U.S. FOOD AND DRUG ADMINISTRATION

NATIONAL INSTITUTES OF HEALTH

CONSUMER HEALTHCARE PRODUCTS ASSOCIATION

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ADOLESCENT OVER-THE-COUNTER (OTC) DRUG PRODUCT USE

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PUBLIC WORKSHOP

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THURSDAY,
DECEMBER 6, 2007

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The public workshop convened at 8:30 a.m. in the auditorium of the NIH Natcher Conference Center, 45 Center Drive, Bethesda, Maryland.

WELCOME

DONALD R. MATTISON, MD, Senior Advisor to the Directors of NICHD and CRMC, Branch Chief, Obstetric and Pediatric Pharmacology Branch, CRMC, NICHD, NIH

DIANNE MURPHY, MD, Director, Office of Pediatric Therapeutics, FDA

HEINZ SCHNEIDER, DrMed, Vice President, Regulatory and Scientific Affairs, CHPA

PLENARY SESSION

ERIC P. BRASS, MD, PhD, Director, Harbor-UCLA Medical Center

LISA L. MATHIS, MD, Associate Director, Pediatric and Maternal Health Staff, Office of New Drugs, CDER, FDA

DONALD R. MATTISON, MD

PANEL I
Chair: HEINZ SCHNEIDER, DrMed
MICHELE WEISSMAN, Senior Vice President, Panel Consulting, Information Resources, Inc.
LEONARD A. WOOD, President, Pharmaceuticals & Healthcare Marketing, Multi-Sponsor Surveys, Inc.
BINDI NIKHAR, MD, Medical Officer, FDA
RICHARD CLELAND, Assistant Director, Division of Advertising Practices, Federal Trade Commission

PANEL II
Chair: SUSAN K. CUMMINS, MD, MPH, FDA
LAURENCE STEINBERG, PhD, Distinguished University Professor of Psychology, Temple University
HEATHER HUSZTI, PhD, Director of Training and Senior Pschologist, Children's Hospital of Orange County
WÄNDI BRUINE DE BRUIN, PhD, Research Faculty, Carnegie Mellon University
ROBERT W. DENNISTON, MA, Director, National Youth Anti-Drug Media Campaign, Office of National Drug Control Policy

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

8:37 a.m.

DR. MATTISON: Good morning. Good morning to all of you. I'm Don Mattison and I'm standing in for Duane Alexander. Duane lives near Ellicott City and has gotten stuck on 108 or 198 or I don't know, one of those little roads in Montgomery County that go sort of east/west that meander through woods and trees and over streams and so he's not going to be able to make it today. So he asked -- this morning, so he asked if I would stand in and introduce the meeting or the discussion that we're going to be having today and tomorrow, and also welcome you.

This two-day workshop is the product of a lot of discussion and energy and activity that's gone on between the partner organizations, the Consumer Health Products Organization, the FDA and NIH. NIH representation in this discussion actually comes from two components. One is just the

topic itself clearly cuts across all of the -- or many of the areas of interest within our institutes but more specifically both in 2002 and in 2007, through the Best Pharmaceuticals for Children's Act Congress has asked NIH to engage itself much more directly in drug development for children and it's clear when you look at the literature in this area, in terms of adolescents and over the counter medications, that there are substantial gaps in our understanding of literacy strategies for directing improvements in health literacy in children of all ages up through the focus of this meeting, adolescents.

And that doesn't even get to the issues that I think, at least from my side I'd like to see us look at in the future, which are pharmacokinetics, pharmacodynamics, issues of dosing and consequences. In the discussions that we had leading up to this meeting, we spent a lot of time talking about how to parcel out the various components and it was clear

that a very, very good beginning would be to try to describe how adolescents use over-the-counter medications and what they understand about their use, how they collect information and how that information goes into improving their health literacy and strategies for dealing with their own health questions.

So that's the topic for the first discussion. As I indicated, I anticipate that there will be others and what I'd like to do now is in Duane's behalf welcome you all to the first of what will be a series of discussions on adolescents and strategies for improving therapeutics and then welcome our partners from the FDA and the consumer health products group. Diane?

DR. MURPHY: I'm delighted to see everybody here who has braved the ice and the snow and I think this is really important because it's been three decades since the American Academy of Pediatrics has said, "We really need to start understanding what the

dose is and whether a product works in the therapeutics that we're giving children".

And it's only been a decade now since we've had some of the tools that had been given t us by Congress to do that. In that last decade, though, we have learned an enormous amount and if I had to summarize it, it would be you don't know what you don't know. And that is because many of the assumptions that we have made in the past are turning out not to be on solid ground.

We have now over 200 products that have been studied the way we would expect them to be studied for adults in children and we know and I'm rounding here, so don't hold me to every little percentage, at the FDA they do nitpick, but I'm rounding to tell you that about a fifth of the time when you study a product, you didn't have the right dose that you thought would work in kids. Another fifth of the time, the product, even though it works in adults, is not going to work in kids and it

doesn’t mean it will never work, it means we just haven’t figured out why it doesn’t work. And then up to a fourth of the time, you’re going get a new safety signal.

Now, that’s just in the first 200 products that we have been looking at. And if you look at the age demographics of those products, there are two ends of the spectrum that we have not studied, the neonate and the adolescent. Now a couple years ago NIH and FDA had a big meeting to talk about what do we not know, we do need to begin to find out about what to do with the neonate. The neonate and the adolescent are most rapidly evolving changing organisms in the pediatric spectrum, and yet they still remain our most enigmatic as far as real solid science in how we use our therapeutics.

For the neonate, we’ve begun to outline some of the things that we know we need to do, but today, we’re going to address the other end of the spectrum and do you know what,

those neonates don't get up and go to the store and self-medicate, you know. So we have a whole other layer of information that we are trying to develop at the agency because we can do all sorts of good scientific studies on how they handle the drug metabolically, what the dose ought to be, what we ought to warn them about, about safety, but if we don't know how to get to them, how to message them and we don't base that message and approach on science and what we know, which is evolving, we are doomed to failure and that's why I'm so delighted that we're here today to really begin this process of how to deal with this age group and I really look forward to the discussion. Don said he would introduce the rest of the -- the beginning of the day for us. Thank you.

DR. SCHNEIDER: Good morning. My name is Heinz Schneider. I'm Vice President, Regulatory and Scientific Affairs at the Consumer Healthcare Products Association. Good morning and welcome.

On behalf of the leading makers of OTC medicines, I want to thank my colleagues at FDA and NIH for this great opportunity to shares insights and data, not assumptions, on this very important topic and I want to add that not assumptions because I think we all can be very quick in making assumptions when it comes to teenagers and teenage related topics from personal experience or from whatever other sources teenagers and we are quick with our assumptions. And some of these assumptions, it's interesting when I asked myself when I was a teenager, some of these assumptions and some of the quick statements we make are pretty much identical with the ones I did about adults when I was a teenager.

The setup of this meeting is somehow unique in that it brings together experts in the areas of market research, clinical/medical behavior science and last but not least from regulatory affairs, so we do look forward to two days of very productive and

insightful presentations and discussions. Thank you very much.

DR. MATTISON: Okay, so we're going to open this first session focusing on a range of issues that I think will set the stage for our discussion and the first speaker is Eric Brass from Harbor-UCLA Medical Center and he's going to be talking about using clinical research to inform our regulatory decisions and we welcome our colleague from the West Coast to the snows and turmoil of travel on the East Coast. Dr. Brass.

DR. BRASS: Thank you. At least I won't be accused of bringing the weather with me. Let me begin by thanking the organizers, not only for the opportunity to join you this morning but also for putting together a program that over the next two days, I think, will be extremely informative and hopefully help move these important public health issues forward in the years to come.

What I'd like to do to start the

program is to review broadly our -- the status of clinical research that's used to inform the public health decisions around OTC drugs, and in particular how these research methodologies relate to addressing the important question of understanding consumer behavior in the OTC marketplace. Now, as you all are aware, making a drug available through OTC access is intrinsically associated with a number of potential risks and benefits. On the benefit side, we have the important improved access to effective drugs to consumers. This may be associated with lower costs and increased efficiencies in the health care system.

We'll have secondary potential benefits of greater consumer autonomy and improved consumer education as they take greater responsibility for their own self-management. But at the same time, there are very clear public health risks. There's the potential for consumers to mis-diagnosis their underlying condition. There may be delay in

treatment of an important clinical condition if the consumer mis-diagnoses. There's the potential for drug interactions with self-management, off-label use of OTC products, increased access in homes and other places leading the changes in the epidemiology of accidental poisonings, inadvertent use during pregnancy or a very important issue that if, in fact, there are superior therapies available under the guidance of a healthcare professional, will we divert consumers from optimal care by making other products available OTC?

It is the balancing of these risks and benefit which must be assessed in making a public health decision whether a drug should be made available OTC. Do the benefits of the increased availability of the drug without the involvement of a learned intermediary outweigh the risks.

And what we're going to talk about is the need to make those decisions evidence-

base, to use data to inform that decision-making and what type of research tools we have and what type of research tools we need further development in.

Critically, to guiding the consumer's self-management of therapy is that the OTC product label is the critical tool for informing consumers as to the proper use of an OTC drug. It may be the sole source of information at the time of purchase and must guide all aspects of self-management of a therapy related to both the indication that's being managed as well as the drug itself. Thus, from a research perspective, the design and validation of the OTC label is central to any OTC development program and regulatory decision-making whether the risks and benefits are favorable with respect to making that drug available through wider access.

Now, the first step, therefore, is to consider how the actual OTC label is developed. And the first step is to identify

the key messages that must be communicated to the consumer to allow the drug to be used properly. What does the consumer need to know? And those kinds of messages can usually be split up into several broad categories. The indication; why should the drug be used and to allow the consumer to make a self-diagnosis of the condition.

There are warnings when not to use the drug due to an individual consumer's health status. This may include the condition actually requires a higher level of care than self-management or use of the drug is not safe based on the individual's own heath history.

Together those messages inform the initial selection decision, an individual consumer's decision to select to use the medication based on their own self-assessment. But the label needs to do more. It needs to communicate the directions for use, and it must also include warnings when to discontinue use, either because the underlying condition changes

and now requires a higher level of care or there may be a drug adverse event that the consumer must recognize. These warnings inform the de-selection decision. That is once a consumer has begun therapy, they must be guided when to discontinue if the continued self-management paradigm is no longer appropriate.

You can see that these mirror what a health professional would do but now we're trying to guide the consumer through this process using the drug label. Once the messages have been defined, there needs to be development of wording for the key messages which are then organized into a proposed OTC drug label. But the question now arises, can the typical consumer understand that label. It's very easy for us to write such algorithms. It's another to do so in ways that consumers actually understand it.

The research tools that are used to assess that are groups of studies called label comprehension studies. Label comprehension

studies share several elements some of which I'll summarize briefly here. Typically, study participants are provided proposed label or sometimes more than one in comparative studies, and asked a series of questions about the drug. Participants answer based on their understanding of the label as provided to them. Multiple choice, open-ended and scenario-based questions are usually included in these types of studies.

Typically, each question is specifically designed to address one of those key communication messages identified at the beginning of the development process. The results are then tabulated to assess the effectiveness of each communication objective, typically centered around percent-correct type data tabulations.

Study recruitment is very important because the study recruitment is designed to enroll a population similar to consumers who would consider the product if they walked into

any marketing venue in the United States. Thus, it's very important to insure that the recruited population includes core sub-populations.

For example, low health literacy consumers must be included. Efforts to insure varied ethnicity, insurance status, social economic status, again, important for generalizability. Study populations may be enriched for groups of special interest based on the drug of interest. For example, if there is a cohort who would be at special risk if they elected to use the drug, making sure the message is directed towards that group or understood by that group become very important.

So let's look at an example of what these types of studies might look like. These are some data from the label comprehension study that was submitted in support of the OTC switch of omeprazole or Prilosec for the treatment of heartburn or gastric reflux. And this particular label comprehension study

recruited 504 participants who were provided the proposed label and asked a series of pre-specified questions. By design, this 504 participants also included a number of cohorts of special interest. For example, it included consumers with frequent heartburn, those who it might be appropriate for them to select to use the drug.

But it also included consumers who did not have frequent heartburn, who should not select to use the drug. It included low literacy consumers and a number of consumers with potential safety contraindications, for example, interacting drugs, who might be pregnant or breast feeding. And let's look at one of the question elements from that study. And the participants were given the question, "You expect to have a very stressful day at work. You usually get heartburn on stressful days like this. You want to take Prilosec 1 to prevent your heartburn on this day. Thinking about this situation, when is the best time to

take Prilosec 1"? And the participants have the label to consult when they're looking at this.

This question had a specific objective. The drug does not work immediately and the label must communicate this so that consumers understand the proper role of the drug in treating. And in this particular case, 81 percent of the respondents gave an answer that was correct or acceptable with respect to this communication objective but fully 19 percent didn't on this very core communication element.

This led to further refinement of how that message should be communicated and revisions to the label and that's common in label development where these types of studies are iterative, where problems are identified, solutions proposed, and retested until a fully functional label results.

Another example; you suffer from seizures and are taking a medicine called phenytoin to help control your seizures. You

also routinely suffer from heartburn several times per week. You have just heard about this new product, Prilosec 1 for the prevention and relief of heartburn. If you were the person described in this situation, and you wanted to use Prilosec 1 to prevent or treat your heartburn, what would you do now? The objective was to avoid a potentially dangerous drug interaction and 90 percent of participants correctly or gave an acceptable answer, either that they would not use or would ask their doctor. And that was very encouraging. It also points out that the answer is almost never 100 percent perfect and that's another fact of life in the OTC arena. There will always be non-heeding and one has to understand the rate of non-heeding and link that to the consequence of that specific failure to heed the label instruction to make the public health decision.

So here we had very effective communication of the drug interaction or so it seemed because when a similar scenario was done

where phenytoin was replaced by Prozac which is not on the label, still over half the consumers responded that they would not use or ask their doctor. So what it is we're actually testing? Are we actually measuring comprehension when we ask this question or simply a universal tendency towards consumers giving safe responses in a testing scenario? Now, from a public health perspective, you might say, who cares, either way they don't use the product. But I would suggest to you that if we're trying to develop labels that communicate key information to allow informed decision-making that will be heeded in the marketplace, there is a difference between comprehension and artificial answers given in the testing scenario. So once we have then developed a label that can be comprehended by the consumer, the next question is, okay, they comprehend it, will they actually follow the directions and that's tested in studies that are called either self-selection or actual use studies.

These are interesting clinical trials that determine how consumers would make decisions and use the drug in the real world OTC setting. The major end points for these trials are behavioral. These are very different than classic drug development clinical trials because remember, for most OTC drugs the efficacy and safety of the drug when used properly has already been established. The question here are the behaviors of consumers compatible with achieving that profile of safety and efficacy.

Will consumers appropriately self-select to use the product? Will consumers self-manage the course of therapy and the design of these trials is extremely challenging because you're trying to replicate in a trial setting the unrestricted OTC marketplace. So some core design elements of actual use studies might include recruitment of participants through pseudo-marketing, trying to attract a cohort to participate that would be similar to

the cohort that would be attracted to the drug in the marketplace.

Participants actually visit a mock pharmacy to see the product display, product packaging, with the proposed label. The consumer then makes a decision whether the product is appropriate for them and if they wish to purchase it. Key demographic data are collected after these primary end point decisions, only after because a common theme is to minimize cuing. Clearly if one took a detailed history of their other medications before they made the selection decision, they'd be highly cued to look and think about interacting medications.

So cuing is kept to a minimum, demographic data collected afterwards. If this is a self-selection study, the study would simply be terminated here. If it's an actual use study, the consumer may actually purchase the product with their own money and elect to use it. They may return to purchase additional

product if the mock pharmacy study site stays open. Data are then collected on purchase, how the product is used and the response of the consumer to change in conditions during the use.

And again, the challenge is to do all this while minimizing cuing or introduction of bias during the data collection. So if you call the consumer every evening and say, “Did you take your medication today”, that might not give us an unbiased view of what would happen in the marketplace. Again, our goal is to predict marketplace consumer behaviors.

So let’s look at an example of some actual use data. This is from the recent switch of orlistat for weight loss and going into this there were a number of key behaviors of interest where one might wonder whether the typical consumer could use a drug like orlistat without supervision. Would orlistat be used with meals as required for efficacy? You can’t take it just any time. It has to be done with

meals. Would consumers exceed the maximum daily dose? Would consumers adhere to chronic therapy? Would consumers use a multivitamin as directed? Would drug interactions be avoided? Would non-overweight or young consumers abuse the weight loss product? And these questions, all behavioral, were tested in an actual use study.

This actual use study recruited 703 subjects to study sites. Now to avoid bias, initial eligibility screening is kept to a minimum. Only subjects where there is a clear ethical or safety concern are ever screened out at this step. So fully 681 were deemed eligible and they were asked whether the medicine is appropriate for you to use after having access to the product with its label? Five hundred and forty-three of the 681, remember these are all consumers interested in weight loss, responded that yes, the drug was appropriate for them. They were then asked whether they'd actually like to purchase the

medicine today. Interestingly, this number then dropped from 543 to 339 and when it actually came to shelling out money and actually using, it fell further to 237. Again, understanding the behaviors and decisions that guide this trend in the flow of study populations is an interesting topic on itself. So let's look how those consumers behaved with respect to the behaviors of interest.

Greater than 95 percent of those consumers were able to use the product appropriately by taking with meals, quite remarkable. Less than three percent exceeded the maximal label dose and again very encouraging given the potential for weight loss products to be abused with respect to dosing, didn't occur. Would consumers adhere to chronic therapy? Forty-six percent of consumers were still on the orlistat after 90 days of the trial. Now, you might say 46 percent isn't very good, but, in fact, that's very similar to adherence rates for orlistat in

the prescription world. So again, a pattern of consumer behavior that's quite compatible with supervised care delivery. Less than 50 percent of the consumers used a multivitamin per the label. Orlisat interferes with fat soluble vitamin absorption, hence the instruction to use a multivitamin. This was viewed as not adequate and again, as an example, iterative improvement led to changes in the label and strengthening of the information about multivitamin use.

Would drug interactions be avoided? Of those 237 consumers who used, only two of the participants were on cyclosporine, one of whom elected to use orlistat. Clearly, one can't draw a conclusion as to whether the drug interaction label instruction -- warnings were effective. And this goes to an important point. Very often, not a single actual use study can address all questions. If you want to understand how people on cyclosporine will use orlistat, you have to study people on

cyclosporine and, in fact, that was done in a subsequent study to confirm the effectiveness of revised labeling to insure that patients on cyclosporine would not self-select to use orlistat.

Would non-overweight consumers abuse the weight loss product? Eight percent of the users had BMI less than 25. Non-optimal, but again, when weighted against the overall pattern and the consequence of this non-heeding, felt to be acceptable. Well, what about adolescent abuse? By design, the core consumer use study excluded any subjects less than 18 years old, so the core actual use study could not address the question of adolescents, but just like with cyclosporine, this issue required -- was important from a public health perspective, required a separate study which focused on the behavior of adolescents, and that study is going to be presented a little bit later this morning.

So we can use these kinds of

studies to develop labels, insure they're understood, and demonstrate their ability to guide consumer behavior effectively, to inform the decision-making and that represents the core of OTC research, but as we all know, there's another part and that is what is actually happening in the marketplace. Do these studies actually predict consumer behavior in the real world? This is an area where we have relatively limited data but it's very interesting to look at some of that data that highlights some opportunities for public health improvement as well as some of our knowledge gaps. So just to illustrate that, I want to show you data from one pilot study of young consumers, not adolescents, but young consumers. This was done in college students, looking at college students in the United States and Germany, using a survey instrument to look at their knowledge and attitudes about OTC analgesics. Now this study is truly a pilot study, has many limitations. It was a

non-random, non-representative convenient sample. There were many factors which could influence the responses of the two cohorts but nonetheless, I think the data are of interest. When these college students were asked, "What OTC analgesic do you use", 75 percent of the college students in the United States identified their analgesic by brand name. In Germany, 100 percent identified their analgesic by generic name. Now why is that important from a public health perspective? One of the major problems faced in safety of OTC analgesics is insuring that consumers do not take more than one product by brand name that have the same active ingredient and if all you know is the brand name, one might think that the risk of taking two products that contain the same generic ingredient might be higher, again emphasizing how differences in knowledge base exist in young consumers.

If you simply look at how much they knew about adverse effects, the total US cohort

can only name 12 potential -- either 12 people naming one event or on person naming two events but only a total of 12 adverse effects could be identified. More than three times that many in the German cohort. So again, clear knowledge differences that might be viewed as relevant for young consumers to make informed decisions about using OTC drugs.

So where are we with respect to research status and needs for the future? There is ongoing evolution of research methodologies for a conduct of OTC trials. The Non-prescription Drugs Advisory Committee met in September of 2006 to discuss the state of this work and made a number of recommendations to try to improve the robustness of research in this area. They encourage pre-specification of research objectives and hypothesis within label comprehension and actual use studies. The pre-definition of benchmarks of what an adequate comprehension or behavior rate would be and the application of robust statistical approaches

and work is still being done to evolve how these principles can be applied to these very complex behavioral types of research studies.

It's also quite clear that specific questions about a specific switch necessitates specific trial design. All of these need to be individualized because all OTC products pose unique public health questions that need to be addressed specifically with designs that are robustly – incorporate challenging those public health issues. And concerns about a specific population requires studying that population, that extrapolation from one population to another is dangerous. But there's also the important need for validation by bridging the type of studies we do pre-approval to what actually occurs in the post-marketing arena and we need more post-marketing research of OTC drugs.

For example, we cannot simply say authoritatively that our current trial designs are absolutely predictive of behavior in the

marketplace, yet that's what we're using them for when we make public health decisions based on them. Further, if we had more information, we'd be able to identify the types of non-heeding that occur in the actual marketplace to design appropriate remediation strategies. But we can't even authoritatively define that component to begin discussing remediation. And we need to recognize that there are influences that are not incorporated into any of our trial designs, the influences of advertising on consumer behavior and particularly when one focuses on populations like adolescents, the role of peer pressure and the availability of misinformation and rumors about a drug effect that might influence how adolescents make decisions.

But the take-home message remains we must use these types of research methodologies to make informed, evidence-based decisions on the risks and benefits of these drugs and need to continue to fill those

research gaps. I thank you very much for your attention and I look forward to the rest of the discussion.

DR. MATTISON: Thank you. We'll have the speakers at the end of the three presentations together for a roundtable discussion. The next presenter is Dr. Lisa Mathis, who is the Associate Director in the Office of New Drugs who is going to be describing OTC drug development in the adolescent population.

DR. MATHIS: Good morning. I'm Lisa Mathis. I'm with the Pediatric and Maternal Health Staff at -- in the Office of New Drugs at the Food and Drug Administration and I want to start out by thanking you all for coming. This is a very important topic to both us and NIH as well as the industry. I'm going to start out by talking a little bit about our pediatric legislation and then go on to describe some of the adolescent data that we've been able to obtain in studies conducted under

that legislation as well as to describe some challenges in the drug development for adolescents.

The first piece of legislation that I'm going to talk about is the voluntary piece of legislation, the Best Pharmaceuticals for Children Act. We've had this law since the late '90s and it was recently renewed or reauthorized on 27 September 2007. And this piece of legislation provides us with the opportunity to issue a written request to drug companies and if those companies do the studies specific to what we requested in our written request then they can get a six-month period of exclusivity, which is basically blocking generic drugs from the market for six months.

We also have a mandatory program or the Pediatric Research Equity Act that allows us to require studies when a drug company submits a marketing application for a drug that may be used in the pediatric population. This, too, was reauthorized on 27 September 2007.

Under these laws we've done a lot of studies and as Dr. Murphy mentioned early on, there are two age groups that we haven't been able to do a lot of studies in as of yet, one is the neonate and really the other is the adolescent.

And one of the reasons why we didn't do a lot of studies in adolescents is because for some time, we have been making some assumptions in adolescents and you've been hearing other people talk today a lot about assumptions and how we need new data. And I think that my talk is going to really help point out why we need to look at adolescents.

We made an early assumption that there would be no significant differences in dosing, absorption, metabolism, elimination and toxicity between adolescents and adults. We did this based on the fact that adolescents are pretty much adult-like. They look like adults. Their skin, heart, lungs, kidney and liver act like adults but one of the major organ systems that we need to consider, especially when we're

looking at over-the-counter drugs isn't exactly like adults and that's the brain.

So when we had adolescents and we needed to get drugs labeled for the adolescents, many of the times we did studies in adults and simply extrapolated both the safety and efficacy down to the age of 12 and then performed clinical trials in the younger children. Here are some examples of where we extrapolated in adolescents and then another example was when I was in the Dermatology Division, we actually had Aldara, which is approved for the treatment of genital warts, we had it approved for patients above 18 and in the clinical trials we had a few patients that were 17 and 18 but when we had to make a decision about studying this product under written request in the pediatric population, we decided that we could extrapolate for that population down to 12 and then require studies in the population under 12. And for multiple reasons we actually ended up looking at another

indication but this product is now labeled down to 12 based on extrapolation.

So are adolescents different than children, younger children and different than adults? Well, we've learned a lot from the studies that we have performed under the Best Pharmaceuticals for Children Act and one of the biggest examples that we like to use are the serotonin-specific reuptake inhibitors or SSRIs used for the treatment of depression. When we looked at the results of the studies, the safety results, what we saw was a safety signal that adolescents actually had an increase in the suicidality or suicidal thinking when they started on these medications when compared to adults. Now, this is actually just contemplating suicide. This was not actual suicides and there were no suicides in the trials, but this was a signal that we picked up and in looking further at the data, we saw the signal carried over even into young adulthood and actually tended to go away as you got into

older adults.

The other thing that we found when we studied this group of drugs was that we had a very hard time demonstrating efficacy. I think that Prozac was the only drug that we were able to demonstrate efficacy in for this population. And with full disclosure, the truth is with depression it is hard to establish efficacy even in the adult population but it's been particularly striking to us for the adolescent population with this class of drugs. Some of the other drugs that we've seen differences with are the triptans. These drugs are used to treat migraines and were first approved in adults and for a long time many of us pediatricians made the assumptions that these products should work equally well in children.

What we learned in the clinical trials was that they didn't work. And we studied both sumatriptan and zolmitriptan and failed to demonstrate efficacy. We've also

seen safety signals emerge that weren't expected. We had betamethasone and betamethasone/clotrimazole combinations that we studied under the Best Pharmaceuticals for Children Act and when we looked at treating tinea pedis or tinea cruris, we saw in both of these trial significant adrenal suppression. We had for tinea pedis 17 of 43 patients who demonstrated adrenal suppression and for tinea cruris, eight out of 17. This was actually very surprising for us because when you look at tinea pedis at least, you're applying the topical cream to a thickened small area of skin and for all of these patients to demonstrate adrenal suppression was very surprising.

We also see differences in metabolism. If you look at methylphenidate, the pharmacokinetic studies demonstrated that as children got older, you had to give them a higher dose.

So why are adolescents different? Why are we seeing these different findings?

Well, one is physical development. And we may need to reassess end points, such as for adolescent migraines and depression because these conditions may be different in adolescent patients.

There may be somewhat of an evolution of these conditions as you go through the age range of the human population. There are also cognitive and psychological development differences and social development differences and these two factors are critical when we're looking at over-the-counter drugs. If you listen to all of the study types that Dr. Brass just described, clearly, many of these are behavioral issues and they need to be specifically looked at in a population that thinks different than the adult population.

So given the previous information that we have learned from studies of prescription products, can we assume that similar pharmacologic effects happen in adults and adolescents? Now, I'm going to deviate a

little bit to talk about extrapolation because this has been such a hot topic in the pediatric research world lately. So we have a decision tree for extrapolation. First, we try and decide if it's reasonable to assume that children, when compared to adults, have the similar disease progression. If the answer is yes, then we ask is it reasonable to assume that children, when compared to adults, have the similar response to the intervention? If the answer is yes, we say, is it reasonable to assume a similar concentration response in children when compared to adults and if the answer is yes, at this point, we simply conduct a PK study to try and match levels in the adolescent or child and the adult. If the answer is no, then we have to go on to look at the pharmaco-dynamics and if there is a pharmaco-dynamic measurement that we can use, then we can use that in a PK/PD study to try and assess safety and efficacy.

If the answers are no from the very

top, then we have to go on and do full safety and efficacy studies in this population. So given behavioral issues with OTC drug use, can we assume that adolescents are the same as adults? And I put in here 12 to 16 years of age, but I think as all of us who live with adolescents know, that the age range can either span below that or above that. And for many of us who have adolescents in college, we know that the behavioral changes actually do go well above age 16 or 17. There are neurocognitive differences, interpretation of labeling may be different and understanding how the instructions apply to the condition that they're trying to treat may actually vary.

The FDA has been given very important tools by Congress to encourage and require studies in the pediatric populations but to date studies have demonstrated that adolescents are different from smaller children and adults and really greater efforts must be made to assess these differences in physical,

cognitive and psychological as well as social development in order to meet the medical needs of adolescents.

Today we would really like to focus on getting additional information on adolescent development, behavior, decision-making, how these developmental differences effect the actual use of products in adolescents and if adolescents must be studied separately from adults, and if this age group needs to be subdivided even more. So we talk about the adolescent age range from 12 to 16 or 18, but do we need to look at sub-groups within that population such as 12 to 14, 14 to 16 or greater than 16.

We also need to look at factors that will help promote safer and more appropriate use of OT medications by adolescents and these factors include communication. And that's it.

DR. MATTISON: Thanks. I'd like to just briefly talk about the implementation at

NIH of the most recent version of BPCA and how it compares to the earlier version; describe a little bit about OTC use and assessment of sources of information and health literacy in this age group; and then end as the two previous speakers have with a description of -- or a request to help us think about improving how we understand and how we approach our understanding of adolescent use of a range of medications, including over-the-counter medications as well as health literacy. Just briefly, as Dr. Mathis mentioned, we're now implementing BPCA in -- under a set of new legislation and in the past the process of identifying drugs began with a catalog of off-patent medications. The current version of the Best Pharmaceuticals for Children's Act asks that NIH identify needs in pediatric therapeutics. We have never done this alone. We've always done it in collaboration with the other institutes and centers, with the FDA, with experts and of course, with the American

Academy of Pediatrics, who've been a strong and staunch partner for both FDA and NIH in this process.

It now mandates that NIH develop the proposed pediatric study request and send that to the FDA for consideration of the development of a written request and then when the written request or if the written request is declined, the written request gets referred back to the NIH for implementation and studies. Now, there clearly are benefits to the use of OTCs for adolescents and adults. They provide individuals with an ability to regulate their health and studies that have looked at self-medication with OTC drugs indicate that that begins early, where it actually begins, the age at which it actually begins, is a function often of the health status and the family structure that the child is in. In most children, it begins roughly at age 11 and by age 16, most adolescents are using self-medication. However, those with chronic

diseases, such as asthma, typically, begin at much younger ages.

Studies in a range of countries have demonstrated in general that over-the-counter use is typically more frequent in adolescent females with the use of analgesics, the use generally increases with age. And typically differences in the use of a broad range of over-the-counter medications vary by ethnicity, age, sex, social economic status and other factors.

A group of investigators using a World Health Organization survey instrument, called the Health Behavior in School Age Children Survey, and this will be referred to several times because that is one of the instruments that provides us with most cross-national or trans-national information on medication use, surveyed 28 countries in 11, 13 and 15-year olds for these four symptoms and the one caveat is we're going to be talking about in the survey medication use. The way

that the survey is structured, medication is anything that's perceived by the individual to be therapeutic whether it's a prescription drug, an over-the-counter drug or a family remedy. So they'll ask these children or adolescents about use of something to respond to the symptom and it could be one of these three categories.

And so this is medication use in the past month in the 28 countries surveyed. The data from the US is in parenthesis, for headache, stomach ache, difficulty sleeping or nervousness and in general, you can see that anywhere from roughly a very small percentage of individuals up to half to two-thirds of adolescents in these age groups, 11, 13 and 15, are taking medications for headache and again, it may be an over-the-counter product or a family remedy. In the US between a half and two-thirds, about a fifth and about a third among boys and girls for stomach ache and perhaps five to 10 percent for difficulty

sleeping and nervousness.

If they look at the impact of age, the use of medications for headache increases in both boys and girls, decreases for stomach ache, difficulty sleeping and nervousness, in boys decreases for difficulty sleeping, and nervousness in girls but increases for the use of medications for stomach ache.

So again, across these countries differences in the way medications, again whether they're OTCs, family remedies or prescription products, are used as a function of age. Now, one of the questions that we would want to know is to what extent do children's reports or adolescents report actually conform with parent's reports or how do they differ and to what extent do they actually represent reality?

So using data from Denmark, the same survey but a 2005 iteration of the Health Behavior in School Aged Children Survey, looking just at 11 and 13-year olds, again with

the same caveat about medications, what they've observed is that depending upon the nature of the symptoms, there is varying degrees of concordance between parent and children's or adolescents' behavior in terms of reporting. What they find is that typically for asthma, nervousness, difficulty sleeping and stomach ache, quite good concordance between parent and adolescent reporting, less so with headache. And typically, in this evaluation, it was observed that the adolescents report more frequent use of medication than do their parents, and I think this simply reflects the fact that these children or young adults are becoming independent and are self-selecting and using more frequently than their parents understand or recognize a range of medications.

In Denmark they were also able to compare across time the use of medications modest, if any change in headache or stomach ache medication use. Interestingly enough, increases in the use of medications for

difficulty sleeping and nervousness. The etiology of that, I think, remains to be described.

The thing I think is interesting is with this WHO instrument, we have the beginnings of a way of looking at cross cultural and cross country use of medications. The -- a group of investigators in the Netherlands looked at a comparison of the use of prescription and over-the-counter medications in adolescents and what they found was that typically a two-fold increase as you go from prescription to over-the-counter medication, again suggesting that these adolescents are beginning to think about their health status and beginning to make decisions on their own and in fact, perhaps, more frequently than they would seek healthcare provider guidance.

This study also looked at use of analgesics by gender and school year and found, typically, analgesic use more frequent among

girls than boys and increasing with age. So the analgesics that were used: acetaminophen, aspirin, ibuprofen, naproxen, as far as they could tell the only association with external activities in analgesic use was TV-viewing and they didn't relate to Internet use or video games. So TV viewing was positively associated at least in this population with analgesic use. There have been a series of papers looking at the use of analgesics for dysmenorrhea in young -- in female adolescents. Prevalence of primary dysmenorrhea is in the range of 60 to 80 percent. It typically increases with age, excuse me. The most common treatments are non-steroidal anti-inflammatories and, where it's been studied, it appears to be reasonably effective, and among adolescents about two-thirds of them report using analgesics for dysmenorrhea across all populations that have been studied. It's anywhere from 30 to 80 percent.

The study by Campbell looked at

individuals who had dysmenorrhea in at least one of their last three menstrual cycles. 93 percent have mild or moderate dysmenorrhea, five percent, severe, and most of them had dysmenorrhea lasting more than one day. Seventy percent used an analgesic. This is a study that took place in Canada, so there are drugs available there to this group of girls that aren't available in the United States. Two-thirds of them used a combination of aspirin, ibuprofen or acetaminophen. There were available, behind the counter, combinations of these drugs with codeine with the exception of several provinces which also put ibuprofen behind the counter.

And within those medications, 55 percent used aspirin, 42 percent used ibuprofen and 95 percent acetaminophen. Twenty percent used the codeine combination. The interesting thing that was observed is that 30 percent of those with dysmenorrhea didn't use any analgesia at all, one-third of those, so 10

percent, had moderate to severe or reported moderate to severe dysmenorrhea. Among those using analgesics, only a third consumed the recommended dose.

Slightly more than half consumed the medication less frequently than was recommended, and six percent consumed the analgesic either at a higher dose or more frequently than was recommended. Now, of course, this doesn't get to the issue of what was the effect of the medication in relieving the discomfort or pain that these individuals had but it's interesting that there is an apparent disconnect between the dosing schedule and the dosing amount and the amount that was actually used.

A group of investigators running a pediatric emergency department actually looked at adolescents' knowledge of OTC toxicity. They asked them, "Do you understand which of these drugs in overdose might be harmful to your health? And 63 percent understood that

aspirin might actually be potentially lethal in an overdose. Fifty-some percent acetaminophen, antihistamines and so on. The authors concluded that many adolescents appear to be -- in the United States at least, appear to be unaware of the potential toxicity of over-the-counter drugs or which over-the-counter drugs in overdose may be fatal.

Well, what do we understand about health literacy? Clearly it's an issue that Healthy People 2010 have asked that we focus on, the degree to which individuals have a capacity to obtain, process and understand basic health information needed to make appropriate health decisions, and using the National Health Education Standards in children and adolescents including critical thinking and problem solving, responsibility and productivity, self-directedness and then effective communication, all of the things that we think need to be included in thinking about health literacy around OTCs.

The study by Nabors looked at the factors related to label-reading among adolescents in high school and college. They looked at individuals purchasing a range of over-the-counter drugs for several different symptoms. Those purchasing analgesics as opposed to any other symptom-driven purchase were more likely to read the label and when they read the label, they reported that the information that they sought included what would the drug be used for, what are its ingredients, how should it be used and then what were the side effects. So in this group, these were the types of medications that were purchased. Slightly less than half reported that they actually used their own money to buy the medications.

Most of them had purchased two or more over-the-counter medications independently and three-fourths indicated that they actually did read the label and again, learning how to take the medication, side effects, symptoms

effected or treated and the ingredients. Now, we know that adolescents are acknowledged users of the Internet and they do use that for a range of reasons. The quality and relevance of health information on the Internet is a concern. In 2003 adults that were surveyed indicated that roughly two-thirds of them used the Internet and of those two-thirds sought health information on the Internet.

A similar survey among adolescents found that they were less likely, interestingly enough, to use the Internet for health information. And a survey of both adults and adolescents searching the Internet for health information, only four percent of those searching the Internet for health information were adolescents. Clearly that changes over time and I think that's one of the issues that we'll have to track. When they asked adolescents for sources of information or where did they learn about health or where would they go, eight percent said that they would look to

the Internet for health information. Forty percent said they'd look to sources within their schools, 12 percent to their parents and a third, roughly, a little bit less than a third, to health professionals.

Where would you go to find health information? Interestingly, only a small increase, 12 percent, again, surprisingly, a third said that they would seek information from their parents and another third from health professionals, again suggesting that as much as they're making independent decisions, they still go back to some of the touchstones that have always been their sources of information. So again, we've described briefly the evolution of BPCA, commented briefly about the use of OTC medications and some assessment of sources of health information and health literacy. We do need to hear from you for research caps and I'd like to end just with a quote from Catherine DeAngelis that was appended to the study on the use of OTC

analgesics that Campbell published.

DeAngelis, after reading the paper, she was an editor of the Journal of Adolescent Medicine at the time, noted that, "A substantial proportion of the adolescents in this study inappropriately used OTC medications for dysmenorrhea. This is probably true for most OTC medications." The question for all of us is, what are we going to do about it? I think the question is as true now as it was a decade ago when the paper by Campbell was published.

I'd like to call up the two other speakers so that the three of us can answer questions from the audience, before we move on to the next part of the presentation. Questions, comments, discussions. No politeness, remember this is a --

MS. FEIBUS: Don, I was --

DR. MATTISON: Maybe, can you go -- there are microphones on both sides. If we could just use the microphones, that would be

great.

MS. FEIBUS: Don, I was very interested in the study by Campbell. It's a really nice study because it does show some really important behavioral information, but I think it would be also interesting to figure out some of the factors that make it different from what may or may not be going on here in the United States.

Because the study was conducted in Canada and it was in 1997, certainly, the adolescents were not dealing with products that had a drug facts label and at least from the products that I've seen in Canada, I think they still use sort of a paragraph format on most of their labels. And so it would be really interesting, especially considering the study that showed that 75 percent of high school and college students actually do look at the label, to see whether that type of dosing errors or non-compliance with recommended dosing and durations of use on labels, whether we still

see that kind of non-compliance here or whether it's actually better with the drug facts or not.

DR. MATTISON: Yes, I think that's an absolutely perfect question. As I looked at the literature, my sense is that there are many, many more questions that we need to explore and I totally agree. I mean, I think we need to have up to date information on how adolescents understand the label and then take that -- translate the understanding into actual use. I totally agree.

DR. BRASS: If I could just expand on that; because I think these types of data point to both the opportunities and the cautions because, for example, one might have viewed the very high rate of response to using the label as very encouraging, but in point of fact, what that actually means is quite obscure, and so that leaves the second part which is when you have these types of non-heeding defined in these types of studies, the

real question is -- the real questions are; 1) why, what is it that led the adolescent to use the drug this way versus that way, and sometimes, it will turn out to be a quite rational reason, and sometimes it will be a quite irrational reason, and 2) from the public health perspective, what is the consequence of it?

So under-dosing particularly if there is efficacy, might not be a problem. Taking 10 times the indicated dose, trying to get relief might be a very different problem. So these begin to define the framework but the real issues, I think, are much deeper than even these types of data are suggesting.

DR. KWEDER: I thank the three speakers. Those were three really interesting presentations. One thing that strikes me in all of them, you know, in looking at the research in all of them is who we're talking about. And I'd like to hear your perspectives on the characterization of the population;

what's an adolescent? I think many -- we typically divide this population by age and years and, you know, given -- at least refer to this, you know, we often think of it in a particular range, yet we know that adolescents probably spans sometimes a couple years below the classic and above.

Is there a better way to divide up the group, to characterize the group, the groups or the distinctions of the spectrum? I'd just like to hear your thoughts on that.

DR. MATHIS: I'll start. From the medical perspective, of course, what we do like to look at is Tanner staging. So we'll look at when a child enters into puberty and the how long before they're fully developed and we use Tanner staging to do that, rather than strict ages.

I think from a psychological perspective, we have to look at a very different framework. We really have to look at how the developing mind thinks. And

fortunately, we do have many experts today who are going to speak to us on that, but obviously, there's great variability from when a child goes from very concrete thinking to very abstract thinking and then being able to make -- use good judgment and decision-making.

I think one of the other things that is really important for us to recognize is that adolescents today are pretty sophisticated, at least compared to when, say, I was an adolescent. If you look at their educational levels, look at what they're studying in school, both middle school and then high school, what they are learning is much more advanced than what I learned at that age. And so I think in some senses, they're very sophisticated and yet, in others, we have to go back to the biologic factor, that they can't possibly develop faster than biology allows them to. So having said that, I'll ask the other panel members to chime in.

DR. BRASS: As the parent of a 27-

year old who is showing unmistakable signs of maturity in the past few weeks, I think it's -- I'm not going to comment on what tools might be used to assess that. But what I would emphasize is the importance of ensuring that study populations are both large enough and diverse enough to capture that heterogeneity.

And the danger is to draw conclusions on a subset that really don't extrapolate. So sometimes just brute force is the solution from a research methodology.

DR. MATTISON: Sandy, I think that the interesting part of your question is that it actually may lay out more a research agenda than it does give us -- I mean, that there's an answer that we can provide. I think we need to look at it from an emotional and intellectual and sort of a physiological, pharmacological perspective. Mark?

MR. DELMONTE: Good morning, thank you very much. Dr. Mathis and Dr. Mattison both mentioned BPCA and PREA as mechanisms to

gain safety and efficacy data on over-the-counter drugs but those would largely be triggered by new over-the-counter medications or new formulations and things. So I'm just curious about what we can do to develop the evidence base for those over-the-counter drugs that are already on the market and being used by adolescents in order to at least be able to improve the labeling of those products for adolescents who are obviously using them.

DR. MATTISON: That's a really good question, Mark, and I've taken as a mandate the new language that says studying pediatric therapeutics, so I think we're going to need to start looking at over-the-counter medications the same way we look at generics that are available by prescription. And, of course, I'd like to reach out to the Academy for help in thinking through how to do that.

DR. MATHIS: Obviously, from a regulatory standpoint, we have a very complex situation because we do have new drug

applications that either start out in the OTC world or are switches from Rx that allow us a little bit more flexibility in obtaining studies. As far as the monograph products go, we have a very different universe there and it's very hard for those of us who live mainly in the Rx world to understand that process and I have to admit that I think many of these issues are probably going to be more adequately addressed from the research perspective and then having that new knowledge move into the monograph world or the OTC/Rx switch world. So I think that we're going to really have to collaborate again, with researchers and with experts to figure out how to increase our knowledge, because this is a class of medications that's available and accessible to everybody, both young children, adolescents and adults, and an area where we really do need to assess safety and efficacy.

DR. RODRIGUEZ: I was sitting there just listening to this fantastic hurdle ahead

of us and I even thought one step further. I said, you know, this country is becoming very, very much involved in the use of alternative medicine and you talk of over-the-counter, the thing is that a lot of the kids and a lot of adults don't -- may be ashamed to share that information. So somehow, somewhere these interactions, this use, we have to develop some way to collect that information so we can see particularly also as some of the population is changing, too, where alternative medicine is also very, very important. So just a commentary that maybe we should think in terms of as we collect information, think about how to collect this other one that may be used.

DR. MATTISON: A group in Rochester has looked at adolescents' understanding and compared their understanding of complimentary and alternative medicines to OTC products and they've noticed several interesting differences. The OTC products are often known by brand name where the complementary and

alternative medicines are actually known by their, I guess, “generic” name. And so the issue again, of sort of different ways of understanding and thinking about the medicines clearly needs to be described as you’ve suggested, Bill.

DR. MATHIS: I’d actually like to add onto that, that of course, as the population changes in the United States, this is something that needs to be addressed. I always laugh; my mother is Mexican and so I was treated with teas and herbals and I always have the joke that everything I ever needed to know to be a doctor, I learned from my mother, which isn’t really true. I don’t treat my patients with non-traditional medications, but I do treat my family that way. So I think it is something that we really need to be cognizant of and thank you for bringing it up.

MS. LEONARD-SEGAL: Don, I have a question regarding some of the information you showed on the relationship between the

adolescents and their parents, that only 30 percent actually seek advice on their health care from their parents. And it makes me wonder how that relationship and that lack of communication impacts the use of prescription products as compared to the OTC products. Do you have any information about that?

DR. MATTISON: There's -- as far as I can -- I'm going to sort of dance around that question a little bit. Adherence to medication schedules at least from the little literature that I've seen, appears to fall off as children age into and through adolescence, and whether that's a communication issue between the adolescent and the parent, or a separate issue, I can't answer. I don't know if someone else has looked at that and can respond to it. And clearly the fact that children would go to their parents or that adolescents would go to their parents for information, I think is reassuring. At the same time, they also need to develop other pathways of information. And

so, using a healthcare provider or using a school resource is, I think, quite good. But I can't answer the question in terms of that -- how effective communication between children -- adolescents and their parents influences adherence to prescription medication schedules, sorry.

DR. MATHIS: I think -- I guess one -- sorry, the access point. When you look at an adolescent using an Rx drug, in general, their parent may know more about that than the OTC drug because they may seek help obtaining their insurance card or scheduling the appointment, and then using the insurance card to get the medication as well.

So I think that there's much broader access to OTC drugs because the adolescent can get up to the CVS or the Eckerd's or the Safeway and actually pay for and use the medication without any other intervening source.

MR. DENNISTON: A question for Dr.

Brass; in your closing slide, you mentioned the unknown or unmeasured influence of advertising for OTCs on youth understanding of risks and benefits, and yet, earlier in the slide comparing German to US adolescents, it seems that US adolescents are far more aware of brands, rather than generics. Is OTC advertising permitted in Germany? Do you know what influence advertising of brands compared to generics -- what difference that would make on understanding not just availability, but also on brands and risks and benefits?

DR. BRASS: I brought along a German expert and I --

MR. DENNISTON: I thought as much.

DR. BRASS: And rather than making up the answer, I'll get the real one.

DR. SCHNEIDER: Sorry, Eric, my first statement in such a context is always, Austrian. I'm Austrian.

DR. BRASS: Yes, I apologize, Heinz, I apologize.

DR. SCHNEIDER: Yes, it is -- OTC advertising is allowed in Germany as it is in my country. I have one comment on that. I think that's a deeper brand versus active ingredient versus what's in these that the concept of that. There are deeper societal and language differences. And to give you an example here, it's a kind of funny example but there is more to it.

In my country, owners of a very prestigious car would say, "I drive a Bavarian car," whereas people in this country would say, "I drive a BMW." So there is something about brand and speaking about brand versus looking one layer deeper on the generic level and often focus on the generic level off brand.

DR. BRASS: Thank you, Heinz. And I was very intentional not drawing any conclusions as to what underlay those differences, because it is complicated. And my point was simply that the differences can be dramatic and if we understood what those

influences were, opportunity for modifying perceptions might be realized.

MR. SEIGEL: Hi, good morning. I enjoyed the presentations. Kind of running a little with the talk about the adolescent having a different CNS developmental process than adults and looking at the algorithm in terms of what studies, whether you do PK, pharmodynamics, whatever, depending upon how they answer questions, how much has been looked into, in terms of looking at biomarkers that are system-related from a developmental point of view and because that may be able to be used as a significant adjunct to the algorithm in terms of product development?

DR. MATHIS: Thank you, and that's a very important question and I'm glad that you asked it. We haven't done a whole lot in this particular area, although the agency certainly is looking much broader at biomarkers in many different areas. There are whole offices and divisions now that spend their entire time

doing that. So it is something that we would hope to get to and something that's very important and we're certainly going to need help and input from experts in the field in order to get to a place were we can actually apply that to drug development.

DR. BRASS: But I think, and I'm sure you'd agree, that it really depends on what domain of development you're talking about here, so that for sexual maturity, we have biomarkers and for other kinds of things we have no idea what the biomarker would be. So there's not going to be a magic, "You are now adolescent, age 17.2 because we measured this thing".

DR. MATTISON: Sorry, to cut off the questions, I apologize. We need, I apologize, to turn onto the next group. Heinz?

DR. SCHNEIDER: In this first panel, in this Panel 1, four speakers will give presentations on marketing data or marketing insights, plus regulatory questions related to

the use of OTC medicine in adolescents. Without further delay, I would like to welcome and introduce our first speaker of this Panel 1, Michele Weissman from Information Resources, Incorporated, or IRI, and I'm -- Michele is an expert and because she's a lady, and when I look at her, I just can't say a long-term expert, but she's a great expert in market research and she will share with us household survey data on adolescent use of OTC medicines. Michele?

MS. WEISSMAN: Thank you for such a nice introduction, Heinz, and thank you and welcome to everyone for coming this morning. How do I get to the next slide? Thank you. Great. Today I'm going to speak to you, as Heinz mentioned, about some consumer research information that my company has collected over the past several years, and the purpose is just to give you a flavor for what consumers are reporting to us in terms of their usage of a number of key products.

First, I'll cover a little bit about our panel and where we gather our data and then I'll show you some key information on acne products, allergy medicine, internal analgesics and finally a menstrual pain product.

The first point I wanted to make is just, for those of you who aren't familiar with Information Resources and the data that we collect, we have roughly 100,000 households in our panel and those households provide us with a number of pieces of information. The first thing that they provide to us is demographic data; so who they are, how much money they make, how many folks are in their homes, and the ages of all the people, ethnic demographic, all those information points.

The second point that they provide us is purchase information and they literally go home from the grocery store and while the rest of us are satisfied to simply be done with the task and take the stuff home and put it

away, these people then scan each item that they've purchased and send that information back to us.

Finally, we have causal information which is provided to us actually by our own auditors in the stores themselves. And that causal information is designed to just give us a sense for how impacted the consumer is on the basis of promotion or price or other in-store factors. For the individual user survey that I'm going to speak of today, what we're doing is we're getting a more granular look at the consumer's household. As I mentioned before we have 100,000 households in our panel.

A household level, obviously, masks anything that's going on on a more individual, person-to-person basis. So for certain categories and brands what we will do is survey the household on their actual usage. This is not intended to be a very precise survey because what we're really asking is among the people in the household and we'll list out,

you've got a male, you've got a female, you've got a child and you've got another child. For this particular product, Motrin, who used it and then the typical respondent would be the head of household, usually the female, and she'll tell us who actually in her opinion used some, most or little of the product.

Jumping into a little bit of information that we gather from our MedProfiler survey which surveys folks on their proclivity to use different medications to treat different ailment types, we survey on a number of different ailments and some of them are here on this slide. What I'm comparing is any sufferer which is the light blue bar, versus sufferers just under the age of 18 and you can see immediately a couple of them pop in terms of a little bit more frequent occurrence. Acne, ADD/ADHD, and infections all are ailments that are incurred more frequently among the 18 and under set than they are against the general population.

In terms of treatment choice, we survey those households and those people on, when you do suffer from this particular condition, how are you most likely to treat it? Do you use an OTC medication, an Rx medication, both or do you choose not to treat at all? Typically, for acne and for menstrual disorder and PMS, one of the things that really shows up the most is an OTC treatment, which is the blue bar. A lot of households are also treating with Rx but they vary for different conditions. ADD/ADHD and infections tend to be those conditions as you would expect, that are treated a little bit more frequently with Rx medication.

What I'm showing now is the number of people typically in a household that consume or use any given product. And this just ranges across a number of categories. Some are OTC, some are not, as you'll see, and I've highlighted in green the three categories that we're going to speak of today.

So the average US household contains 2.3 people and on average for internal analgesics, 2.1 people in the home use any given product that comes in; for cold, allergy and sinus, 1.8, and for facial skin care, 1.4. This is the percent of volume accounted for by females and we do take a look at male versus female behavior and again, typically what you see is a little bit more of female usage among facial skin care, internal analgesics and cold, allergy, sinus. You don't really start to get below that 50 percent mark until you start looking at snack bars. What I'm showing you here is acne products, usage dynamics by age. Of no surprise to anyone who knows anything about this category the 12 to 17, the bright green bar, are the most typical people who are accounting for -- they are accounting for 38 percent of the total volume used among all of the people who potentially could use this particular product within the category.

What I'm showing now is a measure

called penetration and what that is, is simply the percent of households who are buying or who are using this particular product. The total penetration for acne products among all households in the United States is 3.4, which is right there. When you look at 12 to 17, you see a much higher penetration of 12.6 percent. What that means is that 12.6 percent of teenagers between 12 and 17 are reporting to use a particular acne product. Usage rate in ounces also tends to be highest among this age group and the average ounces per person-use for acne products is 2.8. For 12 to 17 that number jumps to 3.4. I know that there is a very high usage rate here in 55 to 64 and that's simply a function of some of the other products that are contained in the product set, so don't get too concerned that you have your best acne years still ahead of you.

What I'm showing you here are different brands. So this is the percent of volume accounted for by each age group across a

variety of OTC acne brands in the category. One of the things I wanted to point out on this chart and the reason I'm showing it to you is, the 12 to 17 group are these folks here and you see a fairly vast difference once you get past this group in terms of all of these other -- in terms of who's actually using it.

The first brand, which is actually the brand that commissioned this study, had a very, very different user profile than the other brands and the point I wanted to make here is that advertising has a lot to do with the difference between OTC brand number 1 and the other brands in the category. This particular brand targets an older audience and a different kind of user. And so one of the points I wanted to make is advertising does, indeed, have an impact on choice.

Moving on into allergy remedies, this slide is showing you the percent of users and volume, users is the bar here and volume is this bar. And it's showing you, by different

age, group who is most responsible for driving usage and driving volume. And you can see that there's not a ton of differentiation between different groups. What we then did is said, "Let's take a look at females and see how they differ," and females are actually pretty close to male usage. Then we took a look at males. And the only thing that really popped is that males under the age of 18 were actually the single largest user group for a branded allergy medication. This is just one brand. However, their usage rate in terms of pills, was actually among the lowest. So they represented the largest user group but not the largest volumetric group. That, actually in this case was accounted for by users 25 to 34.

When you take a look at allergy products and how different genders choose to treat, we see a little bit of a skew, not much, but a little bit of a skew toward female treatment, so it's actually interesting that that brand that we just looked at had a very

different user profile. When we look again at those who choose to treat Rx medication versus OTC only, versus Rx and OTC and suffer-but-don't-treat, we actually see very similar profiles male to female. So what we concluded from this information was that the prior brand that we looked at did in fact, have something in its consumer facing profile that drew in that particular target group.

What I'm showing you here is total internal analgesics category and what I'm showing you is category usage dynamics by age. Charted on here is again, user penetration, percent of households purchasing, graphed against packages per user. And you see a very clean line moving steadily upward. As you'd expect, the 65-plus set tend to have the highest package usage as well as penetration, 18 to 24 and 12 to 17 much lower.

This is demonstrating internal analgesics total category, the percent of packages used by age, and I was very interested

to see the data in the prior presentation because it's a little bit different in our data. We've got about seven percent of the packages that are used are accounted for by the under-18 group and the heaviest percent of packages is the 45 to 64, 65 and older. What we then did was index that to the US population according to the census and we saw that, not unexpected, the under-18 group accounts for seven percent of internal analgesics usage but only 25 percent of -- in fact, 25 percent of the total population. So their index is quite low compared to the 65-plus set who is representing 25 percent of the internal analgesics usage, but 13 percent only of the population.

Again, taking a look at different brands, and once again you see a little bit of a different profile brand to brand. The one thing that does stick out here, though, is that no one brand that we looked at on this particular brand set is really showing up as

this is the brand of choice for the 12 to 17 set. There are a couple of things, private label and two ibuprofen brands that do show up as a little bit more likely to be used by the different -- by the 12 to 17 set but really no one brand is standing out as a heavily used brand among that group.

When you take a look at a menstrual pain product, however, you see a little bit of a different story. This is breaking out by different age groups and predominately female, as you expect since it is a menstrual pain product. I guess if you're desperate enough, you'll take it, but 30 percent of this group -- 30 percent of this brand was accounted for distribution of users by 12 to 17.

Summary and conclusions, the under 18 does over-index for acne but they under-index for allergies and menstrual pain. And again, the difference between our data and the date that you've seen in previous presentations is in large part going to be that 30 percent of

children who report and speak to their parents, the other 70 percent are not and I think there's probably a lot of OTC-purchasing that's going beyond what I'm showing you here.

Teens 12 to 17 account for 38 percent of acne remedies volume and they have the highest penetration and usage rates. Different brands, though, have very, very different age group usage profiles. Males under 18 are the single largest group for any one branded remedy that we looked at for allergy but they do have the lowest pills per user rate. Under-18 accounts for only seven percent of the total internal analgesics category volume at an index of 28 to the total US population. Most brands are no exception; however the one menstrual pain product did see 30 percent of its volume from females 12 to 17.

In conclusion, the preference for OTC remedies and affinities for particular brands within a category, although not necessarily for a category, show that the teen

market is a viable one for our OTC manufacturing partners and in some cases without even direct targeting that the manufacturer is doing. So of course, with acne care you are seeing some direct targeting but for some of the other brands I'm showing you, there isn't anything specific to a particular teen or other group. Thank you very much for your attention.

DR. SCHNEIDER: Thank you, Michele. The last speaker before we take a 15-minute coffee break -- so stay tuned -- is Leonard Wood, President and Founder of Multi-Sponsor Surveys, and in case of Leonard, I can say firmly and loudly, here is a man whose long-term experience in this field, described it, I liked it, experience in tracking consumer attitudes and behaviors and Leonard will take us through varying insight on data on teen surveys on marketed OTC products.

MR. WOOD: Thank you. As Heinz has said, I have been in this business for quite

awhile. Multi-Sponsor Surveys does a lot of syndicated studies on the various pharmaceutical markets as well as many others. What we're going to specifically look at today is acne and dental products and the comparison between the two in terms of usage and the extent to which they rely on their parents and other sources for information.

We'll be looking, as I said, at the acne products, the methodology and conclusions, the dental care products area and then we'll get to the conclusions as well. Overall, the influence impacting the use of OTC products and product brands among teens varies according to the product in question and I've selected two of the most dramatic differences in the two. The comparison and the influence on acne treatment, this is a product that is particularly, obviously, of particular interest to teenagers compared to dental products where they're not particularly teen-oriented in the household. And the comparison between the two

will demonstrate the differences.

We'll first look at the OTC acne products. Our 207 study, and by the way, these are called Gallup studies. We have a marketing agreement with the Gallup organization where we syndicate a lot of the studies that we do. It was conducted online among roughly 500 teens, 13 to 17. It was done in August and September and the sample was weighted to represent the census data.

The survey findings on the acne product use find three things that really drive the use of OTC medication and one is the severity of the condition. We measured it in terms of extremely severe, severe, moderate and mild, by the recommendation of their family and also their peer group and also very much affected by the gender and age of the teen. The product categories reflects a high level of teen involvement in product selection as you would expect. Acne is a serious condition, particularly for teens.

Acne products are heavily advertised directly to teens but the results of that advertising on brand selection appears not to be a particularly influential factor in brand selection and we base that on analysis of advertising recall versus brand used most often. The majority of teens 18 to 13 -- 13 to 17 report experiencing moderate to severe acne, about 6 in 10 indicate they had moderate to severe acne.

The incidents of moderate, severe acne among teen boys is reported at a higher rate than among girls. The incidence among teens by age find that the males tend to report more severe suffering. You can see that eight percent versus a four percent, the 55 percent versus the 48 percent. There really isn't too much difference in terms of when you look at it between 13 to 15 year-olds and 16 and 17 year-olds. Pretty much the similar patterns. As might be expected, the use of OTC acne medication correlates to the severity of the

condition.

Here this slide shows you the medication used by severity. The moderate to severe at 62 percent, a majority, mild 51 and only 10 percent as not a problem. One of the interesting questions that this study does not answer is the not-a-problem. You have high rates of medication, both for OTC and Rx and one of the questions is, do they report it as mild because the medication is taking care of it or vice versa.

Teens report that the OTC acne treatment brand currently used results from the influence of parent's purchases of T1, parents, other family member recommendation and the recommendations of friends. While 70 percent of teens report exposure to advertising for at least one brand within the past three months, fewer than one in five say it impacted their brand usage. And this shows essentially the percentages and the reasons. It's what my mom and dad purchased for me. These are closed-end

questions. They have to pick the categories. At 40 percent recommended by a parent or other relative, 30 and as you can see, the 18 percent saw or heard it advertised is down towards the bottom.

Boys are notably more likely to use the OTC acne treatment purchased for them by a parent than are teenage girls, while girls are more influenced in brand choice by their friends, recommendations than are boys. And you can see the recommended by friends reverses itself where you have 23 percent for boys, 31 percent -- or 23 for boys and 31 percent for females.

As teens mature, they become more involved in the selection of OTC acne treatment products. Regardless of age, female teens are more involved in the selection of the acne treatment brands than are the males. And you can see, again, the table on who generally decides -- when asked who generally decides which brand of facial care products to

purchase, you can see that among males, younger males, it drops from -- it goes up from 44 percent to 56 percent but with females, it goes from 54 percent for those 13 to 15, versus 76 percent for those that are 16 and 17. And of course, the reverse in the parent does.

I'd like to now compare this with the dental care products market. Again, this is a teenage study with approximately the same number of teens, 500 age 13 to 17 and the interviewing is done roughly in the same time period. The findings found that teens' use of dental care products is most heavily influenced by how serious they are about maintaining good oral hygiene and the recommendations of their dentists and hygienists as compared to their parents. Dental product brand use, however, is largely the result of what's in the household.

As I say, the seriousness with what they take oral hygiene drives a lot of their brand use and also what products they use for dental hygiene. About a third say -- indicate

that they take it very seriously and relatively few, less than one in five, say not too seriously or not at all seriously.

This attitude towards dental health has a direct bearing on the use of various dental care products. When you look at this slide, it shows the answers to the questions of brush teeth more often than once a day, floss regularly, use chewing gum formulated for oral health, use dental rinse, mouthwashes, and use tooth whitening kits or strips, broken out by the seriousness with which they take oral hygiene.

And you can see the correlation there among brushed teeth more often than once a day, 88 percent among those who say they are very serious about it compared to only 40 percent of the relatively small group among those not too, or not at all serious. And similar patterns down, except with the exception of tooth whiteners and strips. The clear majority of teens agree that they use the

products recommended by their dentists or dental hygienists. Sixty-five percent agree strongly or agree somewhat with that statement. Here's the graph of it. Forty-two percent agree somewhat, 23 percent agree strongly with the smaller proportions disagreeing.

For the most commonly used dental care products, such as toothpaste, use of the same brand of products as adult members of the household dominates brand usage. As you can see, 74 percent report that they use what is in the household, the brand used within the household as compared to only 24 percent who say they use a different brand.

When asked who selects the brand of toothpaste, toothbrush and dental floss used by the teens, fewer than one in four report they select their own brand. This shows the toothpaste number. Only 16 percent indicate that they select their own brand, a majority, 56 percent, indicate that their parents do. Who usually selects the brand of toothbrush,

similar pattern, a little higher but similar pattern, that the parents are a heavy influence. And the same thing with dental floss, 22 percent of teens select that.

The study also found that adolescent girls are somewhat more involved in brand selection of these products than are boys, but not noticeably so. The one exception to that is the dental floss. For some reason, boys seem a little more involved with selecting the dental floss than is true for the other -- toothpaste or toothbrushes. The influence of parents on teen OTC product and brand selection is key, both in terms of acne, which is a product that's heavily used, and in which they have a very emotional attachment to, but you can also see with things like dental, it's on the other end of the scale where there's not that much involvement in it. So the lesson here is that it really depends on the product category in terms of how much influence parents and other groups and the hygienist have on

usage.

In the case of the OTC treatments, both the age and gender of the teen impact the level of involvement in OTC acne treatment brand use. Seventy-six percent of girls 16 and 17 and 56 percent of boys 16 and 17 select the brand they use. In contrast, far fewer teens report making their own brand decisions for commonly used dental care products, 16 percent, you've seen in the earlier slices, dental floss 22 and toothbrushes, 23 percent.

Acne treatment products reflect the high level of teen involvement in product and brand selection. While acne products are heavily advertised directly to the teens, the results of that advertising on brand selection appear -- not to appear particularly influential compared to parents' influence, et cetera, even on a category that's very important to them. Girls are somewhat more involved than are boys in the selection of those.

In regard to dental care products, products use is most heavily influenced by how serious the teen is about maintaining good oral hygiene and the recommendations of their dentist and hygienist. Brand use is primarily a function of the brand used by the adults in the household. Thank you very much.

DR. SCHNEIDER: Thank you, Leonard. Please hold onto your questions until after the next wave of presentations. We're going to take a break now. Please be back 10:45.

(Whereupon, the above-entitled matter went off the record at 10:34 a.m. and resumed at 10:56 a.m.)

DR. SCHNEIDER: Excuse me, can we make a restart, please? Our next speaker is Dr. Bindi Nikhar, Dr. Bindi Nikhar -- and looking at you not a representative of a teenage organization -- Dr. Bindi Nikhar is a pediatrician who joined FDA in 2003 and since

2006, Bindi works with the Division of Nonprescription Clinical Evaluation and today Bindi will share with us data on FDA consumer studies of adolescents.

DR. NIKHAR: Thank you, Heinz. So my talk covers a brief overview of FDA consumer studies for Rx to OTC switches that have involved adolescents over the last few years. I'm going to discuss two drug products, Plan B, an emergency oral contraceptive and Alli, a weight loss drug. The Rx to OTC switches for these drugs took place over the last 10 years and consumer studies for such switches have enrolled adolescents when appropriate. However, as we've heard this morning, this is still an evolving topic and there are inherent challenges and limitations in the conduct of these studies. I'll leave you with a few points to consider and potential research topics.

Since starting the introduction, we know what over-the-counter drug products are.

They are those drugs that are available to consumers without a prescription. There are numerous therapeutic categories of OTC drugs and our current health climate indicates an increased interest in self-medication and we can expect that adolescents may use more OTC drugs with or without parental supervision. And again, as we've heard this morning, literature reports suggest that adolescents' use of OTC medications increases with age. It starts around age 11 to 12 and goes in general use these drugs, most of the boys, and especially with certain categories. But overall, there is limited information regarding the magnitude and patterns of such use.

In addition, adolescent decision-making skills and risk taking behaviors regarding the use of OTC drugs are not well-studied. The factors influencing the use of OTC drugs may include parents, peers, media, social or socioeconomic circumstances and other factors and the consumer studies that Dr. Brass

just discussed such as label comprehension, self-selection, and actual use for such switches have often excluded adolescents.

And there are inherent study design challenges and limitations such as obtaining informed consent, follow-up, drop? -out, et cetera in enrolling this age group. So, what are the clinical implications about such use? We recognize that adolescents may make decisions to use OTC drugs on their own. However, we have concerns about safe use and overdose and that adolescents may be less aware than adults about the toxicities of OTC drugs and may simply overlook them and that the clinical diagnosis may be confounded by overlooking OTC medications in that adolescents may not be asforthcoming as adults about the use of OTC drugs.

But having mentioned these points, do we really know how adolescents compare to adults in their perception and decision-making regarding the use of OTC drugs? Do adult

always use OTC drugs in a responsible manner? And the concerns that I just mentioned apply equally well to adults. And lastly, if we can influence an appropriate use of OTC drugs in adolescents, would it carry over into adulthood? We would like to think that it makes a positive impact.

Moving on, the considerations for Rx to OTC switch include adequate self-recognition and self-treatment in the OTC environment and if such use is safe and effective. And so a switch candidate must have an acceptable margin of safety based on prior prescription marketing experience and adequate labeling. Now OTC labels are generally targeted towards an eighth grade literacy level and self-treatment and self-monitoring should be possible with minimal physician supervision and benefits should outweigh risks.

Now, coming to the consumers with studies that have involved adolescents we have Plan B for which a label comprehension and

actual use studies were done in 2003 and Alli for which a self-selection study was done in 2005. Given our time constraints, I'll discuss these studies in brief but hopefully, you'll get an idea about the conduct of these studies in general and the limitations.

And the purpose of the label comprehension study for Plan B -- I think I missed a slide. I'm sorry, starting with Plan B, Plan B .75 milligram tablet is levonorgestrel and is a progestin only emergency contraceptive. It is available as a two-tablet package, two doses, 12 hours apart and was approved for emergency contraception in 1999 for Rx use and in 2006 for OTC use in women 18 years and older but retained Rx use for 17 years and younger for reasons discussed later. And so the label comprehension and actual use studies were conducted as part of the switch process.

So the purpose of the label comprehension study was to evaluate the

comprehension of a prototype OTC package label for Plan B emergency contraceptive pills. The communication objectives included its indication, the fact that it's a backup method, not meant for regular contraception, that it does not prevent sexually transmitted diseases or HIV, the timing of the pills and the others.

Six hundred and fifty-six participants enrolled in the study out of which 12 percent were 12 to 16 years of age. Regarding literacy testing, a REALM test was only performed on subjects more than equal to 18 years of age and who had not graduated from college. Now REALM stands for Rapid Estimate of Adult Literacy in Medicine and is the most commonly used test to assess adult health literacy. So out of those tested, 35 percent tested in the lower literacy group and 28 subjects age 17 or younger had not been passed the 8th grade in school. The interviews were conducted in shopping malls and family planning clinics in eight US cities and minors recruited

from clinics did not require parental consent to participate.

So coming to the study design, the participants simply used the Plan B package and label to answer questions. The questionnaires included multiple choice and open-ended questions including hypothetical scenarios and a separate questionnaire about sexual activity was presented at the end. The results for the total sample were provided for each question and results for each communication objective were also provided based on subgroups of literacy, age, race, et cetera.

So these were the results when the key communication objectives were broken down by age. We had three age groups, the 12 to 16, the 17 to 25, and the 26 to 50. So for the first objective, i.e., the indication of Plan B, the oldest group scored the highest. For the second objective, the Plan B is not for regular use, no age group scored very well but the youngest had the lowest scores.

The youngest groups also did not score as well as the older groups for timing of doses but did well on the last two and in fact, comprehended adverse effects better than the oldest group. Here is a breakdown of comprehension rates by literacy levels. As I just mentioned, adolescents were not included in the REALM testing.

Literacy levels clearly played a part in label comprehension. The lower literate groups scored less than the higher literate groups on all key communication objectives. In retrospect, it was felt that REALM testing should have been offered to all participants to make the study experience similar and to test literacy at all educational levels.

So, while the majority of subjects appear to understand key communication objectives, the study had certain limitations. And the main limitation was that a small number of adolescents were included in the study.

Additionally, literacy testing was not performed on all participants and the answers to questions included a yes or no and correct/incorrect variety and so 50 percent may have been correct by chance alone and probing questions were not asked as follow-up. And women with prior experience with emergency contraception were not excluded and so this may have boosted some of the results.

We'll now move on to the Plan B actual use study. Actual use studies are pivotal in determining Rx to OTC switches. Label comprehension studies are generally conducted prior to an actual use study and are meant to guide the formation of an enhanced label that can be used in actual use studies. So this was an open label, multi-center trial using an improved label. The majority of patients were enrolled in family planning clinics because of difficulties in enrolling at other sites.

It was a demographically diverse

population and there was no age restriction except Phoenix, Arizona where 15 and younger were excluded because parental consent was required. Five hundred and forty subjects between 14 to 44 years enrolled took Plan B.

The majority of subjects were 18 to 44 years of age, five percent were 17 years and only four percent were 14 to 16 years. This is a Plan B OTC label, the drug facts, and if you'll note the timing instructions are bolded. So going onto the actual use study design, the objective of this study was to estimate the frequency of contraindicated and incorrect use of Plan B in a simulated OTC environment.

The participants learned about Plan B by reading the product label and self-selected. No education was provided about Plan B or other forms of contraception and the follow-up was at one and four weeks later by phone or at study sites.

The educational level of subjects was as follows. In the 14 to 16 years group,

the majority were in the 9th to 11th grade the more than equal to 17 years group, the majority had completed some form of college. Literacy testing was not done on these subjects.

So now going onto the study results, overall the reasons to use Plan B were similar among different ages, races, ethnicity, et cetera, and the percentage of contraindicated use was 4.4 percent and included pregnancy, unexplained vaginal bleeding and allergy and pregnancy was confirmed in 10 participants who took Plan B and the status of 14 was unknown. And no new adverse events were observed.

And this slide shows the nature of contraception failure in patients using Plan B and we have subgroups of age and education level. So the most common reason, i.e., condom failure, was more or less equal between the younger and the older age groups and those with less than high school and more than high school education. And it's interesting that using no

contraception appeared to be higher in the 17 and older age groups and those with a more than high school education. Now, the next four slides show key study findings divided by subgroups, mainly age. The first one shows timing of taking the first pill and the interval between the first and second pills. And it shows that the majority of patients took the first pill within 72 hours and the second pill by 12 hours after the first dose and so this was in keeping with label directions and there was no age difference.

And this slide shows correct timing of both pills. There was no difference in timing in taking both pills between the younger and the older age groups and in fact, the younger population had slightly better compliance rates for timing compared to adults.

This slide discusses compliance and follow-up. Now, here is where the younger age groups did not fare as well. The study protocol had included two follow-up visits,

either at study site or a phone conversation and the slide shows that a 17 to 44 years age group and those with high school education or higher, were more compliant with follow-up.

And this fourth slide shows contraceptive behavior changes following the use of Plan B. Subjects aged 14 to 16 and 14 to 17 years had no more adverse contraceptive behaviors than the older age groups following the use of Plan B and it also shows that younger age groups, 14 to 17, appear to be more motivated in using effective methods of contraception.

And so lastly in Plan B, while most of the subjects enrolled in the study took Plan B for the right reasons and followed label directions, there were study limitations that governed the age limit for approval. Now, primarily there were a very small number of teenagers enrolled in the study. Five percent of the population was 17 years and only four percent was 14 to 16 years. And the follow-up

was only for a month and so they were unable to assess recurrent use of Plan B and the enrollment was in sort of a preselected setting because teenagers actually came to the clinic seeking contraception.

So the outcome was that Plan B retained Rx status for less than 17 years. The sample size of teenagers 14 to 16 years had been too small to draw effective conclusions.

Next, we come to Alli. Alli is a trade name for orlistat, a weight loss drug. It is a pancreatic lipase inhibitor that acts by inhibiting with gastrointestinal update of ingested fat. Its action is mainly local with very little systemic absorption. It was approved at 60 milligram for OTC use in overweight adults 18 years and older in 2007 and had originally been approved at a higher dose of 120 milligrams for Rx use in 1999 for similar indications.

And as Dr. Brass discussed, there were several consumer studies that were done as

part of the switch process. But bearing in mind that the OTC label indication was a weight loss in overweight adults 18 years and older and adolescents self-selection study was conducted to determine if teenagers 14 to 17 years of age would choose not to use orlistat based on label directions. This is the Alli OTC label showing you the indication. A hundred and forty-seven all comers teenagers interested in losing weight were enrolled in the study from eight different geographic sites. This was probably the first consumer switch study to enroll only adolescents.

At a screening interview, only teens 14 to 17 years continued in the study and the product package and label were reviewed to make self-selection decisions. Sixteen percent of subjects were overweight and 20 percent were at risk of being overweight. And this shows a demographic profile and there was fairly good distribution between the different age groups. The majority were Caucasian and 63 percent were

literate using the REALM, that is the adult REALM test.

So here are the study results. Fifty-nine percent, 87 of the 147 enrolled, selected appropriately orlistat was not appropriate for them. And of those 87, 68 percent indicated that it wasn't appropriate due to their age, 18 percent indicated it wasn't appropriate because they were not overweight, eight percent thought the pill was inappropriate for them and five percent had other reasons.

And 41 percent, 60 of the 147 enrolled, indicated that orlistat was appropriate for them, and of those 60, 68 percent indicated that it was appropriate because they wanted to lose weight, 20 percent believed that they met the requirements for use and so missed the age direction, five percent liked the program, five percent felt is was safe to use and two percent thought they could use it as a preventative.

Next, the subjects were asked if they would purchase orlistat at that particular time. And if you look at the 60 subjects what incorrectly self-selected, 72 percent indicated that they would buy orlistat but when told the price of the product, this fell to 28 percent. And if you look at the whole population, 31 percent indicated that they would buy the product but again, 13 percent indicated that they would buy based on the price. So this slide shows that purchase decisions may be influenced by price, availability of funds and maybe independent of self-selection decisions.

So going onto the next slide, a comparative analysis was performed to cross reference the BMIs of enrolled teens with response to the question, “Based on information provided on the package label is this product appropriate for you to use or not?”

And the BMI results indicated that 16 percent were overweight, that 20 percent were at risk of being overweight, that 63

percent with normal weight and one percent were underweight. And the analysis results showed that an incorrect self-selection and purchase decisions were more likely to be made by those overweight and at risk of being overweight compared to those underweight or normal.

So the conclusions drawn from the self-selection study were that 41 percent of teenagers had made incorrect self-selection decisions and the primary motivation for incorrectly self-selecting was the urge to lose weight and teens overweight or risk of being overweight were more inclined to incorrectly self-select and purchase orlistat. And the price of the product influenced the decision to buy in the appropriate self-selector group.

And so here are a few points to consider. The studies we've discussed so far appear to indicate that the primary motivation to sell selected OTC drug in adolescents age groups appears to be the underlying disease process. The purchase decisions, however, by

adolescents may be independent of self-selection and may be dependent on available funds and other influences and that adolescents may have less comprehension than adults on some communication objectives, for example, in the case of Plan B, the youngest groups scored the lowest in comprehending that Plan B is not meant for regular contraception. But we have to bear in mind that the language and the wording used in these studies can sometimes have a bearing on the comprehension results.

The follow-up was not optimal and higher drop-out rates were noted for adolescents but this is not entirely atypical for this age group and having mentioned these points, the number of FDA studies and patients enrolled is inadequate to allow a clear determination of adolescent comprehension and decision-making regarding the use of OTC drugs.

In the future there may be more OTC drugs that adolescents may use and also the number of adolescents using OTC drugs is likely

to increase bearing in mind that changing social and socioeconomic circumstances, both parents working and adolescents assuming more responsibilities this is more likely to happen. We can also expect that there will be more OTC consumer studies enrolling adolescents. The challenges associated with enrolling adolescent age groups include recruitment difficulties, obtaining informed consent, follow-up, drop-outs, et cetera, and we have to consider literary assessment using appropriate tools such as the REALM or the REALM-Teen Test. Now, the REALM-Teen Test is targeted towards adolescents specifically and has been validated in 2006 and is being increasingly used when appropriate. And lastly, we have to take into account that OTC labels are generally targeted towards an eighth grade literacy level and if we have very young adolescents enrolled, this may be a conundrum because they may be at 6^{th} or 7^{th} grade levels.

And finally, here are few research

issues pertaining to adolescents and their use of OTC medications. The age at which self-administration of OTC medications starts and the patterns of use, adolescent knowledge of potential toxicities of OTC drugs and their decision-making about self-selection and purchase, identifying relevant situations, the differences in information processing and decision-making between adolescents and adults warrant consumer studies specifically in adolescent age groups, an assessment of the impact of low literacy on healthcare and of early interventions help mitigate the impact of low literacy in adolescents and beyond. Methods of all study design challenges involving adolescents and finally a post-marketing validation of Rx to OTC switch to consumer studies, is this even feasible and how much would it contribute to our understanding of this complex issue? And that's the end.

DR. SCHNEIDER: Thank you so much, Bindi. Rounding up this morning's session,

it's my pleasure to introduce Richard Cleland from the Federal Trade Commission. Richard is Assistant Director at the Division of Advertising Practices and his expertise, his specific expertise, is in the advertising and marketing of healthcare products. Richard.

MR. CLELAND: Thank you and good morning. I'm going to shift focus a little bit now. I'm going to give you a brief overview of the regulation of health products by the FTC regulation of the advertising. Before I start, I need to say that my comments today reflect my own views and do not necessarily reflect the views of the Commission or any individual commissioner.

Like I said, my purpose this morning is to give you a brief overview of how the FTC regulates the advertising of OTC drugs and including in that, of course, would be OTC drugs used by adolescents. The FTC Act is different than the Food, Drug and Cosmetic Act. It's an Act of general jurisdiction. The Act

prohibits unfair or deceptive acts or practices in or affecting commerce and the dissemination of any false advertisement for the purpose of inducing the purchase of food, drugs, devices, services or cosmetics.

The general nature of this statute really leads to a totally different approach to regulation than you will find at the FDA. Under this definition, a representation is deceptive if it is likely to mislead a reasonable consumer under the circumstances and the representation, omission or practice is material. Deception does not require that the advertiser have knowledge of the falsity, had an intent to deceive. The FTC does not need to prove actual deception or substantial consumer injury in order to prevail.

A false advertisement is defined in the statute as any advertisement that is misleading in a material respect. So literally speaking, a false advertisement does not have to contain a single false statement if it is

otherwise misleading.

There's a lot of overlap in jurisdiction between the FDA and the FTC in this area and for that reason, in order to coordinate between the two agencies, a long time ago, we entered into a Memorandum of Understanding. Under that Memorandum of Understanding, the FDA has primary jurisdiction over the labels, labeling, and advertising of prescription drugs and over the label and labeling of OTC drugs, of devices, dietary supplements, foods. The FTC has primary jurisdiction over the advertising of foods, OTC drugs, devices and any other health related product. The FTC's jurisdiction and analysis is unique. The third bullet there is actually the most important point that I want to make on this slide. Unlike the FDA, the analysis and regulation of products, of health products by the FTC is unrelated to what the classification of that product is. In other words, we don't first decide whether a product -- pigeon holed

products into a drug, this is a drug, or this is a food, or this is a dietary supplement when we decide how the product is going to be regulated.

The only thing that we look at in the process of that enforcement is what kind of claim is being made for a particular product. For example, for us in evaluating the validity of advertising for orlistat and for an herbal -- not orlistat, but the OTC version, Alli, I guess it is, and for a herbal over-the-counter weight loss product, there would be no difference in the analysis. We're still asking the same questions. We're still imposing the same requirements.

In addition, there's a couple of things, requirements that came along under DSHEA that are just not issues for us. We don't ask whether something is a structure or function claim. We ask whether it's a health claim and what kind of substantiation would consumers reasonably expect and another piece

of the DHSEA legislation was the FDA disclaimer. Again, that is irrelevant for purposes of FTC jurisdiction.

We do make an effort to not conflict with FDA regulatory requirements in our regulations of the advertising. These are two safe harbors that are generally included in all of our orders that involve health-related products. And they reflect the policy, current policy, of the Commission. And essentially, under Part A here, what we're saying is that if the advertising representation is permitted in labeling for a drug under any tentative or final standard, that we're not going to take a contrary position to that. That we've assessed the standard that FDA uses to come to that conclusion, we are satisfied that that meets the FTC substantiation requirement, and therefore, we're not going to come in and say something inconsistent with that point.

Likewise, with regard to products that are regulated under the Nutrition Labeling

and Education Act, if a product -- if a claim is specifically permitted in labeling by regulation under that Act, we would not question that claim.

And you notice in both instances, the safe harbors that are provided here require affirmative action by the FDA to approve a claim. It can't be something by implication or the FDA hasn't taken action on this or there is an informal guidance out there or something, that's not sufficient.

So the core violations that we look at in terms of advertising are first, false statements, omissions of material fact, and unsubstantiated efficacy and safety claims. Some examples of false statements, this is an ad in a case that we brought involving a weight loss product. The "Lose up to two pounds daily without diet or exercise", that's an example of a false claim in this particular ad. But the next statement is probably just as interesting. This is a testimonial, "I lost 44 pounds in 30

days". False statements do not necessarily have to be, as we'll talk about later, expressly -- expressed false statements. There's an implied claim here in this advertisement that the product will enable the consumer to lose as much as 44 pounds in 30 days and that's a false claim.

Here's another one, weight loss example, we do a lot of weight loss cases at the FTC, "blast up to 49 pounds off in 29 days". The allegation in this case, and this was a litigated case, that the product would enable consumers to lose as much as 49 pounds in 30 days.

The most common type of a false claim and the types of cases that we do are what we refer to as establishment claims. These are advertisements where the advertiser has claimed that the product is clinically proven or research proves or scientifically established that a particular product will have an effect. In this case, the false

establishment claim was that this product was clinically proven to increase result in 10 to 25 percent gain in height, and this product was aimed at adolescents and young adults.

The second type of core violation are referred to as omissions of material fact. A misleading omission occurs with a qualifying information necessary to prevent a practice or a claim from being deceptive is not disclosed in an ad. And under this principle an advertisement that contained all truthful statements could still be deceptive if it omitted material facts and the ad was then -- conveyed a misleading impression. The omission must be material and that implies more than just, boy, the consumer would really like to know this information. It has to be the type of information that would, in fact, effect the consumer's decision to purchase a product or how that product was used.

Some examples of deceptive omissions, the first case up here was a case we

brought several years ago. This product, St. John's Kava Kava was being promoted for the treatment of HIV/AIDS and, in fact, because the St. John's Wort content was really contraindicated for the treatment of AIDS and HIV and that was not disclosed in the ads.

Snore Formula here, this is an interesting case. It sort of gets into the sort of the self-treatment and self-diagnosis issue and what our concern was here was the product was being used to promote -- promoted for the use of early stages of sleep apnea and we were concerned that there were no disclosures in the advertising about the potentially serious nature of sleep apnea in the advertising.

And finally our Campbell Soup case, this is a product that was promoted for, as a low fat, low cholesterol soup and yet it had a high sodium content. So it was sort of a mixed message. So as you can see from these ads, it's really that there's a core claim being

made about a product which may be true, may not be true, but there is something that's related to that core message that's being left out of the ad, that's important to consumers and it's going to effect their decision to purchase or use that product.

By far the most common violation are unsubstantiated claims in advertising, particularly in health advertising, health product advertising. The making of an objective claim without a reasonable basis constitutes a deceptive practice, under FTC precedent and our guides, the guidance we've given industry, in general, health claims must be substantiated by competent and reliable scientific evidence and under our precedent again, what constitutes competent and reliable scientific evidence is going to depend in large part on what experts in the field would generally rely on to find agreement or to establish a particular principle or accept a conclusion.

The definition itself defines competent and reliable scientific evidence to mean tests, analysis, research, studies or other evidence based on the expertise of professionals in the relevant area that has been conducted in and evaluated in an objective manner by persons qualified to do so using procedures generally accepted in the profession to yield accurate and reliable results. There's a lot of controversy or has been a lot of controversy about this definition, not so much in the recognized OTC drug area but particularly with regard to dietary supplements and other products. And the controversy is on both sides.

One issue here is, is this -- you know, concern about this definition is, is it specific enough to give guidance to the industry as to what kind of evidence they have to have in order to substantiate their claims? We think it is when it's combined with the precedents, the cases that we have decided. In

most cases involving people who are taking pills for serious health conditions, this standard is going to require randomized clinical studies in order to establish efficacy. So here are some of the types of efficacy claims. This is our HeightMax case again. This was -- here again, the efficacy claim that was made here isn't in this ad, but it was in some of their other ads, was that this product will make you grow two to three inches taller with the use of the product. And it turns out there were no studies at all on the product. So another kind of claim that comes up that's unsubstantiated is the superiority claim. A case -- a couple of years back, we had a case against Doan's. Advertised their product as a back pain medication, that it was special and unique and that part of the advertising claim was true, but there were also comparisons to Advil, Tylenol, and Bayer which suggests that Doan's was superior to these products for those

indications, for the back pain and, in fact, there were not studies that showed that the ingredients in the Doan's product was superior to other analgesics.

Unsubstantiated safety claims, this was -- some of our cases in this are, this was Met-Rx USA, I think we brought this in the late 1980s. This was a product that was promoted to young people for body building. It contained a number of androgen ingredients. It also contained ephedra and it was marketed as a safe product to use in lieu of anabolic steroids. There was no substantiation for that claim.

In our regulation the interpretation of advertising becomes critical and so I'm going to walk through some of the things that we look at when we interpret advertising and evaluate it.

First off, we look at the advertising from the perspective of the target audience. I think that what I've heard today suggests that -- my slide there that I wrote

for the program was that if the target audience is adolescents, the ad will be reviewed from their perspective. And I think one of the take-aways that I had from some of the earlier presentations is, you know, when we look, for example, at an analgesic ad, a headache remedy, we -- the audience that we have in mind instinctually are the adults like ourselves, that are going out and buying this product for a headache, but I think one of the things I saw here is that there's a large percentage of adolescents that may be in that category as well. And it may be true of other products in terms of the audience.

Again, an interpretation of an advertisement will be assumed to be reasonable if it's one that the advertiser intended to convey. It's probably pretty self-apparent that an ad can convey multiple messages to consumers and the rule is that when an ad conveys more than one meaning, only one of which is misleading, the seller is still liable

for deception based on the misleading interpretation of the claim.

And this is the same point, that an interpretation of -- may be reasonable even though it's not shared by a majority of the consumers, so how many people actually have to take away a meaning from an ad for it to be considered a reasonable interpretation? At least at the staff level we think that is about 14 or 15 percent if they're taking a misleading message from the ad, if that large a segment of the population then we would consider the ad deceptive.

The primary evidence of a misleading ad is the ad itself and in terms of the types of the claims, they usually range from express to virtually express to implied types of claims. Where there is an implied claim involved, one that we're sort of, that's the message, even though the literal words aren't in the ad, we really look at the whole ad, what the net impression is of the entire ad

to make those decisions. The Commission has held in a number of cases that it need not have extrinsic evidence before it in order to determine that implied claim is being made in the ad. If the ad is clear enough that the Commission can conclude with confidence that the message is being conveyed to reasonable consumers, then extrinsic evidence is not required. And that position has been upheld by the courts. Extrinsic evidence where it is required and sometimes it will come in whether it's required or not, can include just about anything that is relevant, expert opinions on how an ad might be interpreted, copy tests, behavioral surveys, all of that type of information can come in.

Qualifiers, there are a lot of -- I'll tell you that, you know, while we have a preference towards qualification of claims that are problematic as they first -- sort of the first remedy, qualifiers and disclaimers are generally viewed with skepticism in terms of

their effectiveness. Most of the studies that we have done using qualifiers and disclaimers, have showed that they're not very effective in communicating to people. And that's for a number of reasons. Some is that they're really not observed in most advertisements and that they're often used in situations where the message in the disclaimer and the qualification is contradictory to the main message of the advertising and just that type of -- the negative never overcomes the positive. The footnote never overcomes the headline in those context.

And generally, subsequent disclaimers, that's when you put the right information in the package about a product but you've got the wrong information in your ad, that later information is never adequate to dispel the original deception. Some of the enforcement cases that we have brought involving products aimed at adolescents and kids, the -- involve the efficacy of treatments

of ADHD, the safety of sports and muscle building products, the safety of herbal street knock-off products, efficacy of cold remedies, growth enhancement products, and weight loss products. And we also had a acne product but that was a long time ago. It involved Pat Boone as an endorser.

Well, there's a few more out there. All right, some of the ADHD cases that we have brought here, I won't go through them all but there's quite a few of them. And we've already talked a little bit about our androgen cases so I don't need to do that. This was a case -- a unique case and hopefully, we'll never do another one of these types of cases, but this was a product called Herbal Ecstacy. It was marketed by a company called Global World Media and it was marketed to adolescents and kids as a natural high, a natural legal high. And of course, the product contained ephedra and we challenged the claim and in a relatively unusual action for us, we actually banned the

promotion of this product to audiences of under 21. And this was back in the ‘80s so it --

Another product in an area that is right now is problematic is cold and flu treatment and prevention. This is a case we brought several years ago. We have recently closed a couple of additional cases involving cold and flu products because the companies have agreed to withdraw those claims. This is an area that is of high interest to the FTC and I suspect that we will be taking additional action in products involving cold and flu.

This was a weigh loss of our HeightMax case. I guess the guy in the middle took the most product, and I’m going to close up here talking about a couple of products, weight loss products that are aimed at kids. And it sort of makes my point and one I made earlier. This was another one. There was a third product in this group that all came out about the same time called Skinny Pill for Kids. And the -- I guess the point is we’ve

taken all three of these products off the market. You know, these products were never tested on kids. So there's no data, no efficacy data in terms of the treatments for kids.

The claims can't be substantiated for kids but I think the bigger problem here, particularly in this audience is that these are not the products, not the weight loss products that adolescents are using.

They are using the products that you go to CVS and you go to the diet aisle and you pull those products off the shelves. Those are the ones that they're using. And you know, I think that is a particular problem because I'm not sure we have enough data on how those types of products are being used by this audience. And some of those products, you know, you sort of -- you cannot assume that because those products have herbal ingredients in them or vitamins in them, and they're not OTC drugs, at least not now, that they're safe

to be used by the populations that's using them and we just don't have the data either on the efficacy or the safety of a lot of these weight loss products.

With that, I will close and thank you very much for inviting me. Bye.

DR. SCHNEIDER: Thank you, Richard. It's time for questions now. Michele, Leonard, please join us up here. Please mention your name and your affiliation before you ask a question.

MS. COLLINS: Hi, I'm Felicia Collins with the FDA. My question is for Mr. Cleland. I'm interested -- I appreciate your presentation. That was very interesting and I wanted to know what is the process by which products come to be reviewed by your office and is there any sense of -- or are there any internal mechanisms by which you use to prioritize what products you're going review first?

MR. CLELAND: Thanks. We take

cases from all quarters. Most of our -- the majority of our cases are generated by self-monitoring. We look at -- you know, we look at the advertising like everybody else does and see it that way. We get complaints from competitors. We get complaints from other regulatory agencies. We get complaints from FDA, referrals from FDA. We get referrals from self-regulatory bodies like NAD, National Advertising Division of the Better Business Bureau, consumers, we take consumer complaints. You know, we -- the number of products that we look at or that are out there that are subject to FTC jurisdiction in terms of their advertising, you know, somewhere between 40 and 100,000 products, with several new thousand products a year. So it's tough to decide which ones to look at. We look at -- you know, the first criteria is always safety, are there safety issues involved?

The second is the amount of consumer injury and that's going to depend upon

the egregiousness of the claims. It's -- we give priority to disease type claims that are being made in advertising. Whether the product is being promoted for use by children is another one of the factors that we would give priority to. But at the end of the day there's only, you know, a handful of people that are going to be looking at these ads and conducting these investigations. So you know, there are always more -- our feeling is that there are always more advertisements out there that we could be looking at and that we don't have the opportunity to.

MS. FEIBUS: My name is Karen Feibus, I'm also from the Food and Drug Administration. And you already partially answered my question. My question was also for Mr. Cleland. The kava kava example that you gave was very interesting and I was wondering when you have a situation where you are bringing a suit for a particular product based on the violation of the statutes that you work

under, but there is also a false drug claim, is there a relationship between DDMAC or the Office of Compliance at FDA and the office where you work through the memorandum of understanding where you would bring a situation like that to their attention and say, “Hey, this product is claiming to treat HIV”, or does that kind of communication not occur between the agencies?

MR. CLELAND: It happens, it’s the majority -- it’s the rule and not the exception. Even when we’re looking at a -- may be looking at some advertising for prescription drugs, that we, you know, don’t have primary jurisdiction over the advertising of, you know, we call and consult with DDMAC about those issues. In terms of other types of cases, we are -- we consult regularly with CFSAN, with CDER.

We have brought a number of high profile cases in the last 10 years including the LaneLabs case and the case against

Seasilver USA which involved joint actions and joint investigations by both the FTC and the FDA. So there is a -- there's a high level of coordination between the two agencies.

We often -- you know, we'll seek information, particularly scientific information, from the FDA. We are an agency of lawyers and economists, not doctors and so we frequently will consult with FDA on the scientific issues.

MS. FEIBUS: Thank you.

MS. MEYERS: My name is Beth Meyers. I'm here from FDA's Office of Cosmetics and Colors. And I'm sorry, Mr. Cleland, another one for you. Specifically, I appreciated your explanation of how you do not try to evaluate the regulatory category, whether it's a food, a drug, et cetera, under FDA's classification which we draw from the FD&C Act. But there is sort of an area that becomes relevant in advertising which we, in the cosmetic's section run into all the time,

which is the OTC drug that's being passed off as a cosmetic. And the cosmetic is, of course, under the Act, not subject to approval by FDA for safety, efficacy whereas drugs most certainly are which would mean that a drug being passed off as a cosmetic might actually be advertised with that implied claim that FDA has looked at this, FDA has evaluated this.

So I'm wondering, what does FTC do with this kind of product? I'm familiar with the MOU which, what, dates back 30 years or so but what do you do when you have these pseudo cosmetics, some of which are made by Klein-Becker by the way?

MR. CLELAND: You know, I think that we decided some time ago that we couldn't just look at all claims for all products. And we make a distinction between products that claim to change the appearance of something as opposed to a product -- and now I'm talking about cosmetic products, or what we would think of generically as cosmetic products, as opposed

to those products that actually change the physical structure.

But even under that definition, unless the product is going to pose a safety risk, those types of products don't rise very high on our list of priorities and if you look at the number of cases that we've done over the last 10 years, I'm not sure you'll find any of those cases. In fact, I don't think they're there. And the section of the Act that gives us jurisdiction, the false advertisement jurisdiction also mentions cosmetics, but there's just not a lot of -- there's not a lot of regulation in that area at least by us. I think that's one of the things that, you know, perhaps we've -- it just doesn't rise to the level -- you know, we're making a decision between going after a cancer cure and a wrinkle remover, the cancer cure gets the resources.

MS. MEYERS: Understood, thank you.

MS. O'DONOGHUE: My name is Amy O'Donoghue. I'm from the Division of Drug

Marketing, Advertising and Communications, DDMAC in FDA for those of you who aren't familiar with all the acronyms. My question is actually for Mr. Wood. You mentioned that advertising does not appear to be influential in brand selection for teenagers, and I was wondering if you could go into more detail about how you came to that conclusion, what methodology and what evidence you have for that suggestion.

Mr. WOOD: Sure. As part of the study, we compared advertising recall, the past three months of advertising recall with the brand used most often. And the correlation had some significant anomalies in that which led to the conclusion that the amount of advertising did not necessarily drive the -- what the teenagers were using.

MR. DENNISTON: I'm Bob Denniston, with the Office of National Drug Control Policy. A question for any of the panelists who'd care to respond. It seems by consensus

there's some reason to believe that OTC advertising can't influence brand choice but is there any evidence or inference that advertising in its aggregate can effect overall demand? For example, a pain reliever ad can influence overall demand for pain relievers, not just for that specific brand?

MR. WOOD: I'll answer that. In the case of some things that have become very popular on the depression side, for example, we will see in our studies -- or sleep aids, or whatever. We'll see in our studies an increased levels of saying that they suffer from kinds of things. So to that extent, they drive -- advertising drives usage.

MS. WEISSMAN: We also see instances where advertising will impact category consumption overall in expandable consumption categories, for example, food categories where, you know, where there's not necessarily a definable need.

When you think about drugs, there's

usually more of a typical regiment, so sometimes advertising helps to enforce the regiment, so you're supposed to floss twice a day, you're supposed to brush three times a day. Sometimes advertising, if that messaging is in there, and sometimes, even if it's not, you can see that reflected in sales. What you don't always see is an impact in consumption where it's -- it is not necessarily an expandable consumption category and a lot of the OTC medications are not thought of to be in that class of -- class or category.

MR. DENNISTON: Let me just add, in terms of the medi-messaging that is advertising for a category of products can perhaps help legitimize the use of those products to solve a problem and I know in some other areas there's some view that that -- that advertising, while advertising is an ad for advertising, that it can help, in fact, create aggregate demand for something that people may not even know about or might know about but they don't believe they

have a problem that can be solved by that particular product. So it's kind of the medi-messaging issue that I'm interested in.

MS. WEISSMAN: A lot of marketers struggle with that dilemma because there are many categories where marketers would like to increase the overall consumption and have that overall increase come from their brand. I think that it's just -- it's not necessarily a clean cause and effect relationship. I think it differs very much by category.

DR. BRASS: Yes, I'd just like to hear from the panelists involved in marketing research on a slight extension. The current market research obviously, is directed towards very specific objectives quite legitimately and is methodologically and data analysis-wise and everything centered around that primary purpose.

My question is, what are the potentials for those types of approaches to be expanded to look at issues of relevance to

other aspects of OTC drug use. For example, when we talk about a variety of potential safety concerns, it in fact, is not what the typical average user does. It's the outlier, who's not doing what they're supposed to, who's of most interest? And what is the potential of these types of research methodologies to quantitate the degree to which certain rarer behaviors occur and begin to probe the underlying rationales that guide those types of behaviors?

MR. CLELAND: I didn't even understand the question.

DR. BRASS: I was going to say that's why it wasn't directed towards you. No. No, see, because there's this gap in OTC research between what happens pre-approval and what happens post-approval. Your approaches have the most experience in accessing the post-approval marketplace to understand what's actually happening. But the focus has been in trying to improve sales. That's the underlying

motivation for marketing research.

Therefore, the way everything is structured is a little bit different. So not being familiar with the specific methodologies, the question is the adaptability to steer away from that very focus question to use the access methodologies, the access techniques to probe deeper into what consumers are actually doing in the marketplace and why with an emphasis not on the 80 percent who follow the directions but the 20 percent who don't, things like that.

MR. WOOD: I don't know if this is an answer for it, but we do a lot of segmentation studies in which you identify -- you segment the respondents into various categories. Typically, a certain proportion will revolve around, you mentioned safety, we will have a concern about safety, those that will not have a concern about safety and you can sort of look at what their particular motivations and needs are.

So the techniques exist to identify

that. I mean, you have a market that's a strong possibility but what's holding them up is they're skeptical about the safety or they're just skeptical kinds of people. So the techniques exist to measure that in a fair amount of detail.

MS. WEISSMAN: And from out end, we do occasionally take the results of a segmentation survey and track the results of different marketing efforts on those people in the marketplace. So we would take a survey. We would target -- we would ask our panel to indicate through whatever series of questions the survey created. We would ask our panel which bucket they belonged in and then we would track over time, how those consumers do.

So there is the opportunity to do some follow-up from that perspective. We also can survey our panelists on any number of questions that -- the issue becomes you're looking for outliers within a relatively small sample in some cases to begin with. So

eventually, you know, when you're dealing with 100,000 households, eventually you're going to hit a wall in terms of being able to report back data that's reliable and useful for any kind of serious conclusions.

DR. SCHNEIDER: If there are no further questions, I want to thank the panelists. I want to thank the audience. Please come back 1:45.

(Whereupon at 12:07 p.m. a luncheon recess was taken.)

A-F-T-E-R-N-O-O-N S-E-S-S-I-O-N

(1:45 p.m.)

DR. CUMMINS: Well, I want to welcome everyone back from lunch. Thank you for staying with us this afternoon. We have a wonderful piano plan for you, and I hope all of you will participate as well.

I'm Susan Cummins. I'm with the Pediatric and Maternal Health Group at FDA, and we are going to focus this afternoon on adolescent development, the substrate for all of this discussion.

We're also here about behavior, adolescent behavior, and adolescent decision-making, and their concepts of health and wellness, and how you develop marketing programs to adolescents.

This is an exciting time scientifically to be having this workshop and to have this conversation. You'll hear that the science of adolescent development has really exploded in the last decade, and much

has been learned about the neurologic underpinnings of many qualities that we think about when we think about teenagers.

We're also very fortunate to have an outstanding group of speakers on our panel. I'm going to, in the interest of time, introduce all of them now, and we'll hear first from Drs. Steinberg and Huszti. Then, we'll take a break, and then we'll hear from Dr. Bruine de Bruin and Mr. Denniston.

And then, after their presentations, we'll have about an hour -- we have budgeted about one and a quarter hours for questions and discussion. The discussion is always a very important component of a workshop.

So hold your questions, and we can talk about them during that time.

Dr. Laurence Steinberg is the distinguished university professor and Laura Carnell Professor of Psychology at Temple University. He will discuss adolescent

development, focusing on recent research on adolescent brain development and its implications for common adolescent behavior.

Next we will hear from Dr. Heather Huszti. Dr. Huszti is both a research and clinical psychologist serving as the Director of Training and the Senior Psychologist at Children's Hospital of Orange County, California. She'll present her research on youth concepts of health and wellness.

Then, we're going to take a short break, about 15 minutes. After the break, we'll turn to adolescent decision-making. Dr. Wandi Bruine de Bruin is a cognitive psychologist and member of the research faculty at Carnegie Mellon University, and she'll discuss her research on how youth make decisions.

Finally, we'll hear about social marketing to teens. We are fortunate to have Robert Denniston with us. Mr. Denniston is the Director of the National Youth Anti-Drug Media

Campaign at the White House Office of National Drug Control Policy. He will discuss the process for developing anti-drug media campaigns to youth.

And though the focus of this workshop is on the appropriate use of over-the-counter drug products by adolescents, there is little published marketing research on that topic. So we have much to learn from our colleagues in the drug abuse prevention arena.

So with that, I will turn the podium to Dr. Steinberg.

DR. STEINBERG: Thank you very much. We're going to shift gears a little bit here. I'm not going to say anything about over-the-counter drugs. I'm going to talk more about adolescent brain development and behavior.

I, first, want to just remind you about adolescent risk-taking, because some of what we are concerned about today involves reckless and risky things that kids might do

with over-the-counter medicines. Then, we'll talk about what we know about adolescent brain development and tell you a tale of two brain systems.

Then, I want to present some data from some work that my group has been doing funded by the MacArthur Foundation that provides a behavioral complement to the brain story that I will lead with. And then, I will conclude by talking about some implications for policy and practice.

Lots of people sometimes assert that adolescents actually don't take more risks than adults do, but I think that's kind of silly and really at variance with what we know from actuarial data. Compared to adults, adolescents have more fatal car crashes, even after adjusting for inexperience behind the wheel. They commit more crimes, there is a phenomenon that is known as the age crime curve that has been replicated over many historical cohorts and around the world, which shows that

crime peaks at around age 17 and then declines after that.

According to the CDC, adolescents engage in more binge drinking and more frequent binge drinking than adults do. They are less likely to practice safe sex. They attempt suicide more often. Completed suicide is more common among elderly adults, but attempted suicide is more common among teenagers.

I got interested in this because in looking at efforts to educate adolescents about these and other risky behaviors, it turns out that we spend hundreds and hundreds of millions of dollars a year on health education programs of various sorts, most of which are completely ineffective.

And that leads me to wonder whether providing kids with information or educating them is going to be a sufficient way to deter risky and reckless use of over-the-counter medication, since we know that it doesn't seem to have any effect on their driving, on their

sexual behavior, on their alcohol or tobacco use, or use of other illicit drugs.

So before we go down the road of thinking that we are going to solve this by having labels that teenagers can understand, I want to argue that I think that that is not going to solve this problem, because of what we know about adolescent development.

So let's start by talking about brain development and the tale of two brain systems. What I'm going to present now is really sort of -- in some sense it's an oversimplification in order to condense it into the amount of time I have here. But it is I think reflective of an emerging consensus among those of us who do adolescent brain and behavioral development.

But what do we know about brain development in adolescents that we didn't know as recently as a decade ago? Well, one thing we know for sure is that brain development continues until a much later age than

previously believed. It had been I think believed at some point in time that brain development was more or less complete by the time individuals turned 12 or 13.

We now know that there is anatomical change in the brain that's maturational in nature going on into the early and mid-twenties. And we have several studies, probably the best of which have been done here at NIH, showing continued synaptic pruning and continued myelination of the brain, particularly in the frontal regions of the brain, into the mid-twenties.

Both of those processes -- there's the illumination of unnecessary synaptic connections and the myelination or insulation or the neuro circuitry. Both of those make information processing much more efficient, and that's reflected in changes in behaviors that are subserved by regions of the brain where these processes are going on.

And so this structural or

anatomical change is accompanied by functional changes, patterns of activity. So for those of you who are not familiar with brain science, we typically differentiate between changes in brain structure, so differences in the volume -- in volume of different areas of the brain are in the ratio of white matter to gray matter.

And we differentiate between that and changes in how the brain is acting, if you will, so functional changes in the brain. And so an adolescent and adult, given the same task to perform, may actually activate a very different pattern of brain circuitry performing the very same task. And so we now know that there are changes in patterns of activity in the brain during adolescence as well.

Now, some of this anatomical and functional change is driven by maturation. In other words, it seems kind of encoded in the genetic program that unfolds during adolescence. Some of it is driven by experience, and most of it, we suspect, is

driven by a combination. One of the questions that I'm frequently asked when I talk on this subject is: is there anything we can do to speed up their frontal lobes and get them developed faster?

And, you know, we suspect that experience plays a role in that process, but we don't know what kind of experience it does, and we certainly don't know how to do it in any deliberate way. If any of you has any ideas, I'd like to go into business with you, because I think we could be very successful.

One of the most important lessons that we have learned from studying adolescent brain development is that different brain systems mature at different points within the adolescent decade. And if there is one take-home message that I want to convey during this talk, that's it, because it has really important implications for understanding adolescent risk-taking and decision-making and judgment.

So let's talk about two systems. One system is what we refer to as the socio-emotional system, and this is the system of the brain that is active in the processing of emotions, of social information, reward and punishment. And I've listed there the key nodes in the brain where this system tends to be most localized. And those of you with knowledge of neuroanatomy recognize that this is really the limbic system and the ventral area of the prefrontal cortex.

And this system develops in the following way. It undergoes major changes in early adolescence around the time of puberty. We recently convened -- the National Academy of Sciences recently convened a meeting on this subject. And I think it's fair to say that although some of these changes occur around the time of puberty, we're not sure that they are actually caused by puberty, but they seem to be coincident with it.

And the main changes in this system

are linked to an increase in dopaminergic activity and pathways from the limbic system to the prefrontal cortex. And so dopamine, as many of you probably know, is one of the most important neurotransmitters for the experience of pleasure or reward.

And so there's a lot of remodeling of the dopamine system in the brain around the time of puberty, and, in fact, there is more dopaminergic activity in the prefrontal cortex around puberty than there is at any other point in development. So this change results in increased attentiveness to rewards, increased sensation-seeking, increased or easier emotional arousal for both positive and negative emotions, and increased attentiveness to social information.

This partly explains, for those of you who work with teenagers or have teenage children, why kids seem to be so concerned with whether people are thinking of them, and so attentive, really, to social and emotional

information.

I know when we were raising our son, who is now a young adult, I could have a conversation with him in what I thought was a perfectly normal tone of voice about something that I was unhappy about, and he would say, "Why are you yelling at me?" when I wasn't in fact yelling, but he is -- he was at that stage where he is very, very sensitive to emotional and social information, for better or for worse.

The socio-emotional system is kind of complemented by what we might call a cognitive control system. And this is a system that is engaged in -- that is -- that subserves deliberative reasoning, thinking ahead, planning, regulating impulses, higher order cognitive skills that collectively psychologists refer to as executive functions. And this system is localized mainly in the lateral areas of the prefrontal cortex, and somewhat in the parietal cortices as well.

Now, the cognitive control system, in contrast to the socio-emotional system, follows a different maturational time table. And it's the difference between those two time tables that I want to stress in my talk today.

The cognitive control system develops gradually from pre-adolescence on, so it's not something that has a rapid amping up, like the socio-emotional system does, around the time of puberty. Its development is much slower and much more gradual and extends over a much longer period of time, we think well into the mid-twenties.

And these changes in the cognitive control system result in better impulse control, better emotion regulation, more foresight, more planning ahead, and better reasoning. And these behavioral changes, as I'll show you in a moment, continue throughout late adolescence and into early adulthood.

And as I have mentioned now a couple of times, timing really is everything,

because this arousal of -- or excitation of the socio-emotional system due to the proliferation and then pruning of dopaminergic pathways occurs early in adolescence, around the time of puberty. But the maturation of the cognitive control system is gradual, and it's not complete until late adolescence or early adulthood.

And so one -- you might have seen a quote from me about this in The Washington Post the other day. The Associated Press has been running a series on adolescent brain development and its implications for juvenile justice policy -- is that the accelerator, if you will, is activated before a really good braking system is in place.

And as one of my colleagues has said on many occasions, it's like starting the engines without a skilled driver behind the wheel. So you'll get the metaphor. It actually has implications for driving, but we won't go down that road, so to speak, today.

So a summary so far about what we know about adolescent brain development is that it's a time of a still maturing cognitive control system and still maturing connections between the socio-emotional and cognitive control systems.

And, therefore, if we look and think about this in terms of kids' behavior that indicators of the tendency toward reward-seeking, sensation-seeking, thrill-seeking, experimentation with drugs, and so forth, should show the most significant development during the first half of adolescence when that socio-emotional system is becoming aroused.

And indicators of maturation of the cognitive control system should show more gradual development over the entire adolescent period, and those indicators would be things like planning, thinking ahead, impulse control, and so on.

And when you put these two time tables together, I think it takes you to the

conclusion that middle adolescence, so roughly speaking around the ages of 14 to 16, should be an especially vulnerable period for risky or reckless behavior, because this is when we would see the greatest imbalance between this now amped up, easily aroused, socio-emotional system and the still immature cognitive control system.

I haven't thought a great deal about what this means for marketing to teenagers, but it certainly would suggest that the way that you would want to market something to somebody who is at this place in development would be very different than the way you'd want to market to somebody who is 18 or 19 and has a much more developed cognitive control system.

So I want to show you some data from some work that we have been doing as part of the work of the MacArthur Foundation Research Network on Adolescent Development and Juvenile Justice, which I have directed for the past 10 years.

And this study, which is one of many studies the network has done, is a collaborative effort that evolved these other principal investigators, whose names are up there. This is an interdisciplinary team, including neuroscientists, developmental psychologists, social psychologists, community psychologists, and myself.

So what we were interested in was to examine age differences and capacities affecting judgment and decision-making. And so we collected data in five data collection sites. I wish I could tell you that there was a better reason to choose these sites, other than the fact that that's where all of the collaborators happen to be located.

But it conveniently allowed us to recruit quite an ethnically diverse sample, as you'll see in a bit. This sample involved 935 individuals between the ages of 10 and 30, and they completed a battery that we spent a couple of years developing involving computerized

performance tests of planning, preference for immediate versus delayed gratification, impulsivity, risk-taking, sensation-seeking, reward sensitivity. And we had some standardized self-report questionnaires measuring similar characteristics.

So here is the sample. I'll give you a couple of seconds to process this. We had roughly equal numbers of people in those seven age categories. The way that the sample was recruited was to make sure that the age groups were comparable with respect to race, gender, household education, and IQ.

And you can see from the right-hand panel where we have the data on household education that we did achieve one of our goals, which was to make this kind of an average sample of people. The average level of household education in the United States at the time we collected these data, which was not that long ago, is some college. That is, education beyond high school but not college

graduation.

So the way that we recruited the sample was we went into census tracks where the average level of education was some college and recruited there. You see this sample is equally balanced between males and females, and ethnically quite diverse.

And so there's four areas that we assessed that I want to talk about today. One has to do with aspects of basic intellectual ability. One has to do with outcomes influenced by the socio-emotional system, and these include sensation-seeking, risk-taking, and reward salience.

A third set are outcomes influenced by the cognitive control system, including impulse control, thinking ahead, and resisting peer pressure. And as I mentioned before, we assessed these using both questionnaires and computer-based performance tests.

Is everybody with me so far on how we're doing?

(No response.)

Okay. This is the slide I like to start with, because this is very important to keep in mind. This finding is from our data, but it has been replicated in a bunch of different studies. I hate to break it to you all, but in terms of basic information, processing abilities, and intellectual functioning, you don't get any better than you were when you were 16 years old.

And this asymptotes out at around 16. It varies slightly depending on the measure, but you can see virtually identical curves for three very different types of tasks -- a straight-up memory task with digit span, a working memory task, and a task of verbal fluency.

And if you were to look at data on logical reasoning abilities, and other similar kinds of tasks, you see the exact same curve. So when it comes to basic intellectual functioning, kids and adults don't look any

different by the time they are 16 years old.

I'll come back to that, because I think that that has led us in some senses to overestimate the decision-making competence of adolescence, because on many of the tasks that we've given them to assess their decision-making we test them on -- really on those kinds of abilities in which in fact they don't look any different from adults. I'll return to that a little bit later.

So let's look at some of our data on outcomes influenced by the socio-emotional system. Now, this is self-reported sensation-seeking using a standardized widely-used questionnaire -- the Zuckerman, for those of you who are familiar with this.

So a sample item, as I sometimes like to do things that are a little frightening, and as you see here the predicted pattern, which is an increase in sensation-seeking during the early part of adolescence around the time of puberty, and then a decline

as people get older.

Similar findings if we use a different kind of questionnaire. This was a risk -- a benefit and risk questionnaire in which individuals are asked about all kinds of different risky behaviors -- unprotected sex, riding in a car being driven by somebody who has been drinking, smoking cigarettes, shoplifting, picking a fight with somebody. There is a whole range of health risks and anti-social risk behavior.

And one of the questions on there for each of those behaviors is: how would you compare the benefits or pleasures of doing this thing with the risks? And what you see is that there is an increase during the first half of adolescence in people's ratings of the benefits or rewards or pleasures of these activities, and then a decline during the second half as well.

So we also have tasks that assess these things. A task that a lot of people use

for reward processing is a task called the Iowa Gambling Task, and in the Iowa Gambling Task a subject is presented with four decks of cards face down. Each card contains information about winning and losing.

You can do this with money, with points, with candy, depending upon the age of the subject in the study. The way that we set the task up, you're shown these four cards on the computer, you can't see what they say, and an arrow points to one of the cards and asks you if you want to play that card or not.

Now, in advance, the subject is told that two of these four decks are good decks, and two of these four decks are bad decks. And your goal is to maximize your points or your money by choosing from the correct decks. And what we measure in this is change in how people pick cards over the course of time.

As you can imagine, that when you start the study, and it asks you if you want to

play or pass from deck C, you have no idea. I mean, you know that two of these decks are good and two of these decks are bad, but you don't have any reason to think that Deck C is necessarily a good deck or a bad deck.

And here you find out that Deck C increased your stash by $100, and so now you have a choice about playing Deck B. You still don't have any information about Deck B, and here you find that Deck B decreased your pile by $50. And so you understand that you do this, and over time people develop some sense of what decks they should be pulling from and what decks they shouldn't be pulling from.

Now, the bad decks pair very large gains with very large losses. So every once in a while you hit a really good card with these decks. But if you keep pulling from those decks over time, you ultimately lose money. The winning decks ultimately get you money, but it's through the accumulation of very small gains.

And so choosing the bad decks indicates decision-making that is excessively influenced by the prospect of a big reward. And studies have shown that individuals who have lesions in their ventral-medial prefrontal cortex can't do this task. They keep picking from the bad decks no matter what.

So here is one way of showing data from this. This is the proportion of draws from the good decks, and you would expect that to increase over time as you're learning more about which are the good and which are the bad decks. But what you see here is that the two lowest lines, which are the red line and the yellow line, are the two youngest age groups in this sample, and they learn much more slowly.

Even by Block 3, which is now the 120th card that they have pulled, they are still only pulling a little bit more than 50 percent of the time from the good decks, whereas in the older individuals there is a more rapid increase learning, which the goods

decks are, that occurs even starting between Block 1 and Block 2.

Now, you can get better at this due to two very different processes. You can increase your choices from good decks over time, or you can decrease your choices from bad decks over time, because remember the way the task is set up you can pass on any card.

So your choice of good decks and your choice of bad decks are independent from each other. And so we are one of the only groups to look at the task this way, and I think we've stumbled on something pretty interesting.

This is a hard slide to process, so let me walk you through it. This is the change in pulling from either good decks or bad decks between the beginning of the task and the end of the task, between Block 1 and Block 3. And so if the bar is above the middle line, that means there was an increase. And if the bar is below the middle line, that means that there

was a decrease.

So what I want to draw your attention to are the different patterns for the blue bars, which show changes in pulling -- in choices of good cards, and the green bars, which show changes and choices of pulling bad cards. And so what you see is that younger adolescents who are on the left side of the Y-axis there, that younger -- of the axis -- that younger adolescents are paying much more attention to good cards than they are to bad cards.

That's where the big change is in their card-pulling behavior, as opposed to adults, where, you know, they are paying attention to both pulling good cards and avoiding bad cards, because the green and the blue bars are both fairly substantial for the older individuals.

And we think this is consistent with the basic notion and what we know about brain development, which is that adolescents

are highly reward-sensitive, especially during the early part of the adolescent years.

Now, they are not only reward-sensitive, they are very sensitive toward immediate rewards, toward immediate gratification. This is a task called the delay discounting task, and we start by asking people to choose between an immediate, smaller reward, or a larger delayed reward. So would you rather have $200 today or $1,000 in six months?

Then, depending upon what the person says, we either raise or lower the immediate reward. And we do this over and over again with different time intervals, with different immediate amounts, and so on, and I'll show you what some of the data look like in a second.

But the lower amount accepted for the short term indicates a stronger need for short-term gratification. In other words, if you say that for today you'll take $295 today, as opposed to $1,000 in six months, and I say

you are going to have to give me $525 today, instead of $1,000 in six months, then you are much more focused on getting the immediate reward, because you'll sacrifice all of that to get it sooner. All right? This is a very widely used task in behavioral economics.

And so this is how much a person would accept the next day as opposed to waiting one year for $1,000. And what you see here is that adolescents are a cheap date, at least relative to adults. And so the young kids are willing to take, I mean, really, you know, almost $200 less to get the reward sooner than to wait for the $1,000 later. And we see this at very single delay interval that we have studied.

So not only are they reward-sensitive, they are very drawn toward immediate rewards. So the summary of the socio-emotional system is that the reward system is very sensitive early in adolescence. As I said, it's related to the remodeling of the dopamine

system around puberty. Adolescents become more attentive to rewards, and especially drawn to immediate rewards, and we see this reflected in self-reports of sensation-seeking and risk preference.

So now, remember, that timing is everything, that all of this is going on during the first half of adolescence around puberty and a little bit after that, but that the maturation of the regulatory system, the breaks, occurs over a relatively long period of time. And so let's look at our data on outcomes influenced by the cognitive control system.

So this is self-reported impulsivity, and you get a decline that occurs throughout the whole age range study, even, by the way, from the mid-twenties to age 30. This is people's characterizations of themselves as being less impulsive. And we think this is reflective of development of those regions of the brain that are still maturing into the

twenties.

We measure impulsivity behaviorally using a task called the Tower of London, which used to be called the Tower of Hanoi. And I don't know why they changed the name of it, but now it's called the Tower of London. So we start you with an array of three colored balls that looks like that, and some placeholders where you can move them on a touch screen computer by putting your finger on one of the balls and dragging it over to one of the placeholders.

And we say, "Okay. We want you to rearrange the balls so that they -- it matches the goal." And we want you to do it in as few moves as possible. So if you were given this problem, that would be your first move, that would be your second move, that would be your third move, that would be your fourth move. This is a four-move problem. You can't solve it in fewer than four moves.

And the way that the Tower of

London task is administered, it has a range of difficulty in the problems ranging from, in our lab, three-move problems up to seven-move problems. So you all get the idea of what this task is like. And you try to do it in as few moves as possible.

And one of the things we measure here, in addition to how many moves it takes for people to solve the problem, and how many mistakes they make, is how long they wait before making their first move, because that in some sense is an indication of how impulsive they are.

Obviously, if you've got a seven-move problem facing you, you really want to think it out before you make your first move, because it will cost you time and moves to undo a bad move. And so what's really interesting -- we couldn't have made up the data to look better than this, but this is real.

What you see here is that the easy -- solving the easy problems, the three-move

problems, that's in blue, and the hard problems, six- and seven-move problems, that's in green. And what you see is that for the little kids, the 10 to 13 year-olds, even the 15 year-olds to a certain extent, they don't spend any more time before making their first move on a hard problem than they do on an easy problem.

Whereas you see that nice, great linear increase in the green bars with age over time, showing that as people get older they take a little bit more time, not just a little bit more time, actually twice as much time, 12 seconds versus six seconds, before making this move in this problem. And if that's not impulse control, I don't know what is.

Now, another aspect of maturation of the cognitive control system is resistance to peer pressure. This is a new measure we developed. There is a sample item up there, and it shows this nice linear increase in people's self-characterizations of their

ability to resist peer pressure.

We're interested in this, because adolescent risk-taking usually occurs in groups. I don't know whether this is true for use of over-the-counter medicines. It might be true for things like cough medication and things like that, but most of the risky and stupid things that kids do takes place when they're in groups.

Peers' use of alcohol and illicit drugs is one of the strongest predictors of an adolescent's own substance use. The risk of a serious automobile accident significantly increases with the presence of same-age passengers in the car. Adolescents are more likely to be sexually active when their peers are sexually active, and they are far more likely than adults to commit crimes in groups than by themselves.

So this is from an older experiment that we did using a task called the chicken game, which is the name that one of my grad

students gave to it. And in this game the subject drives a car across the screen, and the longer the car is in motion the more points are accumulated.

The subject is told that a yellow light will appear, signaling that at some point after the yellow signal a wall will pop up out of the ground. If you stop before crashing into the wall you get to keep all the points you've accumulated. If you crash, all of the points are lost.

And in our experiment, performance on this task is correlated with self-reported inclination toward anti-social activity. So people that take more chances in this task in the lab also do more anti-social things in the real world.

Now, the one -- the manipulation that we did here that turned out to be really terrific was that we invited people to come to the lab and told them to bring two friends with them. And then, we randomly assigned them,

either to do this and the other task by themselves, or to do it in the room with their friends watching them. Okay?

And so this is what it looks like. The light turns yellow, you stop in time, points have been added into your account, and so forth. So this is the impact of the presence of friends in the room with you, and this is the number of times the person crashed into the wall.

What you see here is that when people are alone, the adolescents averaged around 14. The youths were college undergraduates; they averaged 20. And the adults were in their early thirties. They all brought friends of the same age and same sex.

So when people are alone, there is no difference in how often adolescents, college students, and adults crash this little car. But as soon as you put friends in the room with them, you see that it doubles the crashes that adolescents make. It increases by 50 percent

the crashes that college students make, and it doesn't affect at all the crashing behavior of adults. We were -- we just love this.

So this was the basis for an application that we made to NIDA which was funded to sort of figure out, what's going on? What's happening when you put peers in the room that is making people take more chances? And so what we're doing now is we're testing a procedure in which the peers are not in the room, because ultimately we want to go into the FMRI magnet, and we can't shove a bunch of people in the same magnet at the same time.

So we've developed a paradigm where you're playing this game in a room, and then the room next door, your friends are sitting, and there is a computer screen in there, and you are told when your friends can see what you're doing and when your friends can't. And there's a mic in there. It's not turned on while you're playing the task, but before the peer condition is implemented, the friends all

say, "Okay, now, John, we're watching you." All right?

And so the adults and the kids all say the same things to each other. That's one way we control that. And so we have some pilot data on 39 subjects that I want to show you, average 19 years old, in the behavioral lab, and we have two subjects that we have imaged in this kind of a design.

So this is a task called the Balloon Analog Risk Task, or BART. Basically, you pump the balloon up, and you accumulate more points or money as the balloon gets bigger and bigger. But if the balloon explodes, you lose everything you've accumulated. And some balloons pop real quickly, some take a long time to pop. You have no way of knowing.

So if the individual is with peers, they explode the balloon twice as often as if they are doing the task alone. This time the peers aren't even in the room with them. They're in another room, and it still makes

them take more chances.

We've looked at this with yet another game called the stoplight game, which is a video driving game. We designed it to mimic the situation that you have all been in where you're driving the car, you approach an intersection, the light turns yellow. You have to decide whether you're going to try to make it through the intersection or whether you're going to stop.

And so what we do is we set up this game where we encouraged the subject to make it through the whole route, which is eight intersections, in as little time as possible. And we tell them that they're going to have to decide when the light turns yellow what to do, and there's three things that can happen.

You can get through the intersection successfully, you don't lose any time at all. You can stop and wait for the light to cycle around to green, so you lose some time. Or you crash, and then you lose a

lot of time. And the time is made very salient. There's a big clock, and it's ticking really loud while you're playing this game.

And so we have an index of how risky the person is, which is really just a ratio of how often they don't brake when the light turns yellow to how often they brake. So this is what it looks like. The light turns yellow, you didn't get so lucky this time, because you crashed the car. And I have the sound turned off, but there's a loud -- squealing tires and crashing and glass breaking, and that sort of thing.

So, again, you know, just having peers in the next room watching you do it increases your risky driving significantly. These are 19 year-olds. We haven't yet started with teenagers.

We brought this into the magnet with two subjects. These are two Princeton undergraduates, and playing the game, even in the magnet, with your -- knowing that your

peers are watching you makes you crash twice as often as when you are by yourself. This is really absolutely astounding to us, I have to tell you.

And so here is what the imaging data look like that during the task in general, regardless of whether you are doing it alone or with your peers, the cognitive control network is what is active here. And you see the lateral prefrontal cortex and the anterior cingulate cortex and the lateral parietal cortex. That's what is active when people are doing the task.

When they're doing the task only in the presence of peers, you get this activation of the socio-emotional network. And so the medial prefrontal cortex, the ventral striatum, are activated only when peers are present and not when peers are not present. So the presence of peers activates a different brain circuit when you're doing the same task.

So my main conclusions here, then,

are that the developmental course of intellectual and psychosocial maturity follow different patterns. Do you remember that graph I had early on in the talk where I showed you intellectual development hitting an asymptote at around 16 or so? So intellectual abilities increase in early adolescence, but they plateau around age 16.

And psychosocial maturity is relatively stable from 10 to 14, and then it steadily increases from 14 to the late twenties, as seen by gains in impulse control, the delay of gratification, planning, future orientation, resistance to peer influence, risk perception, risk aversion, any number of measures.

And certain situations we think exacerbate age differences and decision-making. Social arousal, which we've shown you with the peer data, and now we're doing some stuff in our lab looking at emotional arousal and the different effects of emotional arousal on kids

versus adults when they're doing decision-making tasks.

So we're trying to answer this question, which is I think on the minds of a lot of educators, parents, policymakers, and so forth. Most of us who have teenage children, who had them, know that kids who seem really smart do some just incredibly stupid things.

And it's a puzzle for parents I think to try to figure out why this is, why somebody with a tested IQ of 130, and who does really well in school, and can carry on a really sophisticated intellectual conversation with you, will do something just incredibly stupid like get behind the wheel, you know, drunk and drive a car. And this is what we're trying to answer in our program of work.

And I think the answer is this, is that smartness isn't what it's about, because intellectual -- because intellectual maturity reaches adult levels long before social and emotional maturity does. Social and emotional

maturity is still going on in late adolescence and early adulthood, long after adolescents have become as smart as adults are.

Shakespeare recognized this a long time ago. This is a quote from The Winter's Tale in which he actually proposed that there wouldn't be a period of time between 10 and 23, because kids get into so much trouble as well. Today's version of that is -- it says, "Young men, go to your room and stay there until your cerebral cortex matures."

It's basically the same thing that Shakespeare was saying, you know, several hundred years ago. But I think the idea here is that there is something maturational about adolescence that makes this a very vulnerable and risky time, and we should be concerned about that from a public health standpoint.

So let me just conclude with some implications. It is a period of heightened vulnerability to emotional behavioral problems. I didn't have time to talk about it today, but

if you look at data on things like eating disorders, depression, substance abuse problems, and so on, a lot of mental health problems emerge during adolescence that weren't there beforehand.

And we think that this brain story helps to explain why that's happening. It's due to a timing gap that is normative in the development of two brain systems. And without self-regulation, which adolescents are still lacking when they are 14, 15, 16 years old, adolescents need regulation by others.

And it seems to me that it's a more productive strategy to try to change the context in which kids live rather than change the adolescent through education.

I just leave you with this one observation that despite the billions of dollars that we've spent getting kids to not smoke cigarettes in this country, the most effective intervention ever done was to raise the price of cigarettes, and that had a much

greater impact on kids' smoking behavior than any anti-tobacco program has ever had. And that's what I mean by changing the context.

I'm working with the Allstate Foundation in a promotion of teen safe driving. You know, driver's education, you'd be surprised to know, has absolutely no impact at all on kids' driving abilities. It has been shown -- the National Academy of Sciences published a study on this just last year. But do you know what saves teenagers' lives? Having graduated drivers licensing laws that restrict their driving with passengers in the car or nighttime driving, and so forth.

Again, changing the context, changing the regulatory context, is going to be much more effective in diminishing adolescent risky behavior than changing the adolescent as well.

So I'll leave you with that thought, and then turn it over to the next speaker.

Thank you.

(Applause.)

DR. HUSZTI: Okay. So I'm going to talk a little more about some of the functional findings, so I think that fits well with Dr. Steinberg's talk, and focusing a little bit on concepts of health and wellness. And I will try and draw some parallels as we go along.

And I think, you know, this is one of those talks where, you know, you're -- sort of our initial impression is kind of like it could be very short, and I could just say they don't have any.

But it really is a much more complicated process than that, and that there's a lot of development that occurs during adolescence about health and wellness, and I think -- and just thinking about Dr. Steinberg's talk, as well as those cognitive strategies come into place, there are changes that happen.

And I think that starts to explain

some of the behavior, again, that we get frustrated by, right? Like they seem like they can say this, like they seem to know it, and yet, again, they run off and do these things.

So I wanted to start with, just because I think it's always helpful to say, "What are we talking about?" with some of the definitions of health. I think it's one of those things that's like art, I know it when I see it, but it's nice to actually have the definition. And if you look at World Health Organization's definition, it's a state of complete physical, mental, and social well-being, and not merely the absence of disease and infirmity.

Pender had an interesting addition to that, and I think the two take-home points in that is when we talk about sort of a mature concept of health, we're talking about planful thinking, we're talking about doing things to prevent problems, we're not just talking about an absence of disease.

And I think what you'll see from the data is for adolescents, particularly in early adolescents, their concept of health is really focused around the absence of disease, not in these other strategies, which I think also has some implications for over-the-counter medications.

Okay. I want to also provide a little context, too. You know, Dr. Steinberg talked about some of the neurological development. I think the other thing is experience I think really is something we need to pay attention to. And if you look at, what are the leading causes of death in 15 to 19 year-olds?

You'll notice that everything below accidents, homicide, and suicide, don't add up to suicide alone in terms of what kills 15 to 19 year-olds. And given that, it's not surprising that 15 to 19 year-olds don't really think anything bad is going to happen to them, because they don't see it. It's not a part of

their life.

And it's not until we start to get older, into my age category, that you start going, "Oh, my gosh, I've seen all these people. I know something about -- I need to prevent things." But for adolescents, I think that's a concept that doesn't make sense.

The other thing -- and I do want to -- we've picked a lot on adolescence, pick a little bit on adults, too. The other piece of context is, when you really think about what do we do as adults about health, think for yourself. I mean, this is a room full of people who know better than anybody what are all the health-related regulations, and things that we should do to stay healthy. How many of you do all of them?

You know, have you ever like not taken all of your course of antibiotics? Have you ever like not drunk all of your water? And if you look at adults in the community for any health-related behavior, about 50 percent of

them do not want to make a change in their health-related behavior. And that's doing the bad health. That's not the good health.

So I think sometimes we're expecting more of teens sometimes than we expect of ourselves. So I think that's the other piece of context I want to give in there, too, is, you know, teens are different than adults, but health is one of those very difficult concepts for all of us to engage in and change and do.

So a couple of things I really want to focus on today are a couple of questions that I think will be helpful as we talk about over-the-counter medications. One is how do adolescents conceptualize health and wellness? And what do they think that is?

I think it's also important to know: what do they know about it? Because we can sort of ask people to give back -- like, oh yes, you know, it's this. Here's the definition. But what do they actually know?

Can they use it? Can they actually apply it? And what is happening in there?

And especially as you're thinking about how adolescents' brains are working. Sometimes they've got the knowledge, again, that intellectual ability, but they don't have the capacity yet to do the intellectual -- the control part of applying it. I think that's an important issue.

And then, where do they get information about health and wellness? Because I think that's another important point. If we say, "Okay. Well, let's go label these things," but that's not where adolescents get information about health, it's not going to be very helpful. And so where are the places that adolescents go?

So how do adolescents conceptualize health? There aren't a lot of studies out there that look at that. The studies do tend to be small, and I'm going to present some fairly small data today. They often use

qualitative methodology, but I think that's kind of helpful to get a really nice picture of what's going on. And I think it's helpful, and I feel comfortable giving you some of this, because the results tend to be pretty similar over the study. So over time I think you can sort of accrue some things of saying, ah, you know, that's actually fairly similar.

One study looked at early adolescence, so we're talking about six to eighth graders. And these were from low income, inner city schools. Eighty-five percent of them did participate in the school lunch program. And they asked the kids two questions. How would you define the word "healthy?" And what does being healthy mean to you?

And they used those responses to combine to create categories of health because one of their hypotheses was the taxonomy of health for adolescents is going to be different than it is for adults, and indeed they found

that. So when you look at definitions of health, absence of illness was cited by 12.2 percent.

So it's not, I'm not sick, I don't have a disease, I don't worry about health problems. Physique -- it's a good, strong body. I'm the correct weight, I'm physically fit. And functional ability -- I'm able to run, I'm able to perform sports. Are three of the categories. And if you think about that, this is the very concrete categories about health. You know, it's how you look, it's those very basic simple things that you do.

They also looked some at behaviors like health risk avoidance behavior, not smoking, not using drugs. But, again, when you think about avoiding health risks, they are very simplistic. You know, it really is like I've heard that campaign "Don't Smoke," I've heard that campaign "Don't Use Drugs," that's what I should avoid. But I may not be quite clear why that is.

And then, health-promoting behavior. I should eat healthy food, I should eat vegetables, I should exercise, I should work out, is the second most common category. And what's interesting is to think back to that definition of health from the World Health Organization when the definition includes that sort of holistic approach.

If you look at early adolescence -- and, again, it's not surprising -- that holistic integration is not there. It's very uncommon. And, again, it makes sense, because they're not -- that control and that idea of, okay, there is sort of like future things that happen from my actions today. But, again, that's the way we often approach the message, right, is you want to take care of yourself so nothing bad happens to you in the future.

And that may not be a concept that really works for adolescents. And I think if you want to take something away from my talk, it really is, we need to meet the adolescents

where they are, and sort of understand a little bit better how they process this information, because they are really good sometimes about giving us the answer we want to have. And they kind of know that adult-speak.

But when you sort of probe a little more deeply -- and that's why I'm saying the qualitative studies sometimes are very helpful -- you can see, you know, actually, it's -- there are some other things going on here.

There are a couple of other studies looking, again, at younger kids, six to 11 year-olds. They looked at specific health practices. The older kids, starting in that 11 year-old range, started to use that, "I don't feel ill, I don't feel sick" as the definition of health.

Younger adolescents, again, in another study, tend to describe health as the absence of illness. Older adolescents have greater importance on disease prevention and health maintenance. And in ninth graders they

did tend to start beginning to describe health in terms of well being, absence of illness, being fit, dealing with problems, and taking responsibility.

And this is a lovely picture, but I also want you guys to think about, what is our -- you know, we have a lot of kids saying, you should exercise, you should eat right. What are our rates of obesity now amongst our adolescents? They may understand that, but it's not getting translated.

And again, that's why I think it's very important to sort of do both parts of -- let's ask them the questions, but let's also understand how it's translated, because, again, thinking of Dr. Steinberg's work, intellectually, they understand it, but that putting it into action is a much more difficult issue for them.

I want to talk a little bit about some work we're doing with a group at the Art Center College of Design, which has led to a

whole different methodology than we usually use in research, Children's Hospital of Orange County, and Stanford University. And this is funded by the Robert Wood Johnson. That's part of our team.

And the idea of this is to look at teens and engage teens in their own health and engage teens in their own personal health records, so that they actually can use information and we can approach health and wellness from their perspective and in ways that make sense to them.

So our participants -- we have 35 participants between 14 and 18. We had a group that had a chronic illness, and they invited their best friend to participate as well. We use -- and I'll talk about these in a minute -- a methodology of cultural probes, and this is from a human design perspective, so very different than the psychology and the medical research I've been used to doing. And we also conducted interviews with the identified

subject and their best friend.

So cultural probes are very open-ended activities that ask the adolescents to actually engage in a process of creation and thinking about things differently, so it's not a specific questionnaire or question asked straight on. It's more like, work with this information and kind of tell us how you think about this and what that looks like.

And basically we sent kids home with these kinds of packets that had things like the make your own mix that you see up here -- was very popular. That was an iTunes gift card, and then there were questions that were, tell us something about the song that makes you think of -- makes you feel better, and tell us why that is. Dedicate a song to someone and tell us why you're doing that. Give us a song that says something about your best friend.

And it gave tremendous information in a way that we often aren't pulling from these kids. I'll talk a little more about the

plate in a minute.

And we also had an activity book where they went through, and we asked them to say, "Well, what do you want in your health records?" Let's just throw this out the window. You know what a medical record is. What do you want it to look like? If you're in charge of it, what's important to you to put in there?

We also had them do video blogging, and upload images of their life and things that were going on for them, that was make our own mix. The plate is actually where they -- we ask them to talk about what do they feed their soul, their body, and their mind today. And I'll talk a little bit more about that in a second as well.

The other thing we did during the interviews is we also asked them to talk to us about what are words that have to do with health and wellness and well being. And we plotted those about what was teen-centric, what

applied to everyone, what was well-being or health -- they don't like the word "health" -- and what's fine.

And to kind of try and get a sense of like, okay, well, from a teen-centric standpoint, because we're always asking from -- you know, from an adult standpoint what is health, but from a teen-centric standpoint, what's health? And what this showed us is there is actually a big old gap in there. This is looking at one child's results.

And if you look at the fact that there is actually like a big blank space up there, which if it's just one person you go, well, okay. You know, that area of what's teen-centric, what's well-being? And I don't have any words for that.

Okay. Well, maybe that might be a spurious finding. But when you put everyone's together -- and this includes the blue, includes the friend who doesn't have a chronic illness, the brown includes the child with a

chronic illness, the adolescent with a chronic illness, and you'll note that there's an amazing similarity between them in terms of the words, and the fact that they don't really have words for well-being or health that are teen-centric.

In fact, the only thing about as close as we get are MySpace and friendships. And it scares me a little bit after hearing Dr. Steinberg's talk, too, because when you're with friends, you're a little riskier than you tend to be when you're not. And in the adolescent mind, being with friends and being able to be with friends is part of what means wellness to them, at least from this study. We want to do some more work with this to take a look at this more fully.

The other thing we found is, much like with the other studies, food and exercise are the predominant themes of what is health when you just ask them, "What's healthy?" "The way I eat, and physically, the way I work out

all the time, and stuff." And they start as they get older to go, "Oh, yes, and like not stressed out all the time." School is a huge source of stress for these kids, and something that for them is an important part of health and wellness.

To eat healthy and exercise, the interviewer asked them, "What do you mean by exercise?" and for this kid it was skateboarding. And pretty much everything in his life was about skateboarding, so that was health to him. And just living a healthy life, being athletic and eating the right types of food.

Again, amazingly similar kinds of responses across a wide variety of different studies and different subjects, but -- and, again, when you sort of think about, but what's happening in our population? Teens don't seem to be actually applying that information.

This is the same way when you look at, what did you feed your body? It's

basically food. They took it very literally. When you talk about mind, it's all about school. And when you talk about soul, that's about friends and family and things that are important to them.

And, really, what came across in our interviews was if I can be with my friends, if I can hang out, if I can be connected, I'm healthy. And if I'm not, I'm not healthy, and I'm going to do whatever it takes to be able to do that.

Now, I think that actually has some implications when we start talking about over-the-counter drugs, because if you think about it, I defined this -- "health" as an absence of illness. And I want to hang out with my friends, and I want to be active and go and do things.

Now, I have a headache and it kind of hurts. What might I do with the aspirin or the Tylenol or the -- you know, whatever kind of product you might -- painkiller product you

-- that's over the counter. And, unfortunately, I've seen a number of these in the hospital.

You might take more than the two or more than the three that are recommended. You might, oh, I don't know, take six, 10, because like you really want to get going again, and, you know, if two or three work, six or 10 should, like, work a lot faster, right? And I hear that from them over and over again when I'm going up and doing a risk assessment with them. It's like, well, I just wanted to feel better faster.

They also -- I think it's interesting when we ask kids in their health record, what is their prescription for themselves? Again, sleep, exercise, relax time with friends, and do less procrastinating. Their health recommendations to themselves, again, aren't very health-focused.

They aren't about taking their medicine. They aren't about doing things long

term necessarily. The sleep and exercise is certainly helpful. But they do tend to go around the friends again, and that seems to be very important.

I think the other thing that was very striking to us is, we sort of thought, okay, when we talk about personalizing your health records, like what do you want in your health records, what they wanted was stuff about them. Nothing about their health. They wanted us to know, my friends are very important to me, I like to travel, these are the places I want to go, I like to smile and laugh, I like to talk a lot.

And in talking with some of the teens, their sort of sense was, I just want you to understand me. I want you to know who I am before you start talking at me about here's what I need to do. And if we can come at that level, then, okay, I'll listen to you about the other stuff.

And again, if you sort of think

about what's important at that age, it's the social-emotional connection, why wouldn't they want their doctors or why wouldn't they want health care providers to do exactly that same thing?

I think this is sort of the perfect -- we asked kids to do -- create a cover for their CD. I think this is the perfect adolescent moment. It's all about me, and the back cover is here are my friends. And that's my CD. And it is a very -- you know, that's where they're at, and that's what is important to them.

And if you think about, how are they defining their quality of life or their wellness or their health, they are defining it through the engagement with their social networks and by their mood, not by their illness and not by health. Again, this is one of our young men's personalized health records.

He wants to talk about his prom date, show the awards he has won, that he is

very athletic, that he likes to surf. These are the things that are important. And if I don't get past that, I'm not going to talk to you about anything else.

And then, here is another prescription. I need to remember who my real friends are and not treat them with disrespect. That's my health prescription. I can be a little mean sometimes, and I need not to be. And I need to open myself up a little and make new friends and not be so shy.

Again, to an adolescent, that's what is important. That is what is well-being. To us, not so much, but we're talking, you know, at different -- at different places.

Okay. What do adolescents know about what they consider to be healthy? There was a study looking at 236 ninth to twelfth graders, and they completed questionnaires looking at their self-perception of knowledge across four health-related areas and then completing a knowledge test. And, again, I

think this is important, because it's important to know not only, can I give the right answer, but do I know some in-depth information about that?

So when you looked at questions like exercise, and the questions were things like, if you stop exercising, all your muscle turns to fat. So it's question along those sort of lines. And you'll note that 25 percent got all of those correct, got 70, 80 percent. Only nine percent got them all correct.

You'll also note that the correlation between what I think I know, like I know a lot about this topic, and what I actually know about the topic is pretty much non-existent for exercise and sleep. Adolescents think they know a lot about it, and they know very little.

Interestingly, you have a significant correlation for nutrition and eating disorders. That comes from the female adolescents. And if you think about, again, a

female adolescent sort of world, that diet, that -- you know, the world of eating disorders is a very common thing, and they do generally know a lot about it.

I think the question from this, and the question from some other research is: how do you know what you don't know? You know? I mean, if you think you know it, why would you pay attention to anyone telling you anything because you already know it? And so I think it's important to also sort of understand, sometimes adolescents don't know what they don't know.

And that that can cause problems in labeling, because they just assume they know. I know how to take aspirin. I've known that since I was a baby. I'm not going to read anything over the counter about that. Or here's this new drug, someone told me about it. I know what to do. And I think, again, that's what gets us into trouble.

Okay. Where do teens go for health

information? It was really interesting. Teens want to hear from their healthcare provider, but a lot of things seem to get in the way. For the study that I was showing you earlier, our teens always said, "I have no questions for the physician." Anyone who practices with teens knows you go in and say, "Do you have any questions for me?" and they'll go, "No."

But the interesting thing was when we asked, "What do you want to know more about?" they had like novels of things they wanted to know. And they wanted to know things like, how does this affect my future? Can I do these things that I enjoy doing? So, again, it was how -- what's the approach, and how do I ask the questions?

One study that's a little disturbing in the Journal of Adolescence is looking at adolescents who report a health risk. Seventy-one percent of adolescents presenting to a physician's office reported a health risk, but 63 percent didn't talk to

their physician about it during the visit.

Okay? There's a lot of stuff going on there in teens' lives that they're not sharing with us. Eleven to 19 year-olds said that they prefer health information from a physician, but they're concerned about privacy issues, and they're concerned about a lack of availability, that they can't -- and think about the way the teens communicate in this world.

They are text messaging, they are on the Internet, they are IMing. I mean, there is instantaneous access to information. And the physician, like I have to call his office and wait a week? That's like forever. I need to know right now. And so a lot of times they are not accessing information. That takes too long for them.

And where do they get health information from? Well, the answer to that is interesting, too, because it may depend on what kind of health information they are looking

for. This was a study that looked at high school students.

They gave them health scenarios about a kid with pneumonia, a kid who was smoking, a kid who is ready to initiate sex, and symptoms -- and a child with -- adolescent with symptoms of depression, and asked, "Who would you like to hear this information? Who would you go to for more information about each of these areas?"

What's interesting is for pneumonia -- so something that is seen as a real health risk -- they'd go to the physicians and parents, which is great. For smoking, they would go to friends, parents, and physicians. For initiating sex, no adults are involved in that process. And for depression, they'd go to a partner first. I was glad to see psychologist made the list. And then, friend. But they are not going to parents.

So, again, I think we may need to also pull apart what kinds of questions we're

asking and what sorts of arenas kids see as the experts in this area, and what they are willing to share, because I think some of this is very sensitive information that they don't want to share with adults.

Here is a little good news about the Internet. Obviously, kids are very wired. They are on the Internet all the time. But what's interesting is adolescents do have some concerns about privacy issues on the Internet. I think, though, it is also important for us to understand what privacy means to them, because I think for us privacy means like no one knows anything.

For them, that means I set my MySpace page to 50 people. Well, no, I don't know them very well, but they're like really close friends. And so they have a much broader view about privacy and friendships and those relationships.

The good news is, I think, that they had a lot of concerns about the

reliability of information that's on the Internet. They do see books and magazines as more reliable, and that they would go to them to doublecheck the information they got on the Internet, which is good.

The bad thing is basically -- and I think this is such an illustrative quote -- “They wouldn't print it if it weren't accurate.” So if it's in a book, if it's in a magazine, it's right. So that's a little scary, too.

So, finally, I think part of what I'm giving as a take-home message is to really think about, we're probably defining things differently. We have an adult perception of what we're asking and what we want adolescents to do.

Adolescents may have a really, really different idea for a lot of reasons, for biological reasons, for experience reasons, for the fact that, developmentally, they are moving away from families and connecting with friends,

and we have to be really careful how we frame the questions, what we ask in terms of the questions, because I think we're not going to get good data if we're not careful about making those definitions and figuring out exactly what we're asking and exactly what they're responding to.

Thank you for your time.

(Applause.)

DR. CUMMINS: Okay. We're going to take a break. Let's come back in about 15 minutes.

(Whereupon, the proceedings in the foregoing matter went off the record at 2:55 p.m. and went back on the record at 3:13 p.m.)

DR. CUMMINS: So we're going to reconvene. Thank you all for coming back.

And we'll hear now from Dr. Wandi Bruine de Bruin about adolescent decision-making.

DR. BRUINE DE BRUIN: So what I'm

going to do is I will talk to you about adolescent decision-making, and I'm going to try to answer the following the three questions based on results from the field of behavioral decision-making.

And I'm going to be able to answer some of these questions better than others, and these questions are, first, what skills do people need to make good decisions? Second, do adolescents have the skills to make good decisions? And, third, how can we help adolescents to make good decisions about over-the-counter medication?

And like I said, I may not have the data to answer all of those questions, but I'll do my best.

So to answer the first question, I will give you a brief introduction into theories of decision-making. And so here you have a simplified decision tree, which is a way that decision-making researchers like to represent decisions. And this is a very

simplified decision tree, just give you an introduction into that representation.

So let's say a woman is deciding whether or not to take emergency contraception because she suspects that her method of birth control has failed or maybe she didn't use one. So she has arrived at the decision node on the left of the slide, which is, in decision tree language, usually represented as a square. And in this simplified decision tree, two paths that she can take. She can take emergency contraception or she can decide not to take it. So there are two decision options represented here.

And now let's say she chooses to take emergency contraception, so she would take -- that would mean she takes the path at the top of the slide, and then she will arrive at a chance node where chance will decide whether or not she will get pregnant. Now, of course, the probability of her getting pregnant should be lower if she takes emergency contraception than

if she doesn't take it, so the chances are different depending on the course of action she has chosen.

Now, you can make a decision tree more and more complex by putting more and more information in it. So, for example, if you look now at the top path, taking emergency contraception, whether it's effective depends on when it is taken. The earlier you take it, the more likely it is to prevent pregnancy. And if you take it, you may experience adverse events. And this is how you can make a decision tree more complex to represent a decision.

Now, knowing how decision-making researchers represent decisions will help you to understand the decision-making skills that have been identified by traditional theories of decision-making as relevant to making good decisions.

So the first skill that good decision-makers need, according to traditional

theories of decision-making, is good decision-makers need to be able to structure decisions. They need to be able to identify the options that are available to them and the outcomes that will happen if they choose each of those courses of action, if they choose each of those options. It's not always easy. People don't always know which options are available to them.

The second skill that good decision-makers need is probability assessment because they need to be able to assess how likely it is that different outcomes will happen to them given different options that they might choose.

Then, a third decision-making skill that good decision-makers need is value assessment. For example, if a woman is deciding whether or not to take emergency contraception, she needs to be able to figure it out -- to figure out how important it is for her to avoid a pregnancy. And this is not

always easy either. People don't always know what they want, and what they want sometimes depends on how information is presented to them.

A fourth skill that good decision-makers need is integration. That is, they need to be able to look at all of the information about the different options and the different outcomes, and they need to be able to choose the option that is most likely to lead to the outcome that they want to happen.

And then, finally, a good decision-maker needs meta-cognition, or they need to know how much they know and how much they don't know. And that's important, because if you recognize the limitations of your knowledge, then you know when to go out and find more information by, for example, reading risk communication materials or talking to your doctor, or talking to somebody else who might be able to help you.

So after this brief introduction

into behavioral decision-making theories, let me try to answer the second question. Do adolescents have the skill to make -- skills to make good decisions? And so let me just start by saying that there are no systematic studies that compare adults and adolescents on all of those five skill sets that have been identified by traditional decision-making theories as important to making good decisions.

Most studies that focus on those skill sets compare adults and adolescents on probability assessment, and they show no differences between adults and adolescents. They do find biases in probability assessment in adolescents, but those biases also occur with adults.

And, for example, one of those biases is perceiving oneself to be invulnerable, thinking that that outcome won't happen to you, even though you might think that they would happen to your peers if they engage in the same behaviors.

Another way of looking at whether adolescents can assess good probabilities is to look at whether the probabilities they assess for different things happening to them are related to whether those things actually happen to them.

So to test that what we did is we added probability questions to the national longitudinal study of youth, which follows American adolescents over time, and in 1997 we asked them probability questions about different things happening in their lives, such as getting pregnant in the next year, being in school in the next year, getting a high school diploma by age 20, and other outcomes that they may or may not experience.

And then, we followed them over time, so we looked a year later, did they experience those outcomes? And by age 20, did they experience those outcomes? And to our surprise, we found that probabilities assessed in 1997 with adolescents predicting whether

particular outcomes would happen to them was -- were actually correlated to them experiencing those outcomes a year later and by age 20.

So it seems like, at least for those outcomes, adolescents are able to use probabilities that are valid in the sense that they are related to the outcomes that they experience in their lives.

But like I said, there has been no systematic study that looks at all of the different skills that decision-making theories say you need to make good decisions. So what we tried to do is to develop a measure of decision-making competence that basically is a set of paper and pencil tasks that have been developed in the judgment and decision-making literature, and that measure the skills that you presumably need to make good decisions. So they include probability assessment, value assessment, meta-cognition, etcetera.

And I should tell you that there have been questions, that the field has been

criticized for using kind of hypothetical, unrealistic problems that -- and there have been questions about whether those tasks really -- they may measure decision skills, but there have been questions about whether those tasks really predict anything related to real-world decision-making.

So we wanted to see whether that was the case, so we gave this paper and pencil measure of decision-making competence to adolescents who were participating in a study at the University of Pittsburgh CEDAR Center, which follows adolescents -- has been following them for 10 years I think now.

And we gave them this measure of decision-making competence, those paper and pencil tasks that measure those five decision-making skill sets, and looked at how it related to their real-world decision-making, their risk-taking behavior in this case.

And we found that adolescents with better decision-making competence scores on

this paper and pencil task had fewer risk behaviors in the sense that they were less likely to be juvenile delinquents, they had lower lifetime number of instances of marijuana use, and they had a lower lifetime number of sexual partners.

And those results held even after controlling for socioeconomic status and general cognitive ability, suggesting that, as measured on this paper and pencil task, decision-making skills may be relevant to making real-world decisions, and that decision-making skills are a separate skill from general cognitive ability, such as measured on intelligence tests.

So what we hope to do with this paper and pencil measure but what we have not yet done, because we haven't had funding, is to examine age effects on decision-making competence. So, for example, we would like to follow adolescents over time to see how their decision-making competence develops and how it

compares to adults'.

We would also like to use it to identify levels or ages at which people have good decision-making competence or enough decision-making competence to make decisions on their own about specific topics such as maybe taking over-the-counter medications.

And we could also use it to develop measures or interventions to teach decision-making competence, because presumably, if we can teach people to have better decision-making skills they would experience better outcomes in their lives over time.

Of course, we have to recognize that decision-making skills may not always be used, so even if people have good decision-making skills they may not use them. For example, adolescents may not -- may have very good decision-making skills, but they may not use them when they are overwhelmed by emotions, or when they are in a situation where there is peer pressure.

And also, adolescents need domain-specific knowledge and skills. You can have very good general decisionmaking skills, but if you know nothing or have no experience with a specific topic, such as, for example, emergency contraception, you're not going to be able to make good decisions about it.

Now, if you're a good decision-maker, you would recognize that you don't have those skills and that information, and you would go out to get it. But you would still need to have access to information that teaches you the knowledge and the skills that you need.

And then finally, we hope to use this paper and pencil measure of decision-making skills to adjust domain-specific messages.

So if you're educating adolescents about a specific topic, you might choose to give them different information, depending on how much decision-making competence they have. So you maybe give different information to

people who have high decision-making competence versus people who have low decision-making competence.

So that's really the extent to which I can answer the second question. So now, let me try to answer the third.

How can we help adolescents to make good decisions about over-the-counter medication? And what I'll do here is, I'll give you information about what I know about interventions that target sexual decisions, which is the domain where adolescents have to deal with emotions and peer pressure, and so it might be hard for them to use their decision-making skills in this context.

And then, I'll talk a little bit about some work that is being done right now about adolescents' use and decisions about emergency contraception. So in the domain of sexuality education, there are a lot of ineffective interventions. But literature reviews have tried to -- and meta-analyses have

tried to identify what makes the few effective interventions effective, and they include the following features.

First, effective interventions have a theoretical basis. That is, they represent what experts know, and not just represents what one expert knows but experts in different fields who have studied the specific decision.

Second, effective interventions are based on formative research with members of the intended audience. So in this case, if you're developing risk messages or interventions for adolescents, you need to talk to adolescents to understand how they approach the decision. It's not enough to just ask an expert how adolescents approach it because adolescents can think of decisions in a very different way.

And if you do this kind of formative research, it will be possible to design an intervention that uses wording that adolescents understand, and that may not be the wording that adults or experts use, present

decision contexts that are relevant to adolescents and that they can relate to, and address decision-relevant gaps and misconceptions in knowledge that adolescents may have and that may threaten the usefulness of their knowledge of the basic facts.

And then, finally, effective interventions have -- they provide information, but they also provide behavioral skills training, so they don't just tell adolescents what the problem is and how to solve it, but they also give them the skills to implement their decision once they have made it, and the skills to overcome potential barriers to implementing the decision.

Now, unfortunately, in the domain of sex education, there are a lot of ineffective interventions. In fact, a lot of sex education material has not been evaluated at all, so we don't know whether it is effective. But among the ones that have been evaluated, many are ineffective.

And that is possibly because they lack the features of effective interventions. That is, for example, they use wording that teenagers don't understand, and it might be a simple word like "abstinence." There is actually a group of teenagers that interprets abstinence as including anal sex.

Now, anal sex might have a low risk of leading to pregnancy, but it has a relatively high probability of leading to sexually transmitted infections, including HIV. Also, existing interventions often present just the basic facts, but they leave out information about relevant details, especially on taboo topics. And so one of those taboo topics is anal sex, and if you don't explain to kids what the risks are of that behavior, then they may engage in it, thinking that they are doing something that is abstinence.

And then, finally, existing interventions often fail to give behaviorally realistic advice, so they say, "Just don't have

sex," or "just use condoms if you're going to have sex," and without really explaining to kids how to do that, how to implement that when they are in the situation.

So one approach to developing interventions that explicitly try to avoid those problems is the mental models approach, and it takes the following four steps. First, it asks what should people know, and it tries to answer that by doing an interdisciplinary literature review and convening an expert panel and then representing that in the form of an expert model, which I will show in the next slide.

Then it asks, what do people know? And does formative research with adolescents in this case, conducting qualitative interviews to understand what wording kids use and what decision contexts are relevant to them, and quantitative surveys to see how common it is that kids have those beliefs and how those beliefs are related to each other.

Then the third step is to find out what people still need to know, comparing expert knowledge and lay knowledge, and identify the differences, so you can fix the gaps and misconceptions in what lay people know and address the barriers to implementing decisions.

And then finally, we asked whether the intervention worked, and in that step we conduct a scientifically rigorous study in which we look at whether the intervention actually changes behavior in terms of helping kids to delay sexual behavior or use condoms if they do choose to have sex.

So here is that expert model that I was referring to that is used to represent a literature review in the mental models approach. This is a very simplified expert model. It just shows that when people make a decision they consider perceived risks and perceived benefits. The decision context is relevant, and then that leads to consequences.

So this expert model is not very helpful in trying to understand how people make decisions, but it just shows you how to represent the information.

And now I'm going to scare you.

(Laughter.)

So the only reason that I'm showing this slide is to show you that when you are reviewing the literature and thinking about what is relevant, there may be a lot of different things that are relevant. It's not going to be -- often decisions are not very simple.

There are a lot of variables that come into play, and all I want to say -- I know you're not even going to be able to read this probably in the back, but all I want to say is that the red notes reflect perceived risks. In this case, because it's about sexual decisions, it includes one's own health, one's partner's health, partner's history, and that kind of thing.

The green notes reflect perceived benefit, so they may include the perception that sex feels good, the perception of its influence on your relationship with your partner, and then the purple notes -- oh, the blue notes reflect the social context of the decision, such as alcohol and drug use, external factors such as social norms and that kind of thing. And then, the purple notes reflect outcomes, such as sexually transmitted infections and pregnancy.

Okay. But, yes, so I apologize, but I just wanted to show that there is -- that we try to systematically think about the variables that are relevant and how they are related to each other.

Then in the next step you ask, "What does the audience know?" and this is when there is intensive research with the intended audience of an intervention, and in this case teenagers. And so we conducted interviews with teenagers about their sexual decisions, and I'm

just going to briefly talk about the results.

And one is that, of course, there were gaps and misconceptions underlying otherwise correct knowledge. Actually, kids know a lot of the basic facts about sex, but they don't know a lot of -- when you ask them to explain more and more, then it turns out that they don't really know the details.

So they all can tell you that using condoms, if you're going to have sex, is going to help you to reduce your risk of sexually transmitted infections, but they can't really explain how to use them. Or they may know a lot about HIV, but not about other sexually transmitted infections.

Another finding was is that when adults think about adolescents having sex -- and I know that adults don't like to think about that -- but when they think about it, they think of the risks of that behavior. But when adolescents are deciding whether or not to have sex, they focus more on the perceived

benefits, and one of the benefits is that you're going to have a relationship with -- whether it's a short-term or a long-term relationship, with your partner, and kids are concerned about that.

And then, finally, the third finding is that -- I think the most important one for this talk -- is that female adolescents often perceive that they didn't have choices, so when they -- they perceive a lack of control, so they do see that they can choose, you know, which guy they like and whether they want to hang out with them, but once they decide to hang out with him, what happens next is sort of up to the situation, sort of up to the guy, and they don't really see that there is much -- that there are much decision -- many decision-making points in that interaction, other than that they shouldn't have gone to meet with him in the first place if they didn't want things to go further.

So what we did, based on those

results, is we developed an interactive DVD that we called "What Could You Do?" and it allows you just to select the content that is relevant to them, relevant to their situation, and relevant to what they think they need to know. It used wording that adolescents understand, because it's based on the interviews and on pilot tests of intervention content with adolescents, and addressing the things that they don't know.

So it may repeat some basic facts but also address the underlying details that they have still missing in their knowledge.

And then finally, it includes behavioral skill training, because, as we know about research about effective interventions is they don't just provide information, but they also give kids or the audience behavioral skills training about how to implement their decisions. And because female adolescents didn't see that they had the control, or they didn't see that they could make decisions, we

focused on helping them to identify choice points in interactions with guys.

And after identifying those choice points, they were asked to think about what they would do, so they would see a character interact with a guy, choice points would be identified, and they would be asked, then, to do a cognitive rehearsal of what they would do in that situation, because we know that cognitive rehearsal thinking in your head about what you would do makes it more likely that people will actually implement the strategies that they have thought about. If you think about it beforehand, it's easier to do it when you are faced with the situation.

Now, I'm just going to give -- I know that that was very abstract, so let me just give you a short clip that shows what we did, if I can find it.

(Video presentation begins.)

DR. BRUINE DE BRUIN: There's no sound. I'll just talk through it. So this is

Kaitlyn, and she just met this guy at a party. And so he -- they're kissing, as you can see.

MALE VOICE: Let's go somewhere else.

FEMALE VOICE: What did you have in mind?

MALE VOICE: I don't know, somewhere we can be alone.

MALE NARRATOR VOICE: What next?

FEMALE VOICE: Sure, let's go.

FEMALE VOICE: No, I'm fine where I am.

FEMALE VOICE: No. Jen won't be able to find me.

(Video presentation ends.)

DR. BRUINE DE BRUIN: All right. So this -- and this happens -- as the interaction progresses, the screen freezes to every -- every -- as the interaction progresses, the screen freezes at different points to identify that the girls do have a choice, and that there are different options.

We never tell them what to do. We just show them that they have options.

And then, the narrator comes on. What happens next is that the narrator comes on and asks them to think about what they would do in that situation.

And let me go back to my slides if I could. So -- and then, finally, we conducted an intervention -- or an evaluation of the intervention in which we compared the viewers of the DVD to controls and found that they were more than twice as likely not to have sex at all in the six months that we were following them. They had condom failures half as often if they did choose to have sex, and they were less likely to self-report sexually transmitted infections or to test positive for chlamydia in the tests that we gave them.

Now, currently, Tamar Krishnamurti, a graduate student in our department, is using this same approach to study adolescent decision-making about emergency contraception.

And she has developed an expert model, and she already has conducted qualitative interviews and quantitative surveys with adolescents to find out how they think about emergency contraception and how they view the decision about that.

And she identified potential barriers to the appropriate use of emergency contraception if it were made over the counter. Now, she asked me not to reveal her results because the paper is currently under review. So I'm sorry for the teaser, but this will be followed up. Once the paper is accepted, I'll be happy to share it.

But I guess I could tell you a little bit about other research that has been published about adolescents' use of emergency contraception and -- because one concern that has been expressed about adolescents' use of emergency contraception, if it's over the counter, is that it will increase the chance that adolescents will have unprotected sex.

And so to test whether that might be the case, Melanie Gold at the University of Pittsburgh gave adolescents emergency contraception to take home. And she compared them to controls who were told, "If you need emergency contraception, you should come into the doctor's office."

And it turns out that adolescents who took emergency contraception home, which is sort of comparable to having it over the counter, although it's even more available because you have it right with you, they were not more likely to have unprotected sex over the course, I think, of six months in which those kids were followed. But they were more likely to use emergency contraception, and to use it earlier.

And that might mean that they reduced their risk of getting pregnant, because the earlier you use emergency contraception the more effective it is. And presumably a lot of unprotected sex in teenagers happens over the

weekend, and if they had to wait until Monday until they can see the doctor that might be too long of a wait, or that may increase their risk of getting pregnant.

However, so maybe the idea that kids might have unprotected sex if emergency contraception is made over the counter is perhaps not a big concern, if you believe the results of this study. But there might be other barriers to the appropriate use of making -- of emergency contraception if it were made available over the counter. And Tamar will answer those questions once her paper comes out.

Okay. So, overall, the research that has been done in the field of behavioral decision-making suggests that adolescents and adults may have comparable decision-making skills, but they have not been compared on the full set of decision-making skills. And even if they have good decision-making skills, they may not use them in particular situations where

they are swayed by their emotions or by peer pressure.

And sexual decisions may be one context in which that is the case. But adolescents can make better decisions if we provide them with effective risk communications, even in the context of sexual decisions. So we just have to keep in mind that effective risk communication requires content that is evidence-based and useful to adolescents, so it gives adolescents information that helps them to approach the decision in the way that they see it.

So if risk communication is not effective, then as designers of risk communication we have to -- we can do two things, right? We can blame adolescents and say, "They never listen to us, and they don't -- they don't know how to use our information." Or we can say, "Maybe we didn't provide them with the information that they need."

And just in case you want to read

more about these topics, I have provided a list of references with -- that talk about the different results that are provided in my talk.

Thank you.

(Applause.)

MR. DENNISTON: Good afternoon. I'd like to begin by thanking the previous speakers for their great insights in this issue, in particular Dr. Steinberg's comments I thought were very thoughtful. In fact, it brings to mind a meta-analysis by Robin Room on the research on prevention of tobacco, alcohol, and illicit drugs. And he said, "Popular programs are ineffective; ineffective programs are popular."

And I think when you take a look at the fact that education -- public education is wildly popular, it is not always as effective as we'd like. We need to assume that as sort of a necessary but insufficient factor for the kind of behavior change we'd like to see.

I have been invited here this

afternoon to talk about OTC relevant lessons from the anti-drug campaign, and I'd like to cover, really, three parts. First of all, an overview of social marketing approaches. I was asked specifically to touch on social marketing, what it is, and what we've learned from it; second, talk about some relevant lessons learned from our campaign, a large-scale media campaign designed to prevent or reduce teen drug use; and then, third, identify several OTC-related issues from our environmental scan for your consideration -- in particular, the role of news media coverage of the issue, web content, and parental role and responsibility.

Social marketing, which has been around for about 30 years now, is really an upshot of commercial marketing, and Philip Kotler from Northwestern University, and a number of others, including Allen Andreason from whom this quote is lifted from his most recent book, have worked very hard in this area

to find ways that we can reduce social problems through the application of commercial marketing approaches.

And this is really an analysis and planning discipline, which has been practiced in a variety of areas including here at NIH on the areas such as smoking prevention, breast cancer awareness, and early detection, and a lot of different public policy areas, high blood pressure among them.

One of the great advantages of this is we have from commercial marketing a great amount of experience, great amount of best practices, that we can learn from. And we have found over the years that the commercial application of marketing practices, he derives for us a great deal of wisdom about how to approach particular audiences, really focusing on audience segmentation, consumer analysis, and analysis of the exchange as well.

The four P's of commercial marketing have been put into social marketing

areas as well using product, price, place, and promotion as sort of a framework. It's a little bit of a translation problem sometimes. For example, the price is not $1.99, but the price might be inconvenience of adopting the behavior we like to see, or social disapproval for not using drugs or alcohol at a party.

There is some controversy in this field, having to do with what some of us refer to as the fifth P, and that is policy, trying to move upstream to influence public policy, which then influences downstream individual behavior change.

For example, rather than just relying on individuals to change their behavior having to do with diet and exercise, why not try to influence school principals to change the array of product mix they have in vending machines? Why not try to influence elected officials to increase the amount of parks and playgrounds for teens rather than relying on teens to make that individual level of behavior

change themselves?

This is one of the areas of controversy, particularly when applying a policy lens to the other four P's. For example, what should be our policy on products availability? What should be the policy on price? To Dr. Steinberg's point, if we increase the excise taxes on tobacco, we know use by adolescents will go down.

Likewise, if we have graduated licensing programs, they tend to reduce teen traffic crashes. And minimum 21 for alcohol has been very effective in reducing underage alcohol problems, including drunk driving crashes. So if we apply that policy lens to product, price, place, and promotion, we can really take advantage of both downstream and upstream approaches.

The National Youth Anti-Drug Media Campaign has been underway for about eight years now, established by Congress, designed to prevent and reduce teen drug use. We've had

broad bipartisan support over the years, and unlike most public service campaigns this is a paid campaign. That is, we have sufficient funds to buy media time and space.

In fact, this year the budget is about $100 million, the smallest level since the beginning of the campaign. That is matched 100 percent by media time and space outlets. So, for example, it is basically by one ad and get one free for all of our media outlets.

What that means practically is we have huge levels of media exposure. Right now, for example, we're reaching about 75 percent of teens about three and a half times a week, which is a very heavy level of media exposure. Further, we are able to pinpoint to target that media exposure to the kinds of teens who are most likely to use drugs and the kinds of programs where they are more likely to see the ads and believe the ads.

The Partnership for a Drug-Free America, a 501(c)(3) group, under our direction

creates most of the advertising. We have a strong multicultural audience focus, not because they are particularly at higher risk, but rather today's teens -- particularly African-American and Hispanic teens -- tend to be trendsetters.

Further, African-American teens in particular tend to over-index on media exposure at about 140 level. And we have lots of evaluation, particularly formative process, and I'll talk about some of those steps this afternoon.

We not only use social marketing discipline, but also the theory of reasoned action, social science research, to help drive our campaign, to inform the campaign steps. We all know that nothing is so practical as a good theory.

It's very important for us to take a look at the downturn in teen drug use over the last five years. Basically -- and this is something few people are aware of -- we have

had a 23 percent decline in teen drug use over the last five years. Going back 30 years from monitoring the future research, we know two things tend to drive youth use of drugs, particularly marijuana. One is perception of risk; the other is social disapproval.

When we unpack risk, we can break it down in different forms of risk, whether it's health risk, social risk, academic risk, financial risk. So a campaign, because we have large scale, can help influence the understanding of the risk of drug use, and so that basically is what the campaign is about -- to increase risk -- the understanding of risk, use, and disapproval as well.

So when we look at what role mass media can play, we do believe that in fact the media can play a powerful role here if done correctly. First is confer status on the issues and ideas. That's very important -- to make the issue worthy of dinnertime discussion. If you're off the tube, people have said,

"You're dead," and that's not You Tube, it's the TV tube. At least it used to be the TV tube. I'm not so sure anymore.

Also, refuting myths and counter pro-drug messages. As I'll illustrate in a minute, there is a lot of pro-drug information available through a lot of different channels that youth attend to. So we want to be able to refute those messages, those pro-drug use messages, in a consistent and clear and credible way.

The campaign basically, by using work on the news area to help influence news coverage, advertising -- about 75 percent of our funds are used to buy media time and space -- and also working with the entertainment industry to have influence there to help make sure that messages in the entertainment media on drugs are accurate and up to date.

So between those components, and on the right reach and frequency and saliency, we influence families -- that is, teens and their

parents. We believe this tends to act as an umbrella. That is, it informs not only the families, but it also tends to support those other anti-drug efforts going on in the community, be it schools, the business community, policymakers, the faith community, many other components of society. In a way, it serves as an umbrella message, makes the issue worthy of public discussion.

Now, because we spend 75 percent of our money on time and space, it's important to make sure that our messages, before they go out there, before we spend a nickel of taxpayer's money to buy time and space, are going to be effective. And so we go through a multi-stage process involving both qualitative and quantitative measures to make sure before the ads are aired we have tested them in laboratory and in as a real-world situation as much as possible.

Then, once they are out there, we test in the marketplace through ongoing surveys

to make sure the ads are effective, kids get the message, there is no counterproductive results. We do use on the qualitative research side a lot of consumer insights from organizations such as TRU, Teenage Research Unlimited, MTV Research. We contract with them to provide information to help us keep our finger on the pulse of teenagers around the country.

We look at the national surveys, national survey on drug use and health, many other surveys. Then, we have the creative development of a campaign from a brief that outlines in a nutshell what we're about, what we want to do. We go through our formative evaluation steps, focus groups, and places around the country. We have an outside expert group of people from behavioral research, mass media, telecommunications, et cetera.

We then do quantitative copy testing. We may start off with a dozen different ideas. Through quality research we

boil them down to three, we produce those, then we go to quantitative copy testing to make sure that it will be effective in a quantitative phase before we put them on the air.

Then, once they're on the air, we interview about 150 teens each and every week, 52 weeks a year, to monitor how they perform in the marketplace of ideas. Then, that information is fed back to start the loop all over again.

Campaign evaluations at many different levels, in particular copy testing and market tracking are very important. So we keep our finger on the pulse. We can change out the copy to the ads within a couple of weeks if we really need to.

Now, a couple of lessons learned from this, and I'll try to encapsulate a lot of these and make them as OTC relevant as possible. First is to really understand the challenges, particularly from media and social environments what's going on in the landscape,

the social landscape of teens, look at behavioral issues -- in particular, such as normative effects of advertising. Know the audience -- teens are very sensitive to this topic of drug use, and adult agendas if you will.

We also have to be aware that there's a lot of sensitivity by teens generally, but when it comes to something that -- for example, such as marijuana, which really stands to many youth as a sense of rebellion or growing up or maturing or getting outside the influence of your immediate parents, we're messing with that, they have a problem often.

And also, we want to invest in research, both formative and process research, and performance tracking to make sure the effort is going to be effective. Some of the challenges on this campaign -- and it may be true in other areas as well -- conflicted role. Many parents today want to be their teen's friend, not necessarily a real parent.

And that becomes a problem, often with denial. "My kid would never do that," or "Marijuana? Gee, I used that in high school or college, wouldn't I be a hypocrite if I talked to my teen, because they'll see through me. What do I say if my teenager asks me." So it's much easier not to have the conversation.

With teens, again, it's a sensitive topic, simple rebellion, particularly marijuana. The perception of norms is that virtually everybody is using. It's not true. Isn't true now, as it was five years ago. Nevertheless, because many teens want to fit in, they do things they think will help them fit in. If they overestimate the proportion of their peers who they think are using, they are more likely to use to fit in.

Also, we have some evidence that prescription and OTC drugs are seen as safer to street drugs. They may or may not be, but that misinformation can be harmful. We see rapid changes in media technology.

An example of the rapid changes is this: teens today are master multi-takers. Typically, a teenager will spend 93 hours a week with media. The only way to do that is be watching the TV, talking to somebody on the cell phone, perhaps doing an e-mail or something like this. In fact, teens today spend so much time before computer screens, TV screens, phone screens, some people would say call them “screenagers,” not teenagers -- 93 hours is a lot.

So we're competing in many ways with iPods, which Pepsi, with many other ways to get information across to teens. So it's a very competitive environment in many ways.

We also see from teens themselves they report a disproportionate amount of pro-drug messages. From our analysis, both talking to teens specifically and then monitoring the blogosphere, if you will, we're seeing about a two to one or three to one ratio of pro-drug messages versus anti-drug message in their

social and media environment. Everything from cell phones to websites to T-shirts. Just a lot of pro-drug information, perhaps leading to the belief that drug use in fact is normative.

How to pass a drug test in a fraction of a second, you get 26 million hits, many of them promoting products and processes to defeat legitimate drug testing. Let's face it, teens are -- this is their first language, working the Internet and Web 2.0, the rest of us are like immigrants who don't quite understand the language.

They are very smart about this, particularly with Web 2.0. It's very easy to find out this information, and a lot of it of course is totally, totally bogus.

Even USA Today has been covering this issue of teens IM'ing, finding out who has the best drugs, how to balance the use of alcohol and, say, Percocet in a party situation. There is a lot of conversation in here.

Our concern is -- our concern is that in fact the vital approach here might make the relatively rare event appear normative, because teens spend so much time on the Internet that parents might be -- that in fact a rare event, relatively rare event such as using Oxycontin or Percocet or Adderall, through its dissemination on the web, might in fact lead teens to believe, hey, everybody is doing it, everybody is doing it frequently, everybody is doing it with no negative consequences.

We also see a lot of pro-drug information pushing back against many anti-drug efforts, including your own campaign. It's very easy to mock or to parody anti-drug messages. Here is one -- this is lifted from one of our campaigns done by Wieden and Kennedy, the firm out in Portland, Oregon, that does the Nike ads.

It's funny because guns are perfectly legal, yet they kill almost as many

people as car accidents. There has never been one recorded death from chronic long-term marijuana use. Look it up. I wish people knew the truth.

Every Friday at 6:00 I get the week's dump of e-mail messages and tracking of this, and it's overwhelmingly pro-drug. Now, whether this is coming from teens or coming from adults or coming from organized groups, it's hard for us to tell, because we can't go back and track that. Yet we know, again, this contributes to a lot of pro-drug information on the web, and perhaps a perception that drug use is normative and it's okay.

Now, I want to walk you through a change in our campaign from a couple of years ago. We had for several years the anti-drug campaign. What's your anti-drug? as the brand. And we began to look at teens from a different perspective, learning that kids are changing these days.

Kids today are more likely to have

friends of a different gender, different ethnicity, different religious background, different socioeconomic background. There's more pressure on teens today to perform, and also teens today are less likely to take a firm, clear stand against drug use. It's not quite like they're going to adopt the anti-drug as their personal brand.

So we decided we need to reinvent the campaign, we need to conduct quite a bit of research. And this underscores the kind of research we conduct. It took basically 11 months for us to research this notion of what we're now calling Above the Influence, five phases essentially beginning with some teen insights, reactions to the idea of "above the influence" as opposed to "under the influence."

And this goes to qualitative research, basically ethnographic research, in a number of different markets around the country often involving friendship groups, to Phase 2 validation of the brand, the "Above the

Influence" direction, and going, again, back out to friendship groups. And this is qualitative, but also it is very, very important to our learning.

And a quick anecdote. In Miami, we were doing the friendship groups. We had four boys, tenth graders -- that's our weak spot, that's our target audience -- who began to talk about their personal use of drugs. It was kind of war stories. And we were just about to call it off, because this was not being very useful to us, until the moderator said two words which turned it around.

She said, "Any regrets? Any regrets?" And one of the boys said so quick, he said, "Absolutely." He said, "You know, I'm trying to stay clean and sober. I've tried to quit. Every time we go to party, you guys try to get me to use." He said, "If I use after school like you want, I go to work. If I lose -- if I show up stoned, I will lose my job. If I lose the job, I lose the paycheck. If I lose

the paycheck, I lose the car. If I lose the car, I lose the girl." Right there in a nutshell, he quickly articulated why he didn't want to use. He saw negative consequences, basically social consequences, and financial consequences, to use.

So that helped us understand the audience a little bit better, helped us understand how to craft messages that will be responsive to that belief by young people that just because you used once -- in many ways it's like the national campaign to prevent teen pregnancy. Just because you did it once doesn't mean you have to keep on doing it. Just because you used marijuana once doesn't mean you have to keep on doing it.

The other two phases, optimizing the ad concept -- they're going to quantitative copy testing, 3,600 teens went through the tests to identify what ads are going to be the most effective. And here again we found that a lot of the social consequences, rather than the

health consequences, were big drivers, particularly putting others at risk, letting others down, disappointing your parents, and disappointing your own particular aspirations.

And from that, we do ad tracking to make sure it works in the marketplace. And because with a budget this large we have to keep feeding the beast with new advertising, it helps our new creative advertising testing.

Learned a lot of things about high school being a pool of pressures, a lot of anxiety about performance, athletic, social, academic, getting into good colleges, more pressures today with more severe consequences. Learned about the peer pressure and the teen dreams. How do you strike the balance? And it goes back to some of the comments before.

Kids understand some things, but still the social, emotional, psychosocial patterns lead them to succumb often to peer pressure. They may not think of it as peer pressure, or even peer influence, but we know

that's what happens.

Subliminal pressure, more passive than active, anything that seduces away from the right path, and most of it is related to partying, sex, and drugs, and those are the group activities. Those compromise the teen dreams which are often at this stage lofty and aspirational. Money, sports, college, career, marriage, and live up to the expectations of yourself and of others.

It also helped us to think more about the target audience. In many ways, this campaign is like a political campaign. Some people always vote one way, some people always another. What you want to do is address the malleable middle. Some teens will use no matter what. Some teens will never use no matter what. How can we influence those, looking at the conflicting forces to influence those we can make a difference with, understanding there are reasons to try and there are reasons not to try.

This really helped us understand better the target audience and how we can reach those teens who have not tried.

Now, I'm going to show two ads, and I think the first one is here.

(Video presentation begins.)

FEMALE VOICE: When you give up the ability to decide for yourself, you give up what makes you you.

(Video presentation ends.)

MR. DENNISTON: This ad was created to help establish the brand early on.

(Video presentation begins.)

MALE VOICE: I smoked weed and nobody died. I didn't get into a car accident. I didn't OD on heroin the next day. Nothing happened. We sat on Pete's couch for 11 hours. Know what's going to happen on Pete's couch? Nothing. You have a better shot of dying out there in the real word, driving hard to the rim, ice skating with a girl.

Now, you want to keep yourself

alive, you go over to Pete's, sit on his couch until you're 86. Safest thing in the world.

MALE VOICE: Me? I'll take my chances out there. Call me reckless.

(Video presentation ends.)

MR. DENNISTON: So in many ways this is a risky ad, because, one, it says if you smoke marijuana nothing necessarily bad is going to happen. Second, you've got two out of three teens on Pete's couch having smoked. And the negative consequences of that are not readily apparent, not in the same way.

Our belief is we can't go all negative all the time. We have to talk about aspirations. So by way of examples of negative feedback, here's a few. I decide for myself. I want to know the risk of what will actually happen to me. I do not want to be told, if you do this, then you are uncool, et cetera.

So this is a kind of negative influence -- excuse me, negative feedback we get on the ads each and every week. This one

in particular -- Pete's couch.

Positive as well. "I just wanted to say that your ad, specifically the couch one and the one with the narrator driving the car, are excellent. They are unbiased, effective, and entertaining -- three essential things that are rarely accomplished in the past."

Well, this is really nice. We love to see the positive feedback. On the other hand, we need to quantitatively test these, so this is an ad that was tested very carefully with 300 teens to make sure before it went out, before it went on the air, we tested it to make sure it gets the essential message across by way of comprehension.

It doesn't unintentionally create the fact that two out of three teens are using marijuana or that in fact you can use marijuana and the worst thing that can happen to you is you waste your afternoon on Pete's couch. And we tested that, and we got very good scores. In fact, in the last 26 ads, they were tested

and we keep benchmark scores. Pete's couch ranked sixth in terms of overall effectiveness, so that's the kind of quantitative testing we want to make sure we do.

We also do a lot of different reviews. For example, NIDA reviews the scientific claims before the ads get very far. We go through the testing process, rigorous scientific and audience-based screening process, then monthly surveys. We have a campaign advisory team, as I mentioned before, experts, behavioral researchers, to give us insights all the way through the campaign.

And then, by way of copy testing protocol, here is in a snapshot what we do -- ad expose versus control group, and split sample between younger teens 14 to 16, our sweet spot, and younger teens. We do that in part because there has been some claim that through meta-messaging younger teens aren't really thinking about drugs. They see anti-drug ads. They're saying, "Ah, drugs must be

really important to teenagers because I'm seeing a lot of anti-drug ads."

To some degree, they are claims of reactance and meta-messaging, so we make sure we test for those to make sure that's not happening. And, frankly, we've dumped a lot of ads or revised a lot of ads because the round of testing didn't reveal what we thought was important.

Some of our print ads as well -- we do testing, we certainly do smog testing, that is rehability testing. This particular ad, which we launched last spring, in major consumer magazines -- People, U.S. News, Time Magazine -- this is where your teen goes to get high. In fact, this was endorsed by NIDA, SAMHSA, and FDA.

We test these with parents to make sure they're going to be effective, people understand them. This is a test from another group. We found it's very important for us to include partners there, such as FDA, such as

the American Academy of Pediatrics, for credibility purposes. We want to make sure people understand this is not just the Drug Czar telling you these things. These public health organizations stand shoulder to shoulder consistent with this message.

And likewise, particularly where there's new information -- for example, a link between marijuana and mental health -- we make sure to include scientific footnotes, because this enhances the credibility. Credibility, particularly on the drug issue, is very important.

Youth-tracking protocol, 52 weeks a year. Here, for example, is our data through last May in one of about 19 different metrics. This is awareness of the logo, strong growth since we began. The orange line on the left is when we launched the campaign, and you can see gradually after -- through May we're at 81 percent, which is higher even than the Truth Campaign, a very popular campaign among teens.

We also track for attitudes, for intention to use, and a variety of other areas.

Now, let me turn to prescription and, in particular, over-the-counter drugs. You're probably all aware from NSDUH, from monitoring the future, that the only category of drugs that is actually going up among teens and young adults is prescription drugs, particularly painkillers and products such as Adderall.

And this is an area where we've been doing some research now, because we are intending to launch a campaign aimed at parents, sometime early spring. We have been doing research for about six or eight months on that now. It's a big concern.

So in terms of media coverage, there has been quite a bit of media coverage of this. We do content analyses from time to time to better inform ourselves about what is the public hearing. For example, before we launched the marijuana campaign, we did a

content analysis and found out for a year's media coverage only about seven percent of all of the articles talked about the negative consequences of marijuana use on adolescents.

We did a content analysis of methamphetamine. We found after a year's worth of coverage that only three percent of all of their articles touched on treatment for meth addiction. No wonder the public tends to believe that meth is so addictive it can't even be treated. That's a big myth. Treatment for meth addiction is about the same results as for other stimulants such as cocaine.

So there has been quite a bit of coverage of this, including my boss, the Drug Czar, that their drug dealer is us. When we look at the kind of coverage we see, here is the frequency of drug-specific references we -- we did this kind of analysis. The sampling was 308 articles over the last year. You can see what gets the most coverage, including DXM cough syrup, Robitussin, Tylenol, and some

other over-the-counter available products -- Vicks Formula 44. Give us an idea of what the public is hearing about this.

In addition to that, what is the key message? Clearly, harms and dangers, use is rising, motivations to use to get high, and monitoring -- the importance of monitoring access and availability to these products is getting a lot of news media coverage. As you can see, a lot of this has to do with OTCs.

Sources cited for these products -- home in a medicine cabinet. We know from the NSDUH survey, out of those who use, 70 percent get the -- say they get these products -- prescription products from family or friends for free. So there's a way we think to interrupt the social sources of these products. And so we're trying to increase the news coverage to cover that part of the business.

Terminology -- do we call it abuse, misuse, use? I examined a Department of Education publication not long ago about the

so-called recreational use of Adderall on college campuses. On one page, it was referred to in five different ways -- recreational use, misuse, use, illegal use, and abuse. Sometimes within this field, we just don't talk to ourselves enough, so we can explain it to ourselves, much less explain it to the public. So the terminology challenges here are significant.

Now, in terms of beyond media coverage to web coverage, this is something obviously we are concerned about in terms of street drugs or illicit drugs. When it comes to prescription drugs, and over-the-counter drugs, there is clearly a lot of misinformation out there as well. You can just search on the terms -- teens are searching all the time -- and find out a lot of information.

And, of course, this is the generation of Web 2.0 user-generated content. So it's not hard for any of us to go out there and find out what are the pro-drug messages,

what are the pro-use messages, on the web. A couple of examples here from You Tube, getting drunk off cough syrup. Literally hundreds and hundreds of these video vignettes. Kids are very adept at doing this.

Normalization -- again, this might go to the issue of normalizing. It appears to be that kids can use this stuff, everybody is using it, and what -- there are no negative consequences. You don't need to go to a CVS or drug store to buy DXM. Try a shopping store. I doubt a cashier would take time to card you.

Moving that conversation forward, or backward, what DXM items can a person under 18 buy without getting carded? I haven't been carded yet at CVS. You can get Robitussin cough gels, 50 milligrams, in bottles of 20, et cetera, et cetera.

So there is a whole network out there of not only the so-called benefits of using these products to get high, but how to get them. What are the batches? What's the

mix? What's the right dosage?

User-generated video content -- teens are sharing video clubs depicting their personal encounters with OTC drugs.

Some of these things I have no idea what they are. You probably do. But it's a concern, because it tends, we think, to normalize the perception that it's an okay thing to do.

In fact, some of the websites -- Erowid I think is a particular bad one -- here, for example, in terms of monitoring use, the chart below shows approximate recreational dosages for pure DXM measured in milligrams. So, in other words, there's a lot of information about how to mix, what's the dosage. If you go to a party, how many beers can you have before the Adderall or the Percocet, or what other product, and you'll still be okay? So this has got to be of some concern to us.

Now, when we take a look at from

surveys -- and this is from the Partnership for a Drug-Free America, Teen Partnership Survey, they tend to believe these are safer. After all, they are manufactured by professionals, prescribed by a doctor. You know what you're getting. It's in that bottle. It may not be the same as the marijuana you buy or the other illicit street drugs you buy.

Teens believe there is nothing wrong with using prescription drugs without a prescription. Twenty-nine percent believe painkillers are not addictive.

And when we take a look at what parents are doing about this, are parents aware of it? Teens today tell us their parents are pretty much clueless about drugs and about technology.

Now, here is what parents are saying -- a portion of parents are reporting they talked about drugs a lot, drugs in general, alcohol, cigarettes, and marijuana. We're talking in the high sixties, the low

seventies. When it comes to prescription medicine, not prescribed by a doctor, used to get high, we're talking about the mid-thirties. Non-prescription cold or cough medicine used to get high, the low thirties. And the trend is heading in the wrong direction.

So notwithstanding what teens are receiving, they are not getting much information from parents about the negative consequences, about the risks of these products, and that has got to be a concern.

Now, there are some websites. We've got our content on these products on the "Parents: The Anti-Drug" website we put out about a lot of these different products. Partnership for a Drug-Free America also has one, what every parent needs to know about cough medicine abuse.

The problem here is we have relatively small scale. Even though we think the numbers are pretty good -- about a million user sessions a month on our parent's website -

- in the aggregate that's not very much. So I think those three particular issues, what's the media coverage, how is it influencing people's understanding of the OTC issue; second, what is the web content that teens are accessing far more clearly than parents; and, third, what are parents doing about this to inform their teens.

Some people say, a lot of parents say, you know, I feel hopeless, helpless, because of the pop culture and the promotion of all of these products. Can parents do anything? And yet the research from NSDUH, from many other surveys, suggests that the single most powerful voice in the life of teens about drugs is parents. To disapprove of drug use clearly, consistently, credibly is very, very important.

Let me leave you with a cartoon as others have, because I think it typifies, one, a lot of interest and awareness of the benefits of different medications and prescription over-the-counter, but also the fact that people shop

for drug effects. Teens shop for drug effects, and apparently adults do, too.

For pre-holiday depression, you'd want something a little milder than what you'd take for post-holiday depression. So since we're in the holiday session -- season -- and this is from The Wall Street Journal this last week -- I thought I would leave you with that cartoon.

Thank you.

(Applause.)

DR. CUMMINS: I'd like to thank all our panelists for their presentations and ask them if they could please come up to the podium for some discussion.

Bill?

DR. RODRIGUEZ: I have two questions for Dr. Steinberg. I really enjoyed everybody's conferences. I had some questions when information had been presented in terms of the risk-taking while being observed by friends or peers. Any difference between the males and

females, or do they both fall in – both in the same category?

DR. STEINBERG: The effect is there for both males and females. Now, we haven't experimented with having male subjects bring female friends and female subjects bring male friends. All of our experiments so far had same sex friends, but we see the effect for both boys and girls.

DR. RODRIGUEZ: Okay. Comparable effect.

DR. STEINBERG: I don't know if it was comparable, but there wasn't a statistically significant difference between the size of the effects.

DR. RODRIGUEZ: That's number one. Number two, it's probably a little bit more of a wish from my side, but when I saw your image and demonstration of a simulation of emotional aspect versus the cognitive type aspect, I wonder whether you had any followup on those same participants as they develop or grow to

see the maturity in the brain of those participants, which in a sense may not be necessary but it would probably confirm the maturity process that you are describing so beautifully.

DR. STEINBERG: Well, in the study design that we're doing -- this was pilot work we did -- the study design calls for putting adolescents and adults in the same situation. So we'll be able to compare the patterns of brain activity in adolescents with and without peer exposure with the patterns of brain activity, in adults with and without peer exposure.

So ideally, we'd like to follow people over time, but we're starting with a cross-sectional design.

DR. RODRIGUEZ: Thank you.

DR. CUMMINS: Heinz?

DR. SCHNEIDER: Thank you. Heinz Schneider, Consumer Healthcare Association. I have also a question to Dr. Steinberg. Isn't

it conceivable that reaction to peer pressure is highly dependable on the nature of peer pressure?

And I was thinking about your car simulation test, the male teenager car simulation test. The peers in the next room is the Redskins Fan Club bank versus male teenager. The peers in the next room is the club of the gorgeous girls of the club fast drivers are damn idiots. I drive like Grandma Moses.

DR. STEINBERG: Well, I mean, you're absolutely right. I think that peer pressure gets more of a negative -- universally negative rap than it deserves, because obviously the nature of peer pressure depends on who those peers are.

However, remember that in the design of the experiment we are asking individuals to bring two friends with them to the lab, and so assume that we're getting some random distribution -- well, not perfectly

random, but we're getting some distribution, some kids you would expect would just by virtue of chance come to the lab with friends that wouldn't encourage them to take risks and others would.

And we're seeing a very robust effect in several different samples using several different designs. So I don't know exactly how to explain it, but it -- I think that we -- well, let me just stop there.

MS. SHAY: Yes. Hi, Dr. Steinberg. One more question for you. That large survey that was multi-centered, the age span starting I believe it was 10 -- 10, 11. Did you have to frame -- were the questions framed different for the younger age group? Or was it the same questionnaire for the survey all the way through the older age group?

DR. STEINBERG: It was the same questionnaire. We did a lot of pilot work beforehand, and we do a lot of very careful item analysis after the data are collected.

And we will throw out items that don't seem to be working in one age group or another.

One example, for instance, is that on our risk-taking measure, drinking alcohol was an item that was on there as a risky activity. And we found that a number of kids rated it as a highly risky activity, but people who were 18 and older didn't rate it as a highly risky activity, because, you know, if not a legal drinking age, if close to a legal drinking ago, and so we ended up taking that out of the risk index because it didn't behave in the same way for the different age groups.

So in the end, in terms of the analysis I presented, all of those measures are identical across the different age groups.

DR. CUMMINS: Could you just say your name and where you're from for the record? Thanks.

DR. MATHIS: Lisa Mathis. I'm with the Food and Drug Administration. And this is a question for all of the panelists. We heard

earlier today how Dr. Brass described the studies that are done for over-the-counter drugs -- labeling comprehension, self-selection, actual use.

And then, as I listened to your talks, across the board I really heard that you divided up the adolescent age group sometimes pre-adolescents, adolescents, and looking at a lot of the developmental curves and the studies that are done. You definitely see differences across the age ranges.

And I'm just curious about how all of you would apply this knowledge of differences in the continuum of adolescents to some of those studies that Dr. Brass described, and also if you could give your opinion about whether or not you think those drug -- those studies would actually get to whether or not adolescents can safely use over-the-counter drugs and how we can better communicate to them.

And I can't for you all to get

together with Panel 3 tomorrow, too, because we have a lot of communication experts, and the roundtable is going to be fabulous. But for now, we'll let you answer today's question.

DR. STEINBERG: Okay.

(Laughter.)

I think that where you would draw boundaries -- let me say that I agree with the basic premise of your question, which is that this wide age range that we call adolescence is composed of people -- of subgroups of people of different ages who are not identical in their skills and in their motives and in their knowledge.

I think as a rough guideline in most of our studies kids who are, you know, 15 and younger look different than kids who are 16 and older. And I think that that's consistent with some of the data I presented on intellectual ability, which shows that by 16, you know, kids have a lot of the same intellectual capacities as adults do.

I think -- but yet I think that there is a group of people who are, let's say, from 16 to 21 who themselves are different from people who are in their twenties. So I don't think that we should -- I think we should treat them as somewhere midway between.

It's hard for me to answer your question about, you know, what policies or practices we might engage in to monitor or limit kids' use of over-the-counter medicines. I clearly think that based on our work that a 16 year-old probably comprehends labeling in a way that's not appreciably different from an adult.

So in terms of wording and things like that, you know, obviously there is a lot of individual variability among adults in their intelligence and in their vocabulary, but I think that probably that individual variability among adults and among adolescents is more striking than the age differences once you're talking people 16 and older. Below 16, I think

they probably would require some different kinds of explanations.

You know, I mean, you know my bias on this. I mean, I think that the way to approach this is through better regulation, and I think that labeling is important. But I don't think it's going to -- it's really going to solve the problem by itself.

DR. HUSZTI: I would agree with everything you said, and I guess the other point I'd make is I think it's such a complicated issue for teens in terms of, you know, what they're going to use when and what information they're abstracting when.

And when you think about a -- I mean, when I sort of think about the label, it's like oh, my gosh, I mean, there's not much space there to really change behavior in someone, particularly the younger adolescents, whose, you know, cognitive capabilities and the ability to sort of like stop yourself from doing something aren't so well developed.

And, you know, I certainly -- I will just say from the clinical realm, I will agree with you as well. You know, the impulsivity that happens among these teens where it's just like, oh, yes, this happened, and so I just -- you know, I took this or I, you know, went and did this, and there's not a lot of rational explanation for it.

So, again, when I think about the label, it's kind of like, not so sure what we can do to change that.

MR. DENNISTON: Yes, I could add -- I mean, I don't think anybody would think that a label is a brake, to use your analogy. We actually shifted our target age up. It was tweens before, but we found in the aggregate there are a couple of problems with that.

One, the potential for agenda-setting -- that is, the media don't tell people what to think or whether to think about -- and if you expose younger teens who haven't been thinking about drugs to drug-rated messages,

you might put in on their agendas.

Second, we wanted to get teens more closely linked to the year of decision, to the point of decision, not only by way of age but also by media outlets and time of day -- for example, the more dangerous hours after school.

Third, we got a lot of pushback, frankly, from parents who said, "Sitting in my living room watching TV, and all of a sudden one of your nasty anti-drug messages came on. My kids didn't know a thing about drugs until now. You're educating kids unwittingly."

So there are a variety of factors, but I think based on the science we decided to delay -- or push it back to the tenth grade being our sweet spot.

DR. BRUINE DE BRUIN: First of all, I just want to agree with everybody, just let you know that I agree. But speaking of the label, and how small it is, I am also very concerned that just by putting information on a label that you may not be able to change

behavior. And I wonder whether that is even true in adults, and whether there have been studies conducted on that.

Because just based on what I know about the developing effect of risk messages, I would say -- I would predict that it doesn't change behavior. But, I mean, that's I guess a question for the audience or the other members of the panel.

DR. BRASS: Well, I'll answer that before I ask my question.

(Laughter.)

Because I think there are data that are at least strongly suggestive that in adult typical consumers that how -- how and what you communicate on the label will affect behavior in a trial situation. As I talked about this morning, how we extend that to the real-world marketplace, but clearly changing the message changes the behavior even within the context of a trial.

So I would not be overly

pessimistic in an absolute sense, and I would further point out, as I tried to salvage this morning, that we can't afford to be pessimistic, because without the label to guide behavior we are left with nothing. And that it is the tool we need to look at.

So, in fact, my questions are to follow up this theme in a little bit more focused way, because you've set this up nicely. And my concern is for the moment to put aside the question of abuse, but optimizing proper use when there's a therapeutic intent, because we have heard that adolescents are appropriate OTC users, and that whatever the relative role -- and we haven't heard definitive data on this either -- of judgment versus knowledge gaps and misconceptions.

There is at least a sense that there may be misconceptions about the relative safety and risk of OTC drugs. So I would be very specific in asking, based on your experience in risk communication, are there

approaches to succinct messaging for adolescents that are more or less likely to penetrate the white noise and register at some level that is perhaps different than in other populations.

DR. CUMMINS: Is someone trying?

DR. HUSZTI: I'll try a little bit. You know, I think one of the things, just thinking about health concepts, I think adolescents -- do have a different view of health I think than adults do. I think adults have a sort of more preventative, goal-driven kind of definition often. And I think adolescents may be a little less -- younger adolescents.

And so I think maybe better understanding, as Dr. Bruine de Bruin talked about, better understanding sort of what are the pieces that they are putting into their decision-making, would help guide them what kinds of changes on the label might be helpful in changing the behavior.

I'm a little uncomfortable with the data that is there right now maybe saying, "Well, I think this would work," or "I think that would work," because I'm not sure we know.

DR. BRASS: I mean, maybe just globally, how we communicate risk to affect behavior, I mean, there's a whole literature on what you put on a ladder to prevent people from going to the top step, and how you word that warning changes the likelihood of it being heeded.

So, and maybe the answer there isn't anything that we know about how to risk communicate. But if there was anything, I think it would be very helpful for this audience to hear, to have some sense of what's effective and what's ineffective in succinct messaging.

DR. BRUINE DE BRUIN: I think that in succinct messaging I think that we do know something about given -- given what the experts think people need to know, and given what we

can find out about what the audience needs to know, we can figure out through risk analysis which part of the message is most important and most likely to -- to resonate or to reduce risk.

And if you can't say everything, you need to say the thing that is most important to know. And that may depend on the audience, which may complicate your job, right, because how do you change the label so that even adolescents picks up a medication that has a different label than an adult.

So it would make it more complicated, and I don't know how you would address that. but I think it requires input from experts and from -- and knowledge from the -- about the target audience.

DR. STEINBERG: Let me say just a couple of things based on what we know about adolescent cognitive development, what I think would be thematically important. The first is to be as specific as possible and as concrete

as possible. So I think that phrases like "as needed" are going to be more confusing for a kid than for an adult.

I think to phrase things in terms of what -- in terms of this is the dose that will give you the maximum benefit, that is taking advantage of the fact that we know that kids are more reward-focused than punishment-focused, and so to get them to understand in some kind of language that two pills is the optimum dose to reduce your headache, not three and not one, so I think, again, the specificity and the focus on what -- how can you get out of this product what the manufacturer intends you to get out of it.

And then, you know, I think just, then, as explicit as -- and succinct as possible, because we know that kids -- they don't like to read, so I think that, you know, the fewer words probably the better off you are. But I'm glad that you made another point.

I think it really seems to me like

there is two separate discussions going on here, and I think we shouldn't conflate them. One discussion is for kids that are seeking to use over-the-counter medications for their proper and intended usage, how do we market and package, you know, those products so that kids don't accidentally misuse them? And that includes underuse -- you know, underdose if in fact that's a problem.

And then, the second is how do we protect against kids deliberately and knowingly, you know, abusing those drugs? Because no label -- I mean, if the label says, you know, take two, and I want to abuse it, well, I'm going to know that two is not enough to abuse it. So, you know, I think they are just two completely different conversations, and they shouldn't really be on the same -- you know, on the same agenda in some ways.

MR. DENNISTON: Is the default position label and label only as opposed to a label plus reinforcement point of purchase, et

cetera? I mean, it seems to be that things work better when they're synchronized and there is multiple points of entry -- sorry. If the label only is the default position, why is that not supplemented by point of purchase advertising or other display to help make sure? Rather than have one bite at the apple, why not have two or three?

DR. CUMMINS: Well, I'd like to encourage you to think out of the box in that sense.

DR. MURPHY: Actually, Susan, that was my question -- is we've been talking about risk communication, only related to the label. And as you know, the agencies recently had a big discussion about behind the counter. And not going into all of those limitations, but what information do the people here have on the additional impact of if you're going to go purchase something, such as -- as we're talking about today, of having another source?

Because in everything I've heard

today I haven't heard anybody mention the pharmacist as a resource. And if you have any information in that area as to whether you think that would be something that would not be successful, you'd have to look at it to find out whether it would be successful, just where you -- what data you might have in that arena.

DR. BRUINE DE BRUIN: I guess it -- I guess the pharmacist would be the person that they interact with when they go and get over-the-counter medications, but I am a little concerned -- I think that maybe the pharmacist would need training in how to provide that information.

It's not that easy to be a good communicator, and I think that's one of the problems that we see with sexuality education, where high school teachers who are not trained to give that information have to give it, and they -- one thing that happens is they feel uncomfortable talking about that information, and they leave things out. And they leave

things out that are taboo topics that kids don't get information about, and they're not getting that information from the teacher either.

So pharmacists may not be able to do that, and may need training to be able to do that well. There might be other ways that we can give people information. I wonder -- well, I don't know if we're thinking out of the box -- if it's really -- if it's -- so it depends on what the problems are and what people are buying and how important it is to give them more information.

But, for example, if it's really important to -- that people really understand how to use it, or whatever, you could -- could you give them a license before they -- and do they have to pass a test before they can actually use it? Or if behavioral skills training is especially important in this context as well, could you teach them appropriate use by giving them some guided

experience before they go off in the world with the medication?

I mean, I don't know. Those are some things to consider. Maybe there are other things that the other panelists can suggest.

DR. HUSZTI: I mean, I do think one of the -- and, again, this is really outside of the box and may not be practical, but we're thinking outside the box. I mean, I think one of the things adolescents also like to do is they like to play with options and outcomes, and, you know, I think a lot of what you did with the DVD was great, because there is that sort of like, well, what happens if I do that? Well, what happens if I do -- and you feel that sense of control and that you are discovering something, which I think engages an adolescent a lot more than, okay, here's a talking head sort of talking at you. And, again, I know that's probably impractical for every piece of over-the-counter medication, but something -- I mean, if you -- as you're thinking outside of

the box, if there's something that sort of allows some teen-driven aspect of that, you know, maybe that helps that risk message come home a little more powerfully.

MR. SEIGEL: I don't think it would be that difficult to have a -- kind of a teenage-specific CBT actually at the pharmacy with a little post test before the kid walks out with the drug.

DR. HUSZTI: I mean, the down side is it's -- you know, there's costs involved in creating it. There's certainly costs involved in putting it together correctly and matching it with the right -- with the right thing. But, you know, again, thinking outside of the box can often kind of lead us somewhere where some of those, you know, down sides maybe aren't a part of it.

DR. STEINBERG: I don't know. The cashier at my local CVS can barely ring me up. I'm not sure --

(Laughter.)

-- if this person can deliver CBT, you know, on the spot. So I'm not sure this is happening.

MS. LEONARD-SEGAL: Andrea Leonard-Segal from the FDA. I have a couple of questions. I'm in the division that oversees the non-prescription products for everyone. And a few things -- a few questions come to my mind, because we deal with the nuts and bolts of this on a daily basis. We help sponsors design these trials, and we review the data that comes back in.

And one of the decisions that we always have to make when we see this kind of data, whether it's in children, adolescents, adults, is our tolerance for the risk versus benefit. And I'm curious -- in listening to the panel I sort of get this over -- this thought that maybe kids can't -- we can't trust kids to use over-the-counter drugs. Maybe you're thinking it's not something that's a good idea.

What I'm wondering is, what would your tolerance for error be in adolescents among a population that has a headache and is going in for an analgesic to treat the headache, or who has diarrhea and is going in for something to stop the diarrhea?

The population that's intending to use the product for the purpose intended who could derive benefit from it, who may understand the information on the label the way an adult would but may not have all of the perfect decision-making skills or the -- not that adult decision-making skills are perfect, they're not, but approaching that level, what is the tolerance, and how should we be thinking about this?

DR. STEINBERG: Well, I mean, I need to see some data on how big the problem is for different products. And I have no idea about, you know, how many accidental overdoses there are of particular products among people in this age. It may be such -- it may be

trivial in which case it's not something that we need to spend a lot of time worrying about. On the other hand, it may be more than we're willing to tolerate.

And, clearly, if you phrased your question in a different way, which is if a three year-old walked into a drug store and wanted to buy an anti-diarrheal medication, would we think it would be a good idea for the pharmacist to sell it? And I think most people would probably say no.

So, then, the question is: well, we agree that there is some age below which people shouldn't be able to buy these products on their own, and then we can have a discussion about what that age, you know, ought to be. In my mind, you know, somewhere around 15 or 16 feels pretty good -- feels, you know, reasonable enough to me.

I mean, we're willing to let people drive when they're 16, we certainly ought to be willing to let them take Tylenol when they're

16, so -- because driving is probably a lot riskier. But, again, I don't know how prevalent this is as a public health problem.

MS. LEONARD-SEGAL: Among the adverse events that we see across the board for over-the-counter products, we have not explored every single one in detail for adolescent signals. But in general, we are not seeing much that exceeds -- or anything, really, that exceeds what we're seeing in the adult population.

So, and that's across the board, and that's true for acetaminophen as well. As a matter of fact, if I'm remembering the acetaminophen curves -- and there are people in this audience that know them better than I do -- who have worked more closely with that product, they actually tend to peak in the middle years as I remember for the highest risk for liver failure.

And so it's -- we're not seeing these huge, huge problems, but implicit in any

over-the-counter drug or any drug, whether it's given by prescription, will be a risk. And the question is: what is the tolerance for it? Because that can help us to sort of figure out where we need to be going in this. That's one piece of it.

Another question I have for you -- and I thought all of your presentations were very, very interesting. This approach through a better regulation. Can you put some specifics on that that don't deal with things that we can't control? For example, we can't control the price of drugs that are over the counter. So we can't do it the way cigarettes are dealt with.

Right now, we have two venues. We've got prescription and over-the-counter marketing. We don't have behind-the-counter marketing. So if we go back to our offices tomorrow night after this is over, how can we make practical approaches to providing safe drug environments for adolescents in the short

term and in the long term?

DR. STEINBERG: Well, since I'm the one who advocated taking a regulatory approach on this, I'll give it a try. I mean, I don't understand the law here, and I don't understand why you couldn't have certain products requiring proof of age, you know, for purchase the way we do with cigarettes and other things. And you could take the most dangerous over-the-counter medications and require proof of purchase at the purchase point.

What those medications would be is really, you know, based on your data on adverse events. A second way to regulate kids is to make parents aware of the fact that these -- that just because these medications can be purchased without a prescription doesn't mean that they are completely safe.

And I think a lot of parents don't know that, and so if -- if you told me -- if I'm the parent of a 14 year-old or a 15 year-old and you told me that certain cough

medicines, you know, were being abused on a large scale, I might not keep it in the medicine chest, you know, in the hall bathroom. I mean, I might keep it in a place where only I have access to it, and I can dose my kid when my kid needs it.

So that's another way to promote regulation of kids' use of these products is through advertising to parents.

MS. LEONARD-SEGAL: I guess that one thing that I heard this morning also was that these -- the teenage population doesn't avail themselves of their parents' wisdom in the majority over these kinds of questions. I think I heard a 30 percent number given out this morning. So it seems a very complicated problem.

One other thing I'd like to ask is if we did label our products only down to the age of 18, and we've heard a discussion today about the fact that young people sometimes do things just because they're told not to do

them, do you think that our cutting off the labeling at a certain level would in fact decrease the use of products if there were not some enforcer at the door stopping somebody from purchasing a drug?

DR. STEINBERG: Well, I don't think there is a lot of evidence for the forbidden fruit, you know, model here. So I'm not sure I buy the premise, you know, that kids do things because -- deliberately because we tell them not to.

I think, you know, kids experiment with drugs because drugs feel good, and they find that out one way or the other way. And they don't -- you know, they don't do it because we tell them not to do it. They do it because we tell them to do it probably, but --

MR. DENNISTON: I think that's right. We've looked at some recent MTV research about the new generation of teens, and they are ever more reliant on parents for advice and counsel. So I think the parents'

strategies have got to be effective, and I don't believe there is any meaningful evidence of reactance. And what we do in a very provocative way and many times should incite reactance, but from our small scale and large scale surveys we're seeing hardly any evidence of that.

DR. HUSZTI: Can I just go back to your first question, just for a minute? Because I know probably listening to all of us that there is that moment of like, oh my God, what are we going to do about this for these kids?

This is a huge problem, and I think part of what we're also saying is just it's a different problem, and maybe to kind of think just a little bit that teens' minds and cognitions and the way they make decisions might be a little different from adults and might bear some differences in how you do the post-marketing testing. I think it's more that than like, oh my gosh, we've got, you know,

huge, huge problems.

And I just want to add one other thing about the parents. I think the issue is -- I think teens have -- teens rely on their parents more than sometimes the studies would suggest, I think. And I think part of the problem is a lot of times parents just won't bring up the topic a lot of times, because they don't know how, and they don't know what to say.

And I would think with over-the-counter medicines parents probably are pretty inclined to go, oh, you know, go get that, go get the aspirin out of the medicine cabinet if you have a headache, and there's not a discussion, you know, or there's not a discussion of, hey, you know, sometimes if you take too much that's not a good idea, you know.

But I think teens probably really do look to their parents for guidance a lot more. In fact, in that study that I was showing when we said, you know, dedicate a song

to the most influential person in your life, every single one of the teens dedicated it to their mothers.

DR. BRUINE DE BRUIN: Could I --

MR. DENNISTON: Just quickly, what evidence do we have that parents are good or not so good models for their teen's use? We think that there's something here about drugs and alcohol and tobacco, but what about prescription and over-the-counter medication by where parents become a good model? That's a role they need to understand.

DR. BRUINE DE BRUIN: I also want to say that I think for -- that adolescents may be able to make good decisions about different over-the-counter medications, but it's not something we should assume. It's something we should study and to understand how they approach the decision, and they may -- you might find that they are not different from adults on some drugs, and maybe they are different from adults on some other drugs.

And you may find that they want to talk to their parents about some drugs and not about others. I can imagine that, for example, teenage girls don't want to talk to their parents about emergency contraception, but talking about headache medication is not that much of a problem.

And then, another thing that I wanted to point out is that going through the exercise of talking to adolescents you may find that -- again, it's an empirical question, but you may find that simplifying the label or whatever communication is being given, so that adolescents understand it, may actually help adults as well, because adults may also have some problems understanding the label or understanding how to appropriately use the medication.

And just taking a different view, understanding the problems that adolescents have, may help you to educate adults as well. But I think it's not something we should

assume. It's something that needs to be researched.

MR. SILVER: Hi. Tom Silver, representing the Society for Adolescent Medicine. This has been excellent presentations, and they raise the issue of the balance between adolescents having to learn, practice, and adopt adult behaviors, the role of the parents as educators, and the potential for abuse and misuse.

But the issue that has us preoccupied at the Society is, let's put it this way, the lack of weight of scientific information relating to over-the-counter decisions that affect teenagers. I'll give you a couple of examples.

One, Syrup of Ipecac has been removed from the pharmacopeia in Europe 10 years ago. Four years ago, the American Academy of Pediatrics has decried its use. It is no more in the cabinet for home poisonings.

A panel of the FDA two years ago

made the recommendation that Ipecac be removed because teenagers use it to self-induce vomiting with the eating disorders, they develop myositis, myocarditis, etcetera. They die from it, and it's still out there.

On the other hand, there is not an iota of evidence that emergency contraceptive pills could not very appropriately be used for teenagers that could be protected. So there is a bit of a hypocrisy going on here.

On the one hand, we are having this elaborate discussion on this type of over-the-counter medications which reminds me a little bit of the drunk that loses the key out there, but looks here because there is a light. And we are not addressing those things that are really important about over-the-counter medications.

So I will be interested in your response to that.

DR. BRUINE DE BRUIN: Yes. I think a lot of it is politics.

DR. HUSZTI: And I think the other thing is we do -- I think from the talks today that we recognize that there is different levels of abuse potential, there is different levels of risk potential with different medications. And, again, without the research, as you so well pointed out, it's hard to know.

And so it can be politics if we don't look at it, or it can be we just assume, you know, how many -- how many studies when we finally do them do we go, oh my God, that didn't work. Who knew? We thought it did. And that's why we do research. I'm not telling you anything.

DR. CUMMINS: Lisa?

DR. MATHIS: This is Lisa Mathis again from the FDA. I don't really have so much of a question as much as a clarifying point. And then, I'll turn it over to Dr. Kweder who probably does have a question.

Just as far as when the question was asked of how big of a problem is this in

adolescence, and reflecting on the safety numbers, one of the reasons why -- well, with the adverse event reporting system that we have, the experts in the Office of Surveillance and Epidemiology really tell us that the spontaneous adverse events that we get for prescription products, it's one to 10 percent.

So if we look at over-the-counter products where there is no mandatory reporting, or was no mandatory reporting, and then look at adolescents on top of that, my guess is that we probably don't really know what the safety profiles of these drugs are, especially based on this particular database.

So I'd be careful with that data that we don't have any more on adolescents than we do on adults, because we know that data is not so hot in adults. It's probably worse for adolescents.

DR. CUMMINS: And for -- especially over-the-counter products.

Sandy?

DR. KWEDER: Yes. I'm Sandy Kweder. I'm from the FDA. And, boy, I think -- I have so many questions I can't even articulate them all, but I want to first make a point. And I think Dr. Silverman's comments are certainly appreciated by us, which is exactly why we're here. You know, we have found ourselves in a variety of circumstances over recent years where the question about how adolescents perceive medications has come up.

You know, to be perfectly honest, when we think about over-the-counter drugs, you heard about it this morning, toothpaste is an over-the-counter drug. Okay? Deodorant is an over-the-counter drug. It is regulated as an over-the-counter drug.

Well, I don't think any of us would question whether or not we need to think about how adolescents use deodorant, although in my house I sometimes do.

(Laughter.)

Or don't use it. But we think a

lot differently about internal analgesics so to speak, for example. So our -- one of the things that we're grappling with is -- kind of comes down to when does a drug need to have separate unique considerations for how it will be used or perceived by adolescents?

Sometimes I think the ones that maybe seem most obvious might be when there is a drug that we have any reason to believe might be abused for one thing or another, whether it's to induce vomiting or to get high. We have those same concerns in adults. They are not unique to adolescents, but we may need to be thinking about the adolescent subpopulation of potential users.

But what about other things? You know, are -- one of the questions that comes to mind -- came to my mind as I have been listening over the day is trying to remember when it actually dawned on me that I could -- was old enough to buy Tylenol. You know, I don't know, and I couldn't tell from the data

this morning when adolescents actually -- or teenagers or kids even start to think that they could self-medicate.

You know, we saw a lot of data about they use what's in the household because their parents tell them, but a lot of what we're questioning is the independent use by a teenager. And that's where we're really struggling is when do we need to be worried about that, and particularly where we need information about that, where once we find something that we think needs information, or where adolescents need a unique way -- type of education, how do we achieve that?

So that's where I think Susan is saying -- Susan Cummins is saying think out of the box. What are some ways that we might do that?

I have been surprised in the questions and answers that we haven't heard much from the people from CHPA, and how you guys are thinking about that, because I'm sure

you are. And I know there are several of you here, and so maybe one of you could comment.

Thanks.

PARTICIPANT: That's why we're on the panel tomorrow.

(Laughter.)

DR. KWEDER: You could give us a preview.

DR. STEINBERG: Well, I think you -- in your question you mention two circumstances that might warrant more thinking and more study. One is over-the-counter medications that have the potential to be abused -- to be deliberately abused for recreational purposes. I mean, we know that adolescence is a time when people experiment with drugs.

And if they can -- if somebody discovers that Robitussin is something that you can experiment with, then that -- you know, that ought to be on the list of things that we, you know, require proof of age for or something

like that.

The other I guess would be to go back and to do some better surveillance of adverse events and find out if there are particular products that kids are misusing, not for recreational purposes but because they don't understand the -- you know, the proper dosing or what it's supposed to be used for.

And, you know, then again, I mean, I think that really depends on what the particular product is, and I have no idea whether Pepto-Bismol should be on that list or -- you know, or not. And, I mean, I think we just need some better -- what was said before is that we need some better surveillance data to -- you know, to figure out, you know, which products these are.

MR. SPANGLER: David Spangler with the Consumer Healthcare Products Association. A couple of things. I think on the abuse situation --

DR. CUMMINS: Can you hold that?

MR. SPANGLER: Of course.

DR. CUMMINS: Did --

DR. BRUINE DE BRUIN: Well, I was going to think really out of the box, but I'm not sure --

(Laughter.)

I'm turning my microphone on. I'm from Holland, and in Holland, as you may know, it's very easy to get high. Marijuana is kind of legal. You can use it, and you won't get arrested for it.

There is a minimum drinking age presumably, but I don't know what it is. It's not enforced. And, again, I'm just an n of 1, right, I lived in Holland, and I had never heard of kids using over-the-drug -- over-the-counter drugs to get high. They don't have to.

Maybe my sample was really biased, but, you know, I moved to the United States and my peer group here has all done it or they know about it, and a lot of them have tried it until they turned 21 and then went -- they went crazy

drinking because it was legal and they finally could drink, and they, you know, have the 21 shots on their 21st birthday, which is really dangerous. And I found that shocking.

And so thinking out of the box -- I know you don't have the power to implement this -- but I just wonder whether there -- if there were legal, safer ways to have a little bit of fun, whether that would reduce the risks that our adolescents are exposed to.

If we can give them a glass of wine with, you know, Thanksgiving dinner or Christmas dinner at age 13, maybe they -- maybe getting drunk or getting off in some other way is not that exciting. They just learn slowly how to drink, and they don't seek extremely risky situations.

But this is the kind of out of box thinking you may not want to think about.

(Laughter.)

DR. CUMMINS: Go ahead.

MR. SPANGLER: I have a couple of

comments rather than questions, but one, just on the question of abuse -- and let's -- we may as well talk about cough medicine abuse among teens, because that is a problem, and that's why, yes, we think age restrictions are a great idea.

That's why we met with a number of major retailers across the country to encourage them to put in place voluntary age restrictions and why we have lobbied Congress to have a bill to have age restrictions across the board, so that you can't buy cough medicine with dextramethorpham without, because, yes, both prescription and OTC abuse can be a problem.

So, yes, so when you've got a specific problem on the abuse side, I think that there are tools to deal with it and we want to do that. And we've done a lot of educational work, we've reached 22 million parents since we launched our Five Moms website in May, to get the message across that parents who talk to their teens -- their children,

rather, are half as likely to abuse drugs as those who don't. That's according to the Partnership for a Drug-Free America.

Now, moving on to the -- what we'll call are they using them safely and appropriately and effectively for the conditions for which they are intended, I think Dr. Kweder put her finger on that question. That is, in a lot of instances we have no reason to think that they are any different.

And as you've talked about, Dr. Steinberg, you know, at 16 we let people drive a car, so it would be a little bit silly to say we can't let them take something for a headache or an upset stomach or their acne. So we do have to kind of think through, is there, just as in any, you know, prescription and non-prescription, switch application as Dr. Brass alluded to?

You know, if there is a specific question that we want to answer because teens are different, and we have some rational reason

to believe and think they're different, then absolutely, let's apply the best research tools we can to get at that question.

But anyway, I look forward to talking with you guys more tomorrow when I'm sitting up there.

DR. CUMMINS: Did you want to make a comment?

MR. DENNISTON: Yes, briefly. The notion of harm reduction does come up from time to time, and certainly the minimum purchase age of 21 for alcohol in the U.S. is a topic that is getting more and more attention. If you can go to war at 18, why shouldn't you be able to have a drink at 18?

Well, in fact, if we lower the drinking age, we're going to see roughly 1,000 more teenage deaths each and every year. So where we are now with that product is the situation regarding we've saved a lot of lives -- roughly 1,000 a year -- just in -- mostly in drunk driving crashes, not to speak of falls

and burns and date rapes and all those other kinds of things. So that's just one of the consequences of these policies.

I've heard it said there are basically four kinds of policies -- one, policy supported by data; two, policies contradicted by data; three, policies absent data; and, fourth, data in search of policies. And so I think when we talk about the policy issues we have to look at the data, but we understand at the same time that, frankly, a lot of policies are created by legislative bodies that are not based on data whatsoever, nor is there intent to base them on data, or is there intent to track the impact.

DR. BRUINE DE BRUIN: Right. Yes, we need data. Another thing about the Dutch experience is that kids learn to drink before they learn to drive, and here it's the other way around. But that's --

MR. DENNISTON: We could raise the driving age.

PARTICIPANT: Yes.

(Laughter.)

DR. CUMMINS: Well, given the number of teen deaths from driving in Montgomery County lately, that might not be a bad thing. Heinz, did you --

DR. SCHNEIDER: Yes. I have a brief and a longer comment, a brief comment, almost an Austrian rebuttal to the Dutch sinking out of the books. As a matter of fact, in my country, a 15 year-old who wants to do silly things and wants to get a little bit high can go to the supermarket and easily buy a six-pack of beer, and it's not a better world. It's definitely not.

I agree we need data on the broader question. I think it's really medicine per medicine, and issue per issue. And whenever I would see data which show that adolescents don't understand the communication, go like a drug-drug interaction of a specific medicine, I would first say -- I would first look at the

adult data and say, isn't that a broader problem?

And we don't have to do something here at adolescent-specific and only if -- if our data really show that this is a situation, that this is a medicine, and how it's used and how it's marketed requires specific things, specific communication, specific measures for other lessons, data for if -- if we should go there, but without data I would just not jump to wrong conclusions.

DR. BRUINE DE BRUIN: I don't know. I think I would want to argue that we would standardly include research on adolescents. And we may find that they're the same as adults, and we may find that they're not. But I -- I would assume to -- I would advise to include them.

DR. CUMMINS: Charlie?

DR. GANLEY: Yes. Charlie Ganley from FDA. I think one of the other things, it's not just a question for us and what we do

with adolescents now, but we deal with now with the problem with how adults use OTC medicines and prescription medicine in general.

And the question is well, how did they get to that point? Why do they have these perceptions that they have where they may ignore warnings or they may take more than recommended amount? And so -- and our thinking is that in thinking about this whole issue over the last year is, well, we're trying to attack the problem at the adult stage, and we actually need to look at the adolescent stage and see what is going on there and how can we influence that, whether it be OTC medicines or prescription medicines.

And so I'd be interested in your thoughts on understanding, you know, the -- or the behaviors of adolescents, how predictive of that is it once they get into -- become adults? You know, the -- you know, you showed us various charts about, you know, the changes as they get into their twenties and things.

Well, how is it that some of these adolescents, when they become adults, they still may have behaviors or have -- or maybe they didn't learn behaviors as adolescents that caused them to use medicines incorrectly, because many of our problems that we have with drugs now, including -- you can go back even to some of the issues with the pediatric cold products, is those -- half of the serious adverse events are related to misuse and abuse, and some of it is the parents just give adult formulation, for example.

So that's -- it's a much bigger issue than just addressing adults. It is because we think we have to attack the problem of adult misuse early on in the phase, so I'd be interested in hearing your comments on that.

DR. HUSZTI: I mean, I would say this would be more probably on the prescription drug side, but, you know, there is a literature out there and an interest in looking at transition in care. So, you know, how do you

move from being in a pediatric kind of setting where people do things for you to an adult setting where you have to take this on?

Looking at your charts, and, you know, the -- yes, you're at the cognitive age, and some people make that transition really well, some people make that transition horribly, some people don't pick up until they're in their thirties or forties, and, you know, then they've had some pretty major complications sometimes, and so I -- this is the long way around to say I'm not -- I'm not sure we know. I haven't seen a lot of data that would suggest this is the thing that kind of helps make that transition successful, but other panelists may --

DR. STEINBERG: Well, I think we know that for the most part adolescents don't specialize in substances, you know, to -- you know, for recreational high purposes, so I would suspect that the same factors that predict, you know, marijuana and alcohol and

other illicit drug use would predict, you know, abuse of over-the-counter, you know, medications as well.

And I think there wouldn't be any reason to not hypothesize that the same fact, which is that the earlier you start to use a substance during adolescence the more the chances are you're going to continue using it in adulthood, which has been established now across a wide range of substances, that that's going to hold true for these substances as well.

So, I mean, one way of answering your question is that certainly a strategy for preventing the misuse or abuse of over-the-counter prescription medications among adults is to prevent it among adolescents, because if they're not doing it as adolescents it's very unlikely they're going to abuse them as adults.

DR. BRUINE DE BRUIN: Yes. Ido Erev at the University -- I think the Technion University in Israel has been doing work on the

effect of warnings on risk behavior. And he showed -- and he also does a review of the related literature, that the earlier you give warning the -- in terms of whether you give a warning before people are engaged in a risky behavior or after, it's more effective if you give it to them before, because if they engage in the behavior, a lot of risk behaviors will not lead to negative outcome.

So people engage in the behavior and nothing happens, and they conclude that it's fine. And then, they continue to engage in it, and they may still in the end end up with a negative outcome.

So he has shown that if you get the warnings to people before they have that experience, the warning is more effective than if you give it afterwards. So I think that's another argument for targeting adolescents with information about how to use specific medications.

DR. GANLEY: I just have two more

points. One is a question, and one is a sort of comment. I just want to reiterate Susan Cummins' comment about looking outside the box. And the way I sort of look at this is that our regulatory authority is really dealing with labels now, but I think we have to look at what does the OTC drug market look like in 10 or 20 or 30 years?

You know, because you see all of these technologies out there. You know, there's talking labels, you know, there's various mechanisms to improve health literacy using technology, and I wish we had clear guidance that we had the regulatory authority to use those. That's not entirely clear.

But I think those are the types of things -- where can technology come into play here in influencing behavior, not just -- you know, I have two teenagers, and they are technology savvy. And, you know, they can pick up something, not even read the directions, and they figured out how to use it. And yet we

don't use that -- these type of instruments to convey health literacy.

And so that's where I think we're talking about, too, is what in technology can we use to try to influence use, because that's going to be with these adolescents the rest of their lives, long after we're gone. So --

DR. HUSZTI: I was just -- from our study that -- I mean, I think you're absolutely right. I mean, technology was very teen-centric, and, you know, they talked a lot about, you know, "I fall asleep texting in my bed, and I wake up in the morning and I start texting," and, you know, it's omnipresent.

And one of the things that Robert Wood Johnson Foundation is hoping to do ultimately is put together like what is a prototype that one could use to use technology to help teens make a better transition, to help teens be more healthy, to help address a lot of these issues, because that -- you're right, they're very technology savvy.

That's very -- again, seen as teen-centric and something that's not -- you know, the adults don't know how to do that. This is cool, because I've got this. So I think it's a great idea.

DR. GANLEY: The last question I have has to do with the so-called latchkey kids who come home, they don't have anyone in the house, and how do they function relative to someone who may have -- you know, and I don't want to characterize that they may not have as much parental involvement.

They actually may have more where the parents are setting out these are the things you have to do when you get home. Are there differences in their abilities to make decisions versus kids who, you know, may have a parent at home when they come home and totally depend on the parent?

And I can tell you I have 16 and 17 year-olds and they won't pick up a medicine without asking us. They have never been in

that situation as much I think, you know, on a regular basis where either one of us is not home. So I'm just interested in hearing that perspective, too.

DR. STEINBERG: Well, there's a fair amount of research on differential opportunity and access to substances among kids in the after-school hours who don't have adult supervision. I don't think -- the studies that I'm aware of that have compared the decision-making abilities of kids who are -- who have a lot of time unsupervised after school with those who don't don't find very many differences.

There aren't very many differences in personality, you know, between those samples. But there are differences in behavior that have to do with opportunity, and, you know, clearly the more we can -- and, again, this is outside the auspices of the FDA, but the more we can get funding for adult supervised after-school programming for

teenagers, especially for younger teenagers who tend to be left out of a lot of high school programming, then the more we will keep them in situations where they won't have easy access to these substances.

DR. MURPHY: I just wanted to come back to the separation of what we're struggling with -- of drugs that are being abused for recreational versus what one of our struggles are -- just communicating to the adolescent who wants to go buy, you know, their analgesic and their other drug, and it's not deliberately going to be abused.

And I think they -- you know, Dr. Steinberg said that earlier, and I think we keep sort of crossing back and forth, and we need to be really careful because what I -- we're trying to get at is how do we, for those products -- that's sort of the first level of discussion -- how do we for those products make sure that we have the data on how -- first of all, what's the dose, because extrapolating

from adults we have now learned is -- unless we have the data to tell us we can extrapolate, and then we still need the dosing data and we still need the safety data. We shouldn't be extrapolating until we have that data.

But, so that -- how do we have the data so we know the dose? How do we have the data that tells us how to risk communicate? And then, how do we study if it's working? I mean, those are the huge issues that we're trying to find out of the box, you know, approaches to it.

And, you know, Charlie may be right, maybe it's going to be that when the kid buys it it's got some little -- not a computer chip, but some little micro phone on it or something, and, you know, you get to call in.

And also, get people to understand they have to report when they're having adverse reactions they didn't expect, because, again, as I said this morning, that's the one thing we're finding out. If you don't look and you

don't separate out the kids for adverse events, you aren't going to find them.

DR. CUMMINS: Well, I want to thank our panelists for being here today and for sharing with us all of their knowledge. And I just wanted to ask all of you if you have any closing thoughts that you want to share before we wrap up.

(No response.)

I see a no. Thank you all for being here, and thank you very much. Let's give our panelists a round of applause.

(Applause.)

(Whereupon, at 5:22 p.m., the proceedings in the foregoing matter went off the record.)