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

PUBLIC WORKSHOP

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FRIDAY,
DECEMBER 7, 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/DAY 1 REVIEW
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PANEL III
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LEE M. SANDERS, MD, MPH, Associate Professor of Pediatrics, University of Miami, Miller School of Medicine
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T-A-B-L-E O-F C-O-N-T-E-N-T-S

M-O-R-N-I-N-G S-E-S-S-I-O-N

8:38 a.m.

I. WELCOME AND INTRODUCTION

DR. BRASS: Good morning. I think we will go ahead and get started. I'd like to welcome everybody today to the Adolescent Over-The-Counter ("OTC") Drug Use Workshop and I was given a challenging task and that was to try to recap some of the themes from yesterday to help set the stage for the discussions today.

Clearly, one of the great assets of this workshop is the opportunity to hear about the issues of OTC drug use in adolescents from varied perspectives and having experts in regulatory, scientific, from industry perspective and clinical practice all in the same setting really allows us to share those perspectives and hopefully develop a much more integrated understanding of what these issues are.

I'd just like to recap a couple of the things we heard specifically. We did hear that there are research tools for studying OTC

relevant behaviors preapproval and, importantly, we also heard data from Dr. Nihkar that these tools can be applied to adolescents and we heard results from two specific product development programs about adolescent-specific data.

But I'm not sure we focused adequately on the interpretation of that data. Remember those were studies for both Plan B and for the weight loss product, Orlistat. And it was not at all clear to me that the intent to heed key label instructions were sufficiently uniformly high to give confidence that the adolescents would actually behave properly in the OTC marketplace.

A number of key messages were actually not very well understood, particularly by low literacy adolescents. If you recall the data, there were many key messages where there was only 50 percent comprehension much less behavioral heeding. And I think that highlights that it's not simply collecting the data, but we really need to understand both the data and the

bases for any discrepancies.

The determinants of adolescent behavior even in the actual use studies were not clear. In the case of Orlistat, in fact, it seemed that it behaved very much like we've heard about cigarettes yesterday, that, in fact, the deterrent for adolescent to use Orlistat was not the label instruction but the $60 price tag and that many indicated that they would like to use it but when offered the opportunity to purchase, did not, so again differentiating that we truly understand the determinants of behavior.

And we also know incidentally that age directions per se are not very effectively heeded directions on adult labels where there are age cutoffs and, if you think about it, this goes back to how we communicate the importance of different messages. It is quite reasonable if a label says "Do not use if you're under 50" for somebody who is 49 to decide reasonably that there is no safety issue for them to use it and to not heed the label. Similarly, a label that

says “Do not use if you’re under 18," a lot of 17 year olds may make very informed decisions that use would be proper. So, again, we have to understand the context in which we’re trying to use age differentiations to guide behavior and make sure we understand that those types of directions are not going to be uniformly heeded if expressed simply as an age cutoff.

We also heard quite clearly that as we’ve heard a lot recently kids are not little adults and that adolescents are no different. Adolescents differ from adults. There is quite distinct biology, quite distinct physiology that’s relevant to the pharmacology of drugs, behaviors and decision-making and even underlying neuro-developmental differences that underlie many of these.

In fact, it was very interesting to me that there were, in fact, structural/functional correlates which provide a scientific foundation to the concept of maturation of decision-making during this

critical age range. This is not simply parents' interpreting their kid's behavior, but there truly is a neurobiologic foundation to thinking this and these changes are relevant to both judgment and risk-taking.

What wasn't clear to me at all is whether age is reliable surrogate for the maturation of these decision-making processes. And even when we talked about subdividing adolescence to 12 to 14, 14 to 16, 16 to, whatever subdivision you wanted, I was struck that that seemed artificial and that really I think one of the messages is we have to recognize the heterogeneity within that age group and studying it, recognizing the heterogeneity because any finer delineation based on chronologic age is unlikely to be sufficiently specific for any maturation level. And those of us who lived through this for the geriatrics question and took 20 years to recognize that chronologic age isn't an index of how drugs are handled in a geriatrics population, how the

geriatric population accesses health care, it's the same message that chronologic age is the crudest of surrogates for understanding underlying health status and behaviors.

We also heard quite clearly that there are environmental factors that interact with host factors. It is not simply peer pressure. It is peer presence that can alter how adolescence behave in any given environment for any given decision tree and it made me think whether we actually need now a new standard warning on all OTC packages. So we have our "Do not use" warnings, "Do not use if you're allergic." "Do not use if any of your friends are in the room because that clearly impairs your decision-making and you won't be able to use the drug properly."

I'd like to focus just for a minute on the issue of OTC used by adolescents with therapeutic intent. Again, I think it's very important conceptually to differentiate any issues with drug abuse to ensuring the proper use

of drugs when there's a therapeutic intent.

Despite the discussion and despite many biases, it's not at all clear if there is a problem in this arena, but I want to emphasize the absence of evidence is never evidence of absence. We simply do not know. We do not have enough data about how adolescents use these products. What data we have can be interpreted in a variety of ways. But even whether or not this represents a sizable public health problem isn't clear.

If there is a problem, it's not clear whether it's one of simply judgment and decision-making or whether there are genuine knowledge gaps or misconceptions about factual information and clearly understanding which of these two domains any problems lie is key to any remediation or mitigation strategy.

While we saw a variety of data on adolescent OTC use, I would characterize it as very broad but not very deep. It doesn't allow me to have an in-depth understanding of how

subgroups of adolescents are making decisions using and actually using the products in detail. So this goes back to it's not clear there's a problem.

This breadth in the absence of depth has the potential to mask a great deal of heterogeneity on how these drugs are used in the adolescent population. And this is not surprising because it would be consistent with the heterogeneity in the population we already talked about and it's no different than any other OTC cohort. That is, you begin to look at adults. It makes a big difference whether you're talking about low literacy or high literacy adults. It makes a big difference if you're talking about adult consumers who have access to health care versus those who don't have access to health care. And those same -- I'm sure there's a large number of analogous factors that contribute to the heterogeneity.

But another important issue that came up yesterday that I want to emphasize is that

even if one thinks there's an absolute problem of non-heeding with any specific direction on an OTC label by any group, the real question is whether it is an important issue of misuse and how big a problem it represents and how much effort should be expended to try to correct it in a finite resource world.

I just want to reiterate a construct that I have consistently found useful when I think about these problems. And that is that the magnitude of a clinical problem whether it's from a public health perspective or an individual health perspective is determined by two factors.

First is the frequency at which there is non-heeding. What percent of users disregard a certain instruction in a certain way? But that's not enough. You have to understand the risk that's associated with that specific non-heeding. And those two factors together give you an estimate of the problem.

For example, if you take the age restriction at age 50 arbitrarily and you have

lots of people at age 49 using it, but they're at no incremental risk and are likely to get benefit from the product, even if the frequency is high, that doesn't represent a public health problem. It is not worth expending great effort to try to fine tune that.

However, we take a situation where an overdose of just two or three times the recommended dose may expose the population to a health risk that is potentially serious, we would insist on a demonstrably very low frequency of non-heeding because of the larger public health consequence. So there is no single answer to this, but for every single example one has to formulate this way and decide how much effort on those very small labels is going to be required and whether or not it impacts the overall public health benefit of the increased access of the drug.

In other words, I want to emphasize just because there is a non-heeding doesn't mean it's a public health problem. Just because

there's a non-heeding doesn't mean that it is not an appropriate OTC product and understanding this in the context of adolescent decision-making, I think, is important.

We heard that there's a mandate from the public, at least, to the degree that Congress can be thought of as the public to understand factors specific to pediatric and adolescent use of drugs and that's quite appropriate and those in the clinical arena have been supporting such activity for a long time. We need to understand the public health issues to apply whatever new learnings we get about the population to truly incremental improvement of public health.

As we indicated, intellectually we need to differentiate the approach to drug abuse from errors with therapeutic intent and then we can begin talking about issue-specific interventions and I would suggest that those are broadly going to be in two categories. One example would be broad public health communications. For example, we heard a lot

about the drug abuse campaign and insights into the effective elements of such a public health campaign and I think for a number of general issues about OTC use these tools may be very important and very effective. If we focus also on the secondary goal that if we turn adolescents into well-informed consumer of health care products we will end up a generation from now with adults who are well-educated consumers of health care products. So it really is also the secondary goal of instilling good lifelong behaviors during this formative stage.

But then we may also need drug-specific labeling to address adolescent behaviors that are identified in the context of clinical research when there is a risk for adolescents behaving differentially in a way that may affect their individual or public health and this differentiation in terms of interventions is again dependent on specificity in identifying what the problem is that we're mitigating and that it justifies the public health effort.

So hopefully what yesterday has done is set us up nicely for Day Two where we're going to focus on how do we communicate with adolescents in general but also specifically extrapolating that to issues of OTC drug use and then this afternoon in our roundtable begin to set a more specific agenda as to how to move forward in taking the lessons learned to translate into improved public health through improvements in how adolescents use OTC drugs.

Before I turn it over to the first panel this morning, I've been asked to make just a couple of announcements. The original schedule listed at 11:30 this morning, an open public hearing, it is our understanding that nobody has requested time to speak during that open public hearing. Thus, unless there is strenuous objection, what we will do is shift the timeframe for the day up a half an hour. So we'll do lunch at 11:30 a.m. The roundtable will begin at 12:30 p.m. and the day will end at 3:00 p.m. instead of 3:30 p.m.

The other point that I'd like to mention is that those who would need a taxi to leave this afternoon if you could allow the Event Staff sitting outside the auditorium to know where you'd like to go and at what time, they will try to coordinate arranging cabs to be available to transport people to trains, planes or whatever.

With that, I'd like to again thank you for your attention and I will turn the podium over to Dr. Bosco for the first panel.

II. PANEL III

DR. BOSCO: So that was a great kickoff, I think. That was very helpful.

So, anyway, I am Lynn Bosco and I am within the NIH Office of the Director and the Office of Behavioral and Social Sciences Research and so why am I here? Well, I started my career at FDA and Drug Safety. So I've always had a soft spot in my heart for FDA issues.

We are one of the cosponsors of this meeting and the focus of our office is to

encourage research and, in particular, behavioral and social sciences research, what ends up being called Applied Research. You are sitting in the midst here of a $30 billion research enterprise. Welcome. And it's a lot of money, but it's not a lot of money that gets spent on things like applied research. I think when we looked at this topic we didn't really find a lot of research out there. So one of my goals here is to encourage more research in this area and we'll do a little bit more talking about that at the roundtable.

But without further ado, I'm going to introduce my panel. I'm going to introduce everybody all at once just to keep us on track for our schedule and tell you a little bit about the theme of this panel. The theme of this panel is basically adolescent communication and communicating with this unique group of people or groups of people as we've talked a little bit about during the meeting is that it's not one group of people. It's a number of groups of people and a number of age groups with a number

of different needs.

So our first speaker is going to be Jim Jaccard who serves as Distinguished Professor at the University of New York in Albany. He has conducted research on applications of theoretical psychology to the alleviation of social problems in the United States. His topic is going to be "Models for Communicating to Adolescents."

And then we'll have Dr. Lee Sanders. Dr. Sanders is the Associate Professor of Pediatrics at University of Miami, Leonard M. Miller School of Medicine. Dr. Sanders is a general pediatrician. His topic is going to be "Health Literacy Among Teens."

And then we have Cornelia Pechmann who is actually Connie Pechmann. She is Professor of Marketing at the Graduate School of Management, University of California, Irvine, UCI. Dr. Pechmann conducts controlled experiments to study the effects of advertising on consumers. Her topic is going to be "Teen Marketing Psychology Research."

Julie Aker is President and CEO of Concentrics Research in Indianapolis, Indiana. This is a contract research organization which specializes in custom late-stage, clinical regulated, health care marketing and regulatory research solutions including Rx to OTC switch. The topic is “Design of Consumer Studies in Adolescents.”

I’d also before I sit down acknowledge the Committee members who helped with the planning of this panel and that’s Lisa Mathis from FDA and Dara Blackman from our office. Without further ado.

DR. JACCARD: Hi. Thank you very much. I recently moved to Florida International University, Miami. That’s where I am now. I was at Albany, State University of New York at Albany prior to this. My wife is Argentinian and she grew up in Buenos Aires and she referred to Albany as a small village near the North Pole.

(Laughter.)

DR. JACCARD: So she was very happy

when we decided to go to Miami and live there.

I am going to be talking about communication models, but most of my work is with parent-adolescent communication. So I'm going to frame my discussion of communication models in the context of that research. I also was very heartened to hear yesterday several people talk about the importance of parents in this whole process and so I want to reinforce that and drive home the importance of parents.

Let me start by saying there's a variety of different intervention strategies that people have used in approaching adolescent risk behaviors and adolescent behaviors in general. There's a whole set of intervention strategies that adopt legal or policy-based interventions to try and impact behaviors. This might be, for example, with a Plan B contraception of making it over-the-counter for people over 18, but for kids that are less than 18 they have to have a doctor's prescription for it and this in turn impacts the behavior of the adolescent in terms

of access to it and use of it.

In addition, another type of intervention strategy that we often use is to try and alter the environment or the context or the product itself with the idea that that in turn will impact adolescent behavior. So, for example, you might keep certain over-the-counter drugs behind the desk of the pharmacist and that in turn will impact access to it and behavior with respect to it.

Then there's the ubiquitous education or counseling strategies that we use and there are many different approaches based on education to try to impact adolescent behavior. There are school-based approaches that rely on education in the schools and the health classes and outreach through schools. There are clinic-based approaches where clinics outreach to adolescent or through contact to health professionals or a family physician, you might try and impact adolescent behavior. There are public service announcements on television and different media

outlets that we try and impact behavior with and, finally, there are internet or web-based approaches that are very commonly used.

I'm taking a slightly different perspective in the way that I'm going at this and basically in my research I'm developing parent-based interventions. And I try to influence adolescents indirectly by influencing the parents of adolescents. In the work that I do, I try to teach parents how to parent their adolescents their adolescents more effectively, how to communicate effectively with their adolescents with the assumption that they in turn could have an impact on their adolescent behavior.

I started doing this work some 25 years ago and I was one of the first to start exploring parent-based perspectives in the area of adolescent sexual risk behavior and I'll never forget when I told my colleagues that this was the direction I was going to go they all told me I was nuts and that there was no way that these kinds of interventions would have any type of an

effect.

And the kinds of disadvantages or the objections that I heard quite frequently were, first, “Families are dysfunctional, Jim, and they’re not going to work in dysfunctional families. So how can you hope to have an impact that way?” And I agree. A parent-based approach isn’t going to work in dysfunctional families. However, there are a lot of non-dysfunctional families in the United States and that actually it’s a huge audience that we have and a lot depends on how you define dysfunctional. And across a wide range of families, I’m absolutely convinced that parent-based interventions can have an effect.

The second objection I heard is that parents just lack knowledge. They don’t know enough about these topics. They don’t know enough about sex, alcohol, drugs, health, things like that to be effective. To explore this, I went out and I did a whole bunch of studies looking at how knowledgeable parents were and it

was kind of scary, the results that I got, because they weren't very knowledgeable about a lot of things. The key thing here though is that parents can be educated. They can learn these things and so the knowledge they don't have you can teach them and help them convey that to their adolescents.

The other thing is that parents are not just transmitters of technical information about health-related issues. Parents have a much, much broader role than that. They motivate their kids. They monitor their kids. They shape the behavior of their kids in many ways beyond just the provision of simple technical information. So this didn't deter me.

The final main objection I got is "Jim, are you nuts?" All right. Adolescents are trying to get as far away from parents as they can during this stage of life. They're totally peer-oriented. Any intervention that is aimed at parents is not going to have an effect. I spent many, many years trying to demonstrate through

empirical means that parents do make a big difference kids' lives, in adolescents' lives, and I think the empirical base for that is fairly convincing at this point. So I'm pretty comfortable with that.

I also think that the peer influences on adolescents have been way oversold. The impact of peers is not nearly as strong as people think it is and that it's a common myth even among fairly informed social scientists that peers have a dramatic and pervasive effect on their kids.

This is an example. I worked with the Add Health data set and did an analysis where I kind of explored these things. It's definitely true that when you look at wide range of studies that a very strong correlate of adolescent risk behavior is the number of friends they have who engage in that risk behavior and that's a very ubiquitous finding. However, there are a lot of uncontrolled variables and alternative explanations to those correlations in what you

see.

So, for example, one alternative explanation focuses on selection effects in friendship selection. We know from psychological work that kids like to hang out and choose friends who are similar to themselves. So you might have a kid who or an adolescent who has a risk-taking propensity for reasons that have nothing to do with peer influence and that adolescent chooses to hang out with other adolescents that have that same risk-taking propensity. There is no peer influence going on. It's merely a friendship selection effect.

So when you look at peer influence studies, you need to control for those friendship selection effects. One way of doing that that we've done in our work and others have done is to start with intact dyads where the selection has already gone on and then follow the adolescents longitudinally and see if across time if one of the peers' behavior changes does the adolescent behavior change as well and if you see

concomitant changes over time for already selected dyads, then that would be consistent with peer influence.

There are problems even with those designs however because there are parallel events that can happen to both kids that impact their behaviors so that the behavior change occurs concomitantly when, in fact, there has been no peer influence. So, for example, two kids might experience puberty at about the same time and these hormonal changes might cause them to alter their behavior around the same point in time. So you have these parallel events that are operating that will also create concomitant changes over time.

I did an analysis of about 5,000 kids where we interviewed every single kid in the school. We had them nominate who their best friends were. I then, by interviewing every single kid in the school was able to link the data of best friends. John would say his best friend was Joe. I had Joe in my sample. I asked

Joe a bunch of questions about risk behaviors. I asked John a bunch of questions about risk behavior. So I could pair up the dyad and then look at their behavior over time, over a one year period, to see that if Joe started drinking did John start drinking and look at concomitant changes over time. One of the first things I found -- I did this. So that controlled for the selection effects and then I thought of about 40 or 50 parallel events and I statistically controlled for those in the context of this as well.

One of the first things that was very interesting is that over a period of one year the kids had nominated their best friends. One year later, 50 percent of them were no longer hanging out with those best friends at all. Peer relations are very dynamic. Friendships change all over the place and so in some respects often peers don't have time to have effects on the kids because the peer changes so much. The bottom line is when I controlled for all the parallel

events, I controlled for selection effects, there was a negligible effect of the peers in this. There was a small consistent effect on binge drinking and on sexual risk-taking but the effects were very, very small.

One of the things I did that was interesting is that I had looked at who they nominated as their best friend and looked at concomitant behavior over time and then I tried an analysis. Instead of using their best friend's data and look at concomitant, I just randomly picked someone out from the school and said, "Let's pretend they're the best friend." So it was a random best friend. The only requirement I had would be that it had to be the same gender and the same age. I looked at the effect of this pseudo-peer and it was just as strong as the effect of the true best friend. Something else was going on. I think if we do rigorous well-controlled studies of peer effects, it's much more complicated than we realize.

There are certain advantages of parent-

based interventions that I emphasized and found in my work over the years. The first thing is that parents can tailor the information that they present to kids based on the characteristics and needs of the adolescent. They have special knowledge about their kids. They know what will work and what may not work and they can tailor information to the maturity levels of the kids, the personalities of the kids and their knowledge of the kids.

Second, there's flexible timing. If a kid is having a bad day and the parent had planned on talking about things, the parent can back off and just not talk about it and talk about it on another occasion. They can be very flexible when they deliver these messages. In school-based settings, that flexibility isn't there. They usually have a schedule on which they teach certain topics and they're going to teach them no matter what and if a kid is having a bad day, too bad.

Finally, you can implement these

interventions in the context of the values of the family. You can take into account the value systems of the family and there's a lot of controversy surrounding some things like Plan B and stuff like that and you can develop interventions and communication-type strategies in the context of the values of the individual families that are involved.

As I approach my parent interventions, there are four key parenting dimensions that I look at and I think are really important. One is parent-adolescent communication and that's what I'm going to talk about today.

The second is parental monitoring and supervision, the extent to which parents supervise what their kids are doing and monitor their kids. This is a very, very important variable for adolescents and has a fairly big impact on a wide range of adolescent behaviors.

A third key dimension is parent-adolescent relationship satisfaction. Are the parents happy with their relationship with their

kids and are the kids happy with their relationship with their parents? This also can be a very, very important variable in this and it's even important from the standpoint of over-the-counter drug use, for example, because kids that have very positive relationships with their parents are much more likely to self-disclose things to their parents. They would disclose health concerns that they have, how they're dealing with those health concerns. Whereas, if you had a bad relationship with your parent, you're going to be less likely to engage in self-disclosure. So this is an important factor that way.

And then finally, how parents discipline their kids and their use of reasoning when they discipline kids versus just straight out discipline and the types of discipline strategies they use.

I'm going to be focusing just on the parent-adolescent communication part of this today. I'm going to talk about communication

models from the parent-adolescent perspective and I'm going to start with one class of models that we call top-down communication models and these are models where you have some source who is trying to convince someone to do something. It's not really looking at the dynamics of two-way communication, but it's a top-down communication where a parent is trying to convince an adolescent to do or not to do something or a physician is trying to convince an adolescent to do something or not to do something.

I'm going to frame a lot of these issues in the context of parents. But you can take a lot of these processes that I'll be talking about and apply them to, for example, physician-patient communication or communication in general between many dyads.

Let's look first of all at the key cognitive processes that are involved in communication and giving you sense of what we know and how we frame communication research. First, for communication to be effective, someone

has to attend to the communication. If they don't attend to the communication, then it's not going to have any effect. So attention is a key cognitive process that's involved in communication.

Attending to it is not enough. They also have to comprehend it. They have to understand the message. So comprehension is the second key process.

After they've attended to it and they understand it, the adolescent has to accept the message and say, "Yeah, I agree. That's right. I go with that."

After they've accepted the message, then they have to retain that information over time. You don't want people to pay attention, understand, accept a message and then completely forget it. So retention is another key factor in all this.

And, finally, there's retrieval. At some point down the line, you want them to be able to retrieve the information and actually use

it as they consider decisions. So attention, comprehension, acceptance, retention and retrieval are highly interrelated cognitive processes that we have to think about when we think about communication and we're trying to maximize all of these key processes when we communicate.

On the independent variable side, those are key dependent variables, we ask what are factors that can impact communication and there are a half of dozen or so ones that are key in most communication models. First, there's the source of the message, who is giving the message, and you can find that the effects of a communication will differ depending upon who is delivering it. Is it a parent? Is it a peer? Is it a physician? Source of the message is critical.

The timing of the message, when it is said and how often do you say it. When should you be talking about these issues with kids? At what point do you start talking about certain

issues with kids and how often do you talk about them? These are issues that I address with parents when I talk with them about communication.

The context of the message, where the communication happens. What is the environmental setting where the communication occurs and that can have an impact on message effectiveness.

The content of the message, what is said. What is it that we say in message style? How do we say it? Those are very, very important factors.

And finally, there's the issue of the audience. Who is the message directed at? And depending upon who the audience is, the message might look different.

We can combine the different independent variables with the different cognitive processes and you end up with what researchers in the communication field call the Communication Matrix and the idea is that there are source variables that can influence

attention, comprehension, acceptance, retention, retrieval. There are content variables that can affect attention, comprehension, acceptance, retention and retrieval and there are actually very active bodies of research in every single cell of this matrix and there's a huge wealth of knowledge for us to draw on from this communication matrix and what we've learned from social psychology, psychology, communication and other fields.

This is kind of an orientation that I have is I talk with parents. I'm going to make some comments today about source content, timing context, style and audience factors, highlight just a few odds and ends with respect to them, but it's a very, very rich framework from which to be thinking about communication.

Let me start with some audience characteristics and talk about that, some issues with that. One of the first things that I address with parents when they ask me "What should I be saying to my kids about things" is I

say, “How old is your kid” and as we’ve talked about we need to recognize that there are huge differences with kids depending upon whether or not they’re early adolescence, middle adolescence and late adolescence. And there’s a lot of controversy over how we split up adolescence, but roughly speaking, early adolescence maps upon middle school age, middle adolescence to high school and late adolescence into college and vocational school kinds of ages.

To those of us who work with adolescents, we like to make distinctions even within those. I think of people saying how there’s, what is it, seven dog years for every adult human year. Well, it’s kind of like the same thing for adolescents. A year in the life of an adolescent is a huge amount of time and if just within middle school if you look at the difference between a sixth grader and an eighth grader it’s absolutely stunning the difference that’s going on there. And even in terms of risk behaviors, for a lot of risk behaviors, for

example, for sexual activity or alcohol use, in the sixth and seventh grades maybe seven percent, eight percent, of the kids are engaging in these behaviors. In eighth grade, 20 percent. There's a huge jump between sixth and seventh grade and eighth grade that goes on in middle school.

The transitions from middle school to high school, eighth grade to ninth grade, have very dramatic effects on kids, just like the transitions from elementary school to middle school do. And even within high school, the difference between a ninth graders and a twelfth grader are very dramatic. So one thing that is very important is to take into account in deciding your message the age of the audience.

I really resonated with Eric's comments earlier that there's a lot more to heterogeneity than age and we have to look at maturation and different levels of development. So let me talk about that very quickly. Developmental scientists generally talk about five major areas of development of kids in general and one area is

cognitive development and we've heard about some of these yesterday. It's cognitive development which is problem solving, decision-making, interest in academics, kind of general cognitive and problem solving skills and that's the type of development we want to maximize. There's emotional development in terms of emotion regulation, being able to recognize your emotions, being able to deal with those emotions and we want kids that have good emotional skills, feel good about themselves and have good emotional development. There is social development which are social skills, being able to interact effectively with people, having meaningful friendships and being able to maintain friendships and, in general, social development.

Another major area that developmentalists look at is moral development, being able to base your behaviors on a solid value system and developing values and moral reasoning and being able to think about values and think about morals and apply moral reasoning

to your behavior. And, finally, there's physical development, being physically fit, healthy, having an active life, not being overweight and maintaining a good physical state in the context of development.

Now you can actually put together and get a developmental matrix, the different ages of adolescents and the five major areas of development and kids vary in how much mature they are in terms of their cognitive development, their emotional development, their social development, their moral development and their physical development. There are huge individual differences in these developmental domains within early adolescence, within middle adolescence and within late adolescence and when I do my market segmentation studies and kind of decide how to segment things, I don't necessary segment by age. I segment by development and levels of maturation in these areas. As we frame communication to our audiences, we have to be thinking about what are the cognitive skills they're bringing, what

levels of emotional development are they bringing to the situation, what are their social skills, what are their moral reasoning capabilities and what are their physical states as we contemplate how to structure messages for audiences.

Source characteristics, there are tons of research on source characteristics but in terms of parents there are three key dimensions that seem to be really critical that a ton of research is validated. The first is that messages tend to be more effective if the source is seen as an expert. And by having expertise, I mean that they're capable of giving good advice. From the standpoint of an adolescent and their parent, if they think their parent has good advice to offer, they'll talk with their parent and their parent can be more effective. But if they think their parent doesn't know what they're talking about, they're not going to consult their parent and the parent is not going to have an effect. There's a ton of research that shows that identical messages given to kids but

attributed to different sources that vary in their expertise will have dramatic effects on the acceptance of those messages.

It's not enough to be an expert, but you also have to be trustworthy. The adolescent has to think that you're looking out for their good. You may be an expert about something, but if you aren't looking out for the good of them, if you don't care about them and you sincerely want them to be better and if they can't trust you, then you're not going to be effective.

And the final component that seems to be very important is accessibility. If a parent is not accessible, then the kid is not going to talk to them very much. So these three dimensions of expertise, trustworthiness and accessibility are critical and part of my interventions are designed to help parents establish these things, these dimensions, that they get those.

It's very interesting if you ask parents, for example, how accessible are you to

your kids and you ask the kids how accessible you are or your parents are to you, the correlation between those is about 0.2. They're not very strong and the parents see themselves as being much more accessible than the kids do. The same kind of finding with expertise and trustworthiness, there seems to be a disconnect between how much the parents think their kids see them as experts and trust them and how accessible they are as compared to how parents really are and these are very key sources dimensions we have to look at.

What is it that the parents should be saying about the content of the message? This is really important. What is it that you say to a kid and if you're trying to look at drug abuse and abuse of over-the-counter drugs like kids using too much cough medicine and things like that and actually abusing the drugs to get high and things, then we might invoke a lot of theories of risk behavior, classic theories of risk behavior, that social scientists have used

to inform us and to tell parents about what they should be talking about with their kids.

Work with communication is really challenging because not only do you have to talk to parents how to communicate and how to communicate effectively, but you have to know what's driving the kids' behaviors so that you can tell them what buttons they should be pushing and what they should be talking about with their kids. It's not enough that we tell them how to communicate. We have to know what is impacting these kids' behaviors so that we can tell them what to focus their communications on. One thing that I do in this context when I think of message when I'm trying to deal with drug abuse in risk behavior situations is I just take the standard theories of risk behavior and draw on constructs from those.

There was a very interesting conference that was done by NIMH a few years ago. They noticed that a large number of grant proposals that they were seeing on health-related topics

involved the same theoretical models over and over and over again. So you see the theory of reasoned action, Bandura's social learning theory, the health belief model, self regulation models and in a cross-cultural context, you see a theory of subjective culture developed by Harry Triandis. What they did was, it was a very interesting meeting, they took the primary architects of each of those theories, they took Marty Fishbein for the theory of reasoned action, Albert Bandura for social learning theory, Marshall Becker for the health belief model, Fred Kanfer for self regulation and Harry Triandis and they basically locked them in a room for a week and said come up with a common theory, integrate your stuff and see what you get.

Now I train under Marty Fishbein and I got a blow-by-blow account of what went on in that meeting and they couldn't come to an agreement, didn't work out too well.

But they did agree on classes of variables that they all agreed were very

important. They just disagreed on how you measure, how you conceptualize, and the causal priority of those.

And some of the constructs that they emphasized and that I have my parents address with kids in the context of the communications are what kids see as the advantages and disadvantages of behaviors, norms and peer influence and how can parents help kids minimize peer influence and put norms into perspective, issues surrounding self-concept images and social prototypes. The kids often engage in behaviors based on the kind of images they think it's going to convey and self images and self concept and just prototypes of the kind of person who does this seemed to be critical in a lot of adolescent behaviors. These are issues that parents sometimes need to address. Emotions and affect, emotional reactions that kids have and affective factors that drive their decisions. Feelings of self efficacy and feelings that they can do something and, finally, high risk situations and

how kids deal with high risk situations, how to avoid high risk situations and when you get into high risk situations, how to deal with them and how to act in them and what you should be doing. So these are concepts that we talk about in training parents and teaching parents how to talk about these kinds of issues with their kids.

If instead of trying to influence a risk behavior you're trying to talk about medicating some kind of condition that the kid has, then essentially the parent becomes the label. And all the concepts that we talk about with what goes into a label, the parent should talk about with the child. So I'm essentially saying that all the things we carefully think about in putting into a label, those are things we want to teach parents to be able to talk about with their kids.

When we look at labels, we should not only look at how the label is understood and interpreted by adolescents. We should also look at how the parents understand those labels and

think about those labels because so many times it's the parent who is supervising and overseeing the medication. So I think that becomes very important. The one thing that parents can do that the labels can't do is that they can monitor the kid and they can develop joint monitoring plans with the kids over time and make sure that everything is done properly across time as medication occurs.

Message timing and context, most parents for a lot of these topics think that you have to have the big talk with kids. You have to have the big talk about sex, the big talk about drugs, the big talk about alcohol, whatever and they get very nervous about these big talks. When they have them, they're totally relieved and they think they're through. They're not. Okay? Adolescence is a long time.

One of the things that I spend time doing is telling parents "Forget the big talk. Break this up into a series of smaller talks. Make it a more manageable task. Revisit these

things many times over the years. Adolescence is an extended period and don't be thinking about the big talk. Look for teachable moments. It's very important." One of the things that parents really have a problem with is how do they get conversations going. "Help me get conversation starters. How do I start talking about some of these topics?" And we need to alert them to teachable moments and how to be sensitive to those and how to get conversations going.

Listen. Don't lecture your kids. I always tell my parents in terms of style. I tell them about Socrates and the Socratic method on how he would convince people of his position by only asking questions. He does nothing but ask questions, "Why do you think that's the case" and things like that and that encourages a dialogue.

Many parents tell me that they don't get respect from their kids. Well, you get respect by giving respect and you have to be respectful.

In the communication theory, there is

an eight factor theory of communication styles which I won't bore you with, but they involve respect and all kinds of strategies that we can use to frame messages in different ways.

I'm winding down now. Sorry about this.

In addition to parent-adolescent communication, there are other communication models that we work with. There is internet and webpage communication theory, how to design communications taking into account web-based design and internet kinds of issues and then there are also media-based communications theories that are important.

I think the most important thing in all of this that I want to drive home is the key importance of building partnerships and it's very trite to say that because all of us have heard this a million times. But I do this in practice and it makes such a difference. We take university researchers who have a vast amount of knowledge about these risk behaviors and we

partner them with schools, universities and clinics in our work and I'd love to talk about the strategies that we use to do this. But I'll just leave you with the ideal.

Imagine if you could take and sit down for an hour a parent, the adolescent, a physician, an expert researcher and a school counselor and a health professional in the schools and sit down and work out together how you're going to deal with health issues for that kid for the next three or four months. And imagine that you worked out and coordinated your efforts and thought about "Physician, here's what you're going to do and here's your role," "Parent, here's what you're going to do and here's your role," "And here is how you guys are going to communicate with each other." And if you built those partnerships between the physicians, the schools, the parents and those of us who do research, you can be so, so much more effective.

We've been doing that in our work in

New York City and it's very dramatic, the effects that can result from that. We use the schools to outreach to parents and we literally can reach almost every single parent who has a kid in the schools through the outreach efforts that we do. In the clinics, we have outreach efforts where, for example, all the kids in the schools have to get a physical exam before they attend school in a given year.

In the low income neighborhoods we work with, there's generally one health center where almost everybody goes and they go to get their physicals and they usually go with a parent, usually the mother, and they usually wait about 45 minutes. Then the kid goes in for the physical and the mother is sitting there for another 20 minutes, 30 minutes, while the kid gets the physical. Well, we have social workers sitting in the waiting room just waiting for these down times and we basically take the mother while the kid is in getting the physical and administer communication programs to them and

tell them how to communicate effectively with their kids about topics and use that time to reach out to the mother. We coordinate those efforts with the physicians. So the physicians know we're doing that. They know what we're saying and they actually tell the kid that "Look. Your mother is being told now about some issues to talk with you about and here are some of the issues they're going to talk with you about." And we can coordinate those efforts accordingly.

That's it. I'll end there. Thank you.

(Applause.)

Dr. Sanders: Good morning. It looks like it's a Miami morning. I have the good fortune to find out that Jim Jaccard is now a neighbor of mine in Miami.

I work at the University of Miami as a general pediatrician and also spent the past five years as a Robert Wood Johnson General Physician's scholar looking at the relationship between parent health literacy, so much an overlap with Jim's work, and child health

outcomes. But I tried to put some of my research in the context of the purpose of today's workshop. Here's where I work, the view out my window. A little bit warmer there today than it is here.

With that in mind, I wanted to give you an overview of my understanding of the way in which health literacy impacts adolescence and may impact the use of over-the-counter drugs. First, I'll give you a brief overview of the status and what's known about health literacy in the United States generally, then what's known about the health literacy of adolescents and young adults, finally the very little we know about how health literacy impacts over-the-counter drug use among adolescents and finally leave you on the theme of today with some thoughts about how this inform a research agenda.

A recent Institute of Medicine report, not so recent anymore, it was released in 2004, concluded that at least 78 million U.S. adults or 36 percent of U.S. adults do not have adequate

health literacy defined as the capacity to obtain, process and understand basic health information, that information necessary to make appropriate health decisions for themselves and their families. This is supported by work done by the National Center for Education Statistics, the National Assessment of Adult Literacy, which was performed in 2003 and the Report of Health Literacy Skills came out in 2006 that supported this finding.

Just to put it in very real fundamental terms, approximately 14 percent of U.S. adults have below basic literacy skills and the remainder of that 36 percent have basic literacy skills. Examples of below basic skills in the pediatric context are the ability to use the dosage chart on an over-the-counter medication or to give two pieces of information back from a health information pamphlet. And examples of basic skills are the ability to interpret an immunization schedule for your child, to interpret a growth chart given to you by a

physician or to follow instructions in a prescription to take medicine on an empty stomach.

What's interesting about adult literacy skills is that in many context, at least clinical context where I speak about this, many feel that this is just a restatement of the known health gradient associated with income and educational status. But we know that many adults with below basic health literacy skills have graduated from high school or college and that it really is a separate construct.

Further we know that controlling for many of these other socioeconomic factors poor health literacy in adults is significantly related with a number of health outcomes in these general categories: health outcomes and access to health services, health behaviors and knowledge about health. Many of these factors that have been studied relate directly to some of the greatest concerns for adolescent health, namely, substance abuse, violent behavior, STDs and

knowledge about birth control and so forth.

Most of my research I mentioned before looks at the impact of adult literacy on the health of children of all ages, particularly more recently actually the health of younger children. We know that young children of adults with low literacy are twice as likely to lack the basic components of a medical home even after controlling for many of the other significant socioeconomic factors that are normally associated with that outcome.

We also know that child use of urgent health care services is significantly related to parent health literacy and that those with low literacy skills are more likely to have additional unscheduled visits to the clinician for their child.

Overall, the health system costs of low health literacy are actually difficult to come by. Very well done health economic analyses have not yet been done, but the estimates are a cost of $25 to $70 billion to health care system a

year just based on disparities between the health literacy of the population and the complexity of information that goes through the health care system. So it's based on this. I mentioned the Institute of Medicine report that was put out a couple of years ago and a number of research and policy initiatives put forward to try to address the factors in health literacy that contribute to health care disparities and increasing cost.

I want to turn now to what we know about the health literacy of adolescents and young adults to focus more on the topic of today's discussion. There are a handful of tools available to measure adolescent health literacy. I'll make the case that none of them are quite sufficient really to most of the clinical problems that I see as a general pediatrician taking care of adolescents and many of the research questions coming up right now.

The most recent tool developed by Terry Davis was an adaptation of a tool she calls the Rapid Estimate of Adult Learning in Medicine, but

this was adapted for teenagers. It's simply a list of words that has medical content in it that's appropriate for child in middle school/high schools levels. Child are asked to read the list of words aloud and they're graded on the number of words that they can read without tripping over them. It's a proxy for general readability and it has fairly good correlation with other measures of readability.

Another test developed that has not been validated for the adolescent population, this was developed by Ruth Parker and others, is called the Test of Functional Health Literacy for Adults. The short version of this is 36 items. It takes about seven minutes to complete. It tests only what's called prose literacy and it has content really from the adult health care environment, preparing for an upper GI, understanding the Patient Bill of Rights, the sort of things that most adolescents don't often use. Although I'll show you in a second that some of these tests have been used with

adolescents with some interesting results.

And, then finally, I alluded before to the most recent and most comprehensive study of health literacy done nationally. This was the National Assessment of Adult Literacy. It was performed on over 18,000 adults across the United States, nationally a representative sample of whom about 1,000 were in the age of 16 to 18. In that test, there were 28 health literacy or health specific items covering three different domains of adult health literacy: prose, document and quantitative and three different areas of health content, namely, health prevention, systems navigation and medical treatment.

An example of the sort of questions asked in this test by the interviewers was an open-ended question related to this brochure. According to this brochure, why is it difficult for people to know that they have high blood pressure and they need to track through the prose and find the answer to that question.

So from that study again done in 2003

and released in 2006, we actually know something about the health literacy of older adolescents, namely, 16 to 18 years which is mainly that it maps pretty closely to the health literacy skills of the general adult population. Eleven percent have below basic health literacy skills. Those are the same sort of categories of skills I described earlier and 23 percent have basic skills, again, suggesting that roughly one-third have profoundly limited health literacy skills.

We know that health literacy skills in general decrease with age, but the most of this decrease isn't until much later in adult. We also know a little bit about health literacy from other estimates done on other age populations. Not many studies have been done of this, but using the tools I mentioned before, all of them seem to congregate around finding that roughly one-third of adolescents and young adults have significant problems performing the numeracy or prose tasks necessary to use most health documents. A couple of the studies that I did,

one was a high risk group of younger children who were part of a birth cohort that we follow at my institution and another of teen and young adult parents.

Recent study in the *Journal of School Health* also looked at adolescent self-report of their health literacy. It didn't actually use any of these standardized measures I mentioned before, but it did ask teenagers to report their own self assessment of their difficulty understanding health information and surprisingly they were quite insightful, although not quite one-third, 22 percent of them did report that they had difficulty understanding health information. This study was done through area health education centers in partnership with schools and so they were in the context of receiving some health information through those programs and, like I said, about one-fifth of them reported some difficulty. They also reported many different sources of health information, very much in line with the larger

body of literature that Jim was alluding to and that schools and clinics were their main sources of health information in these early preteen and early teen years and that interestingly the interest in learning about health information decreased with increasingly age in this, again, very young adolescent population and with decreasing self efficacy.

Again, back to some of the research we've been doing with this birth cohort, we looked at number of factors, both cognitive, developmental and social, and tried to find out what most mapped with adolescent scores in a couple of the instruments I mentioned before, namely, the REALM-Teen and the S-TOFHLA measures of adolescent health literacy, and really the most marked factor that correlated with adolescent health literacy, again reinforcing some of the themes that Jim just brought up, were the health literacy of the mothers and other care givers in their environment.

We don't know a lot about the way in

which health outcomes are associated with health literacy as I've just described it's currently measured. But we do know something about the relationship between a teen's performance in school particularly in the area of reading and their own health outcomes. We know that adolescents who read below grade level are an increased risk of many health outcomes. One of them is school dropout which is really in this age group one of the greatest predictors of the worst health outcomes, certainly, risky sexual behaviors and substance abuse are closely correlated in terms with school dropout and we know that teens who are reading below grade level when they enter 9th grade are much more likely to drop out of school.

We know that tobacco and substance use are associated with reading below grade level, sexually transmitted illnesses, and, intriguingly, violent behaviors and just to give you an example of that, again, Terry Davis who I mentioned before has been doing a lot of this

work at LSU, documented about seven years ago some very significant and independent relationships between teen reading ability based on performance in schools and their likelihood to be involved in a variety of violent behaviors whether that would be carrying weapons, specifically guns, or having been in a fight resulting in injuries in the previous 12 months. Again, this was controlled for the other socioeconomic and demographic factors and this association is still being teased out by others perhaps related to self-esteem and some of the other issues in adolescents' lives during this time period.

I want to turn now to what again little I mentioned we know about adolescent health literacy/young adult health literacy and the use of over-the-counter medications. Just to review my own clinical perspective on this, again much of this was reviewed yesterday and Eric and Jim went over this, but from a clinician's point of view we think about these sort of factors known

to influence adolescent health behaviors and likely their use of over-the-counter medications by transference, namely, social factors, ethnicity, peer, family, systems factors that have been mentioned before that will be reviewed at this meeting and then, finally, individual factors and as I mentioned parent and child health literacy likely have some influence on an adolescent's and young adult's choice of medications. But we know little about that.

Back to, again, our best national source of evidence on adolescent and young adult health literacy, namely, the National Assessment of Adult Literacy, there was one of the 23 items that did investigate the use of over-the-counter medication. Basically an over-the-counter box of cough medication was presented to the respondent and the interviewer actually pointed to the paragraph about what to do in the case of an overdose of this medication. And the question was asked, "What should you do? What does the label say a person would do in the case of an

overdose?" And more than half of the individuals responded incorrectly to that item.

We don't have any breakdowns of many of these responses by age. However, just this month, that data set has been opened up to more public use and investigation and I'll suggest for our research later there might be some interesting research questions that we can ask of this data now that it's publicly available.

A couple of my colleagues and I at Vanderbilt, University of North Carolina Chapel Hill and at the University of Miami were interested in further investigating and developing a tool to measure actually parent health literacy. Namely, we developed something we call the Parent Health Activity Test. It has the acronym PHAT which appeals to several of our adolescent patients and it's 22 items that attempts to explore the document, literacy and numeracy of parents in a health context, really focusing on daily care practices very important to young parents when their children are young

and includes the use of four common, over-the-counter cough and cold medications for their infants, not for themselves. It was validated against a couple of the existing measures. One I mentioned before, the S-TOFHLA. The other a measure of math skills, namely, the WRAT-3.

Here's an example of one of the items from that 22 item test. Your three-year-old, 35 pound nephew comes to visit and he suddenly has a fever. How much of this product should you give him? And we did give them the label. That should come up there and asked them, basically challenged them to negotiate whether to dose this medication by age or by weight and to see what conclusions they came up with. There were about four of those items in addition and they related to, I'm sorry, six items that related to four different cough and cold products.

I'm not going to present all of the results from the validation of that study or all of the items, but I will summarize some of the hot-off-the-press issues. This has been

submitted as currently under review by JAMA for publication. We investigated 182 parents of infants less than 12 months of age and again across the three institutions and found again similar findings about their health literacy skills. But since we were looking specifically also at numeracy skills, we found that many, most, 83 percent of these parents had less than 9th grade numeracy skills. This is a pretty varied population, a little lower income than the general population, but again a pretty varied population at these university-based clinics.

Eighty-six percent of these parents considered over-the-counter cough and cold medications appropriate for children less than age two without consulting a physician. Again, some of these findings are not relevant only to today's discussion, but also the recent FDA Advisory Council commentary on use of over-the-counter products for younger children.

Interestingly, fewer than half of parents even when presented and given plenty of

time with the package choose to read the dosing instructions in the context of being asked many questions about the indications for these products and when asked to reflect on what influence their use of over-the-counter medications, their understanding of the reasons and indications for these products, there were really two factors that most influenced those responses. One were the parent numeracy skills themselves, so those 17 percent who had adequate skills versus the 83 percent who did not and then aspects of the packaging itself, particularly infant-related content on that packaging that they spoke to, both the word “infant” being on the packaging and very responsive to the graphics, not the words and the dosing part of the instruction but the graphics, infants, teddy bears, droppers, etc.

Here is just a few of the data to support that finding. Again, looking at with each increasing grade level of numeracy skills, there was less of a propensity for parents to

report that an over-the-counter cough medicine was appropriate for children, less than two, and with their statement that they were responsive to each of these package components. Whether it was the word “infant,” infant-related graphics or other language related to that, there were increased odds of reporting that the medication was appropriate for younger children and infants.

I mentioned I wouldn’t go into this in too much detail. We’re just completing the write-up of this manuscript to describe the actual answers to individual questions about skills in using packaging to dose over-the-counter medication. Actually stating the indications for medication packages, there weren’t too many incorrect responses there. But the greater difficulty that parents had were in converting teaspoons to milliliters and being confused about those components of the dosing recommendations, understanding how to dose by weight and understanding which of four medications to choose for various indications,

sort of that effect of going to the pharmacy and trying to figure out what to choose from what's on the shelf. Still on packing of that information and haven't fully analyzed that yet.

So based on my perspective as a clinician and as someone who has been spending the past four years sort of thinking about this relationship between health literacy and health outcomes, health behaviors, health choices, what research do I think is needed going forward? Here are some of my suggestions and I'm happy to be challenged about that here and also in this afternoon's session. Really in four different categories would I urge further work.

First is better tools to measure what we mean by teen and young adult health literacy, really first looking at more in detail at the individual items from that National Assessment of Adult Literacy and going on from there, working with experts in communications such as JAMA and others to understand what else do we need to be measuring on a routine basis.

Second is understanding the relationship between teen health literacy once we've measured it well enough and teen health behaviors generally, the risky health behaviors that really portend major health problems, not just for adolescents during their adolescent years but across the life course.

Specific to the questions being considered today, namely, over-the-counter medication use and medication use, what is the relationship between health literacy and that use? Particularly in two areas of interest to us as physicians, one is the adherence and error rates among teens with chronic illness. I'm not sure how much that was discussed yesterday. This is a very special population of children and teens, namely, those 10 to 15 percent or so with special health care needs who require regular medication and some of my colleagues including a rising star at the University of Rochester are really trying to take a closer look at this.

Secondly, moderating effects of

medication costs and packaging on teen use, this was alluded to before. There's more and more literature indicating that we shouldn't forget about those, that very fundamental, sort of obvious component of cost driving teen behavior and choices as well as those of their parents.

And then, finally, without going into too much detail, this was discussed earlier today and will be continued to be discussed, interventions to reduce literacy-related health disparities. This overlaps with -- Doesn't need really to be literacy-related but in terms of some of the early findings both in the world of adult health literacy and parent health literacy. We know that what needs to be done is to work on better partnerships, to improve doctor/teen communication, including the parent in that partnership, health information kiosks as well as individuals placed in particular settings. Jim talked about the teachable moments and whether they be in waiting rooms or in schools and so forth to deliver tailored messages. It's part of

eHealth, enhanced health curricula in schools, social marketing as well as I mentioned, eHealth, electronic health information systems.

So those are the comments that I have. I want to thank you and again thank the Robert Wood Johnson Foundation for supporting my work in this area. Thank you.

(Applause.)

DR. BOSCO: So the government gives and the government takes away and we're 15 minutes late. I apologize. But we will have a break here which I have we'll be back here about 10:10 a.m., I guess, for our next two speakers. Off the record.

(Whereupon, at 9:58 a.m., the above-entitled matter recessed and reconvened at 10:12 a.m.)

DR. BOSCO: On the record. We're going to get started with Connie Pechmann's presentation and just another quick announcement. The people who are on the roundtable should meet in F-1 for lunch and discussion about how the

roundtable is going to go.

DR. PECHMANN: Good morning, everyone. I'll give you a chance to sit down. That was a short break. Tough.

My name is Connie Pechmann. I'm from the Paul Merage School of Business at the University of California, Irvine, and I'm going to talking to you about what I've learned over the years about teen psychology as it relates to the marketing to teens.

To begin with, I'll just give you a brief overview of my background in my research and then we'll talk about psychology and adolescent drug use, marketing and adolescent drug use, industry self regulation. So we have quite a bit of experience how do other related industries like alcohol and tobacco self regulate to protect adolescents from marketing and then the role of public service announcements or social marketing, what kinds of messages could be used either by the industry or the government to ensure safety and effective use of over-the-

counter drugs. And then after each point, I'll talk about, since my background is a little different and it's more on tobacco and alcohol and marijuana, how might this apply to over-the-counter drugs and what are the unanswered research questions in each area.

As I said, I'm a professor in the School of Business. I'm a Marketing Professor. I have an MBA, a masters in Psychology and a PhD in Business and originally I did work on just general advertising and price advertising and deception in advertising and then about 1990 got involved with tobacco-related advertising. So I've had five grants from the California Tobacco-Related Disease Research Program studying how adolescents respond to cigarette ads, how they respond to anti-smoking ads, product placements and movies, ads before movies that would try to mitigate the effects of smoking in movies and most recently, portrayals of smoking in television and television shows including entertainment education.

So, basically, I've been studying primarily in the 8th and 9th grades because I find them to be the most interesting group in terms of being very malleable about whether they're going to use drugs and where they're going to smoke. And I think because of my experience with tobacco I was brought in with the ONDCP, the Office of National Drug Control Policies' Anti-Drug Ad Campaign, and for several years was on what's called the Behavioral Change Expert Panel which was a small group of academics with backgrounds in communication and marketing and public health to ensure the campaign was changing behavior. In that campaign, I was responsible for helping to create the strategies for the messages and testing of the ads before they went on the air and after they were on the air. So we had a lot of real world experience about how the messages were working in the anti-drug arena.

Now I want to say obviously there's a big difference, many differences, between tobacco, marijuana and over-the-counter drugs.

But there probably are some important lessons we can learn from those arenas in terms of understanding adolescents, especially adolescents' misuse of prescription drugs and also maybe something just about their general use of prescription drugs. Or in any event what are the research questions that were important in these arenas and would they apply in this new arena?

To begin with in terms of the psychology, you've discussed this a little bit yesterday and today also, how prevalent is adolescent drug use and abuse and why are adolescents using drugs and which adolescents use and abuse drugs? These are very important from a marketing perspective because you can't go on to create messages unless you can answer these questions.

The classic source of information that we use in the tobacco and alcohol and marijuana arena is Monitoring The Future. You can pull those data form the website and you're going to

see that illicit drug use is pretty high. They start with 8th grade and then go to 10th and 12th and you're seeing steady increases with 37 percent, the same percent basically that's health illiterate in 12th grade using an illicit drug and if you see marijuana, that's the primary illicit drug being used. The numbers are pretty high, one-third of 12th graders are using this illicit drug. It's kind of scary and they're down from the past.

Alcohol even higher. You have one third in 8th grade using up to two-thirds using and in terms of drunk which is six drinks I think we have half who are drunk.

In the past year, cigarette is lower, but still you have almost one-quarter or one-fifth anyway using cigarettes in the past month. Those numbers are big. This is where many of us have been focusing our attention and because you look at the numbers for over-the-counter drug use with these standard surveys and these are focusing on -- because Monitoring The Future is

focusing on abuse, then these questions focus on abuse, too. Use of cough/cold over-the-counter to get high are in about the five percent range, a slight increase with age and then use of steroids in the past year, I assume that's illicit use, is about one percent.

I think the interesting issue here is that we don't have much data other than these two questions that have added recently about how big an issue this is because it's under the radar from the standard survey questions. There are just a few questions and I'm not certain these are the only questions. But I guess we would have to think about what other questions should be added to this survey if we're concerned.

Now why do they use and abuse drugs? I think there are several reasons. One is that in adolescents youth are extremely self-conscious and insecure. So they're looking for props to make themselves feel more comfortable in social situations and they're looking for a way to fit in and they think that cigarettes or whatever

help them feel more comfortable. And also there's a body of literature on how unhappy adolescents are which is sad because you think back that's the best years of your life. But actually when you look at it objectively, scientifically, teenagers are the unhappiest group. They have extreme negative mood swings. They've very sad, angry, anxious and the research especially University of California Irvine where they're monitoring kids with Palm Pilots, you're finding when they feel anxious and sad. Then that's when they're prone to grab a cigarette and after they smoke they don't feel any better, but they think they do or anyway that's why they're using it.

Then, of course, because of the psychology of adolescents across species and the nature of adolescents, they are prone to risky, impulsive behavior, some of which is adaptive, some of which is not. So drug use fits into this idea of a risky, impulsive behavior.

They attribute their use to peer

pressure and part of that is complete miscomprehension of the use. Every time I look at the percentage of teens that use versus how many actually use in the schools, it's double or triple the perceived prevalence versus the actual prevalence. So the drug use sticks out like a sore thumb and everyone notices it and it seems like the prevalence is very high and everyone is doing it and therefore I have to do it too.

And if you ask them about marketing, they say it plays absolutely no role whatsoever, you know, ads, movies. Maybe there are some kids that will mention it if they had an media literacy class. But most kids will say, no, it's peers. But what my own research shows is that the marketing just accentuates their attention that they pay to drug use. So if they've seen a cigarette ad, they notice more people smoking. Everyone who smokes looks cooler. So it's distorting their perceptions or priming their perceptions. This tendency to see everyone using it and cool people using it is accentuated after

they've seen the marketing communication. Everyone looks like Joe Camel or Marlboro Man or Virginia Slims after they've seen those ads and they have no idea this is happening.

Of course, we also know there is considerable co-morbidity in use so that all of these are one big picture that they're drinking, they're smoking, they're using marijuana. So there's a lot of co-morbidity.

And which adolescents use, I think essentially what we're seeing is a lot of personality traits and also psychological disorders are predictive of abuse. But in terms of personality traits, the two that seem to stand out most commonly are conduct disorder, those are kids who disobey and break rules, and of all the predictors I've looked at, that's the No. 1 predictor abuse. It's just another way of breaking the rule.

And sensation-seeking, so adolescents overall are seeking riskier, more high sensation experiences than those are even more likely who

just want excitement and change and novelty in their life. Drug use is a real simple way to get that kind of high that they're looking for.

And on a more clinical arena, you're seeing kids with attention deficit and more serious disorders and adults alcoholics and people with schizophrenia are using tobacco as self-medication. So at the more extreme level, you're seeing that happening. At least with adolescents, demographics aren't predictive abuse and aren't predictive of reactions to marketing. So male/female, different ethnic groups, some slight variations, but basically demographics aren't very predictive.

But the No. 1 predictor of smoking in adults is socioeconomic status by far. But you don't see that in adolescents. You start to see that when they go to college that the college-bound ones aren't smoking. They stop. They don't become addicted. They were occasional smokers and they stop when they get to college.

What does this have to do with over-

the-counter drug use? As I said, if you look at the statistics, you could argue more money should be spent and has been spent on tobacco and alcohol because those problems are much bigger. If we're going to argue that this problem is big, we need to get better data to see where is the problem, how big is the problem, is it a serious problem, so not just the frequency but the outcome.

But overall what we see is, for the other drugs, if we're talking about abuse, the reasons for abuse are similar and the abuser groups are similar. It's because of negative affect and sensation seeking that you see this in the other areas.

The unanswered research questions here, I think, are is there anything different about over-the-counter drug abuse or misuse relative to what we've already learned from years and decades of research in the illicit drug arena. Are there different reasons for abuse or for misuse? Maybe everything we've learned doesn't apply. So there

are just completely different reasons. I don't think that's the case. I think a lot of it is still going to be about insecurity and looking better and negative mood and self medication. But there might be some new reasons, too. And are there different groups who abuse? Maybe there are some different segments who are or who misuse that just are off the radar because it's not related to other drug use.

Marketing in adolescent drug use. So here, we're going to now talk about how marketers, who market correctly or incorrectly to adolescents, market to them. We're going to talk about marketers' beliefs about teens and how they can reach teens, what media they can use, what role models they can use, what messages they use and what we know about the impact of marketing on adolescent drug use. Again, given my background, we're going to talking mostly about tobacco and alcohol.

Now the first thing is there's extensive quantitative data that allows marketers

to reach adolescents. Every major media is going to document the demographics of their readership or their viewing group and so they can market themselves, “This is a youth-oriented media” and they market it two ways, what percent of teens you can reach and what’s the total number that you can reach, what percentage of their readership is teens and then how many teens you can reach and what percent of the teens can be reached.

So marketers, I mean, there’s just huge media departments who are analysts that use these data and figure out what media to choose. So they are very astute at reaching teens. With cigarettes, this was before the Master Settlement Agreement. There wasn’t officially the agreement not to target teens. But you’re seeing these kinds of numbers. If there was a magazine with four percent youth readership, you’d only get a 32 percent odds of seeing a youth brand ad; whereas, if there was a 34 percent readership, it was a 92 percent odds. So there’s just lots of

data to show that marketers can reach adolescents if they want to. The data are available. No problem. Very quantitative.

And how do they reach them? They tend to use very young, edgy role models, role models who are just slightly older than the audience they want to reach, not the same age, but slightly older. We know the most about this with tobacco because there's been a lot of research. Joe Camel was chosen to appeal and, of course, their segments are very specific about the personality trait of the person they're trying to reach.

For Joe Camel, he was chosen to appeal to 14 to 18 year old underachievers with insecure futures who therefore were very concerned about immediate peer acceptance and social acceptance because that's what their life was all about. Joe Camel's whole character and persona was designed so that if you smoked Camels you would be like Joe Camel and you could belong to this group and you could feel like you really belong

to this group and fit in.

And, in terms of messages, the message that is overwhelmingly used with adolescents is peer acceptance, much more so than with adults where we have more benefit messages and be a good mom, be a good dad, that sort of thing or this product will work for you or cost. The whole thing with adolescents is peer acceptance.

When marketers design platforms, they'll talk about exactly what benefits they're trying to sell with the product that are allusive. In the case of Joe Camel, they were trying to convey the message that smokers are masculine which I guess women like, too, individualistic, admired and respected by friends, young, contemporary and fun/exciting. I think this was in contrast to the Marlboro Man who is older and more sedate. For any campaign, you're going to see these types of benefits which are not actual. They're psychological benefits. They're not true benefits of using. They're created benefits. They're created by marketing.

And then in terms of the impact, now this is a very robust finding that adolescents are more responsive to marketing than adults because they're at the age where they're starting to choose their own brands and, to some extent, they might choose brands of their parents. But often, they will choose brands that are not what their parents chose. Overall, there is no good prediction from inter-generational influences because some people reject, some people don't care, some people accept. Overall, there is no effect of parents.

They're trying to choose their own brands and then they'll be lifetime users very often because they choose the brand and then they stick with it. In the case of tobacco, there was a very quantitative study done that showed that the impact of ad expenditures on the youth brands for youth was three times larger than the effects on adults. So you got three times as much for your money if you were promoting a youth brand than if you were promoting an adult brand because

the youth were more receptive to the message because this is the time when they're choosing brands.

It's directly increasing primary demand and also demand for certain -- it has to increase primary demand because there was actually an increase in the total market because of the advertising. And we don't see a lot of imitation even in this quantitative research where what's happening is we're affecting adults with advertising and then the adults in turn are affecting adolescents. Really, these are adolescent-specific campaigns targeted with adolescent messages, adolescent role models, adolescent media and adolescents are responding individually.

The conclusion is when marketers have products that could potentially appeal to adolescents they're going to go for it and they know how to reach them. They know what media to use. They know what models. They know what messages and they're going to be highly effective

and adolescents are going to respond very favorably because they monitor this. I know because I monitored it for the Anti-Drug Campaign. They're going to monitor the effects. They're going to see that youths are even more responsive and in turn they're going to spend more. There's a natural tendency for marketers to target adolescents if the product is at all remotely of interest to adolescents.

The unanswered research questions would be should be -- First of all, we don't even know, I don't know, what over-the-counter medicines are targeted specifically to adolescents, how much money is being spent and maybe it's not important to know. But unless we know that, we can't answer these questions. Are different messages being used in the over-the-counter arena? Are the messages more health-related or more objective, more factual or is it still image-oriented, peer appeal, peer acceptance messages that can't be verified? And do we care? And are there different effects on adolescents for these

over-the-counter campaigns versus drug campaigns? Is there anything different at all? Is there anything we need to worry about? Are there new messages being conveyed that we're not aware of?

And there is some evidence that there are unique over-the-counter ad effects with adults but not with kids and the two most important ones are on this slide. One shows risk compensation. So there's extensive research in economics about risk compensation. Essentially, it says that if you lower the risk of something, you may just increase other risky behaviors because every person has a set level of risk that they want to live with, that they're comfortable living with and with adolescents that risk level is higher and the classic example is with seatbelts. When you had people wear seatbelts which reduces the risk of driving, it's not clear cut evidence, but there's substantial evidence indicating people drove faster and so there were more accidents involving say pedestrians who, of course, don't have seatbelts on. So they were

adversely effected because people felt safer. So they then drove faster because they want to go up to that risk level. We have this need for arousal and risk which is even higher among adolescents.

What's happen is a series of studies were done showing this is the case with things like nicotine patches, debt reduction and things like this that if you advertise remedies people go "Oh, there's a solution" and so they are actually less likely to want to quit or less likely to do anything now because they know that in the future it sort of reduces the risk of that behavior and therefore they're more likely to continue with the behavior or engage in more of the behavior because they know there's a solution. And I know this was a problem with the AIDS drugs when the AIDS drugs came out. People were concerned. "Okay. Well, I can engage in this risky behavior because there's a medicine there" and there was no proof of it. But now there's a series of studies that indicate this

could be happening. So that's a particularly unique effect for over-the-counter ad effects that you can inadvertently by saying there's a remedy, you can actually increase the risky behavior the remedy is supposed to cure.

The other is a placebo effect which is again unique for the over-the-counter drugs or drugs that there's a series of studies here, these are pretty recent studies, on over-the-counter energy drinks, Sobe and those kinds of things, that basically amazingly enough that in a controlled experiment, so people didn't know what condition they were in, if they got a higher priced drink, they behaved -- it was a classical placebo effect in a marketing context. Just a higher price of the Sobe, $2 versus $1, $4 versus $2, got people significantly more life. They felt they had more energy and they solved more puzzles. And then if they saw an ad, that like doubled the effect. An ad and the high price made the this product seem very good and you saw these really strong effects on people where they

were actually performing better.

What are the implications of that for over-the-counter drugs? Are we creating in some ways this benefit that is psychological and is it going to be worse with adolescents because they are looking for risky kinds of things? Are we encouraging some behaviors that might not be good?

The industry self-regulation. There are industries that have been worried about targeting youth with drug messages and this talks about what they feel are problems and how they try to resolve them. Overall, there's a concern about media. The idea with media since it's so easy for us quantitatively to reach adolescents if we shouldn't be, let's set some very quantitative rules about how not to reach them.

The standard rule is to look at the percent of the youth in the population. There is roughly 30 percent of the population under 21. Alcohol, the Beer Institute, has a marketing code, a voluntary code, that they themselves

established and they themselves monitor to the extent they monitor it. And they say they won't use media reach by 30 percent -- that reach where the readership or the viewership is comprised of 30 percent or more youths. Since youth is 30 percent of the population, they'll use media that reaches up to 30 percent of the readership being youth. But beyond that, they're differentially targeting youth with the media and they say they voluntarily won't use that.

Then in the case of tobacco, they've said under 18 is 26 percent of the population, but they're not going to touch any media which is read by 15 percent of the youth. They're really careful about trying to reach youth now. All the tobacco companies have agreed to that. Then Philip Morris has also said we won't use any magazines with more than two million youths because it might not just be the percent but the total number of youths. So two million seems to be an important number, too. We don't want to reach more than two million youths.

The point is that if you ask them not to reach youths, they can set up quantitative standards that are easily followed not to reach them and they themselves have done some of this themselves. It's a clear set of rules.

In terms of role models, the Cigarette Advertising and Promotions Code says that cigarette ads should not suggest that -- remember all the messages are about peer acceptance and these sorts of things, what their codes essentially say is that you can't say smoking is essential to any of these benefits -- the only way you can be attractive, prominent, successful is by smoking. That's their code.

The Master Settlement Agreement said no cartoons because that's clearly targeting to youths and the FDA proposal said "We think all images are bad" and saying smoking's not essential to sexual attractiveness doesn't mean that they clearly imply it's related to attractiveness even though it's not essential to. Therefore, no images at all, we're just not going

to not allow any images because we know that the images you're going to choose are going to be attractive. So you can't use any images, just words."

Beer has a code very similar to the tobacco code saying you can't represent that beer consumption is essential for success or status. You can associate it with success or status as long as it's not essential to success or status. It's kind of hard to monitor those kinds of rules. And then they also have a voluntary code that you can't show excessive drinking, intoxication, illegal activity, promiscuity, sexual passion. So they have a set of things that those are way too edgy and inappropriate and you can't show those in beer ads. It would be basically not showing any type of abuse.

Now in terms of the impact of the industry regulation, we have no idea. We don't know compliance because it's voluntary. So there's no one monitoring at all. So we have no idea and we don't know whether this has been

beneficial at all. But it's at least an attempt.

In terms of adolescents and over-the-counter drug use, if we do encounter problems, likely the industry could and may adopt some voluntary regulations so the government wouldn't have to get involved. Once you identify the problem, often the industry will come forward and say, "We'll try to fix that with some kind of voluntary regulation." We don't know if they work, but, at least, they would be on the books and the more quantitative they are, the easier they are to monitor and the more subjective they are the harder they are to monitor. But as to whether this is really helpful, we're not sure. It seems to make sense. But there's no research.

In terms of public service announcements, this is where you'd require or ask for warnings or the government would come in with public service announcements. So what I'm going to talk about here is what the messages that have been used with adolescents in the past, what do we know about the impact on drug use and what we

know about inadvertent adverse effects because there's quite a bit known on that.

The kinds of messages that are used fall into these general categories. The classic one is there is a severe health risk associated with this. Watch out. Social risk which is the one I focus on a lot is just basically countering the messages in cigarette ads or movies saying this is going to lead to disapproval and the more, say, in California where second-hand smoke is such a big issue, that's a very credible message that it can lead to disapprove.

And to whether these are objectively true, they're not objectively true in the case of the (Laughter) either. Do you know what I'm saying? It's just an image. So it's actually very credible to tell adolescents this is going to lead to disapproval. And overall, the research in psychology shows that negative messages are very powerful.

There's an issue of behavioral efficacy. So you could scare them as much as you

like. But unless they feel they're able to perform the behavior, you're not going to be able to persuade them. They may even deny the risk. If there is an issue of efficacy, you have to reassure them, say, in the case of condom use that they know how to do it, they can do it, they can get their partner to use it.

Social norms are a big issue, trying to say "Most people are doing this right. You should be part of it. This is what everyone else does. So you should do it, too."

Then in the case of tobacco, we have a lot of these anti-industry ads that are trying to say, "Don't let them fool with marketing. Resist the marketing."

Now the impact of these in my research, we have compared the different ones sort of head on. The social messages seem to be the most effective which is consistent with the commercial messages and they've also found though which is kind of a surprise to me that you have to have both positive messages and negative messages and

I think I learned this from the Anti-Drug Campaign because we came in as public health people saying, “You have to have negative messages. Talk about risk. Talk about social risk. Scare the living daylights out of them. Get them to stop.”

And the Ogilvy & Mather people were running the ad campaign and we were like “We never do negative messages with adolescents. It’s all positive. ‘How cool you are. How much you can fit in.’” And we thought, “Wow. Isn’t that weird? There’s this huge discrepancy between public health and these people with tons of experience with adolescents but in the commercial realm.”

And so we did a study to show there’s actually two groups of adolescents and including smokers. There are some adolescents that are security and safety oriented. Those probably end up being public health people and they like the negative messages. They want to be scared. They want to be told about risk.

But then there's another group who often maybe ended up being more marketing kinds who are much more persuaded by positive messages. "Tell me what's good." They just turn off the negative message. They want to hear, "What will make me happy. What will make me" -- So you need actually -- It's just two sides of the same thing. You could say "Smoke and be rejected" or "Don't smoke and be accepted." And we just kind of changed the amount of time in a 30 second ad. You spend 25 seconds on the negative versus five seconds on the negative. It's the same message, but it's whether it's half empty/half full or like 20 seconds versus 10 seconds. You can get a big change in response and essentially by having these two valence messages you can reach both groups which I think is an important message no matter what we do.

And then there are some messages that will actually be counterproductive. So the "smoking kills you" message the more you say "smoking kills you" the more it's like forbidden

fruit and this has been shown with labels on movies. If you say “R” you’re going to increase adolescent’s response they want the R-rated movie, just the same movie, same description, but you say R rating and their intent to buy it or their actual choice goes way up because you’re signaling something that’s actually alluring to them as long as they don’t view themselves vulnerable to the risk.

They go on the scariest amusement park rides. They want the riskiest things. And I remember we used to smoke and go “Ha-ha. One minute off our lives. Ha-ha.” That was our big joke. So that’s not a good thing.

And normative messages can also have very negative adverse effects. A lot of work has been done on college campuses about drinking and scientists objectively figured out what was the norm and conveyed the norm in the message and the norm was most students have five or fewer drinks. That’s still a lot of drinks. So what you end up having is conveying messages to those who are

naive and saying, “People drink five drinks. Drink more.” So you actually get these boomerang effects and you see it with energy use where you say most people use this much energy and some say, “I use more than that. I should increase my energy use.” So it’s really hard to use these normative messages because the people who weren’t at risk now of a sudden are because you’ve told them about what the majority does which is worse than what they did.

Also there are a lot of examples of anti-drug ads that seem to be possibly counterproductive from the research like some ads which would say, “No risk to drug use.” And you think why did people create this ad, but I’m just saying that they did. And the tagline was “Marijuana can make nothing happen to you, too.” I think the idea was nothing would happen good, but they got the idea nothing would happen bad. So you just have to be very careful because a lot of very smart people put together that ad and thought it would work, but it looks like it was

counterproductive.

Or benefit to drug use, a lot of ads will tend to show attractive drug users so that people will pay attention to the ad. And so there will be criticisms. The woman looks like Winona Ryder. She's wearing a tight tank top. No visible track marks. The visual message people are getting is "drug users are cool." And the verbal message they may not even hear. So it's just very tricky to make sure you don't have -- by having fun sensation seeking ads you may inadvertently say the wrong message and we found a lot of that happening with the Anti-Drug Campaign. So we didn't produce certain ads because they had the potential to create adverse effects.

So the conclusion here is that public service announcements aren't a panacea, that they could be used be either the government or the industry to inform the people, but they could also do more harm than good. So if they are done, they have to be done very, very carefully

because they could actually make the problem much worse.

And unanswered questions, are there any messages that should be conveyed to adolescents about over-the-counter drug use? Which ones should be conveyed? Who do we target these to? Who should pay for them? How effective would they be? And, again, are there any adverse effects that we aren't sure of because of these other effects that we see with over-the-counter drug ads?

I think that's it. These are ways you can reach me and then I'll be here later for the panel discussion.

(Applause.)

MS. AKER: Good morning. My name is Julie Aker and I'm here from Concentrics Research. Concentrics is a CRO that specializes in consumer health care research. I've been delighted with the talks up until now and I've learned quite a bit.

Today what I'm going to be covering is

the context of consumer health care research in terms of the goals, the rigor and the approaches that are used in this type of research, also how we apply this to testing in adolescents, how we define that population, the goals of research in this population and I've been asked to speak a little bit about the consenting procedures and ethics as well. Also we will share some of our learnings and challenges of doing this type of research and then offer some potential solutions.

In terms of the context of consumer research, I wanted to compare and contrast against the more traditional clinical research that we're all aware of. In clinical research, we're understanding how the drug reacts physiologically in the person. But in consumer research, we're trying to understand how the person reacts behaviorally with the drug.

A typical OTC development program big picture view might look something like this. We've heard quite a bit about how important the OTC label is and certainly that is the very first

starting point and I will offer to you that sponsors go through quite a bit of time and trouble to get it right with the labels. So there are many, many iterations of this type of research.

Once we have a label that we feel is the best label, we'll start into label comprehension research and I'll talk a little bit more about what that means. Often there are standalone, self-selection and self-diagnosis studies that are conducted so that we can learn a bit more prior to an actual use study about whether or not the consumer can, in fact, correctly self-diagnose themselves for the condition and whether they can self-select the product correctly.

We then move into an actual use study in which we are behaviorally looking at self-selection, we're looking at overall safety and we're looking at compliance with the label directions and warnings. We also have an option for post approval work, but I will tell you that

it's not commonly done in consumer health care research. But I think that's an area that we can further explore to see if there are other answers that we can gain from post approval work.

I also want to point out that there may be additional clinical studies that are done during this time but not always and that not all of these studies are necessary for every program.

Eric did a nice job yesterday of pointing out some of the details about how each of these studies are run. So I'm not going to go back through that again. But I would like to talk a little bit about the focus, the focal points, for each of these types of research. In a label comprehension study, our focus is really the label. We're looking at a wide range of individuals here, demographically, geographically dispersed and also various literacy levels and what we're really trying to understand is if the label is strong enough and clear enough to speak to a wide variety of individuals and will it specifically communicate about the product use,

directions and warnings.

In a self-selection study though, we are more concerned about consumer judgment. And, in this particular type of study, we're really trying to understand if the consumer can make the appropriate judgment about whether the product is appropriate for them to use based on two key things. The first is what the product label tells them to do and the second is the consumer's own personal and relevant health history.

In actual use study, we're very interested in the consumer behavior and, in this case, we're looking for safety in an unsupervised OTC environment as it relates to self-selection and compliance behaviors and really what we're seeking to understand at the highest level is do the benefits exceed the risks.

I wanted to take a minute and talk about how consumer research studies are rigorous. I'm going to just review some things that might be very familiar to all of us in clinical research, typical study procedures and how this

compares and contrasts to label comprehension studies and to actual use studies that are conducted. In clinical trials, a protocol is put together. We go through an IRB. Sites are selected. We screen subjects and go through informed consent. Often there are procedures done, medical history taken. We enroll those subjects. They take the drug home to use it and then we gather data in the form of a diary or other means and then conduct follow-up visits, collect the paperwork and the drug at the end and sometimes post approval studies are done.

In a label comprehension study, some of these things are similar and some are different. But there is the rigor of a protocol. We do not send these studies to an IRB because there are no exams that are done, no procedures done. The drug is not taken. We do select sites that are across the United States that are nicely distributed. We do screen the subjects, however, it's minimal unless we have some special populations that we're looking at. Informed

consent is not done specifically. A confidentiality is done.

Again, there is no drug being taken. No procedures being done. Minimal medical history often in the form of a self-administered medical history. We are enrolling subjects. They do not take the drug home and use it. It's one day interview. So there is no diary or usage data that's collected. No drug is collected at the end. And then, of course, no post approval study is necessarily here.

In actual use study, you can see that there are many parallels between an actual use study and a clinical trial. In this case again, we have the protocol. We do use an IRB because in these cases the drug is being used by the individual. Sites are being selected. Minimal screening again because in these cases we are trying to attract an all-comers type of population. So we're really trying to understand who will be seeking this drug out, who is interested in this type of drug.

And we will do an informed consent. There may be again a self-administered medical history of sorts. Rarely procedures are done. We do enroll these individuals. We will not let them go on into the use portion of these studies if they are in a contraindicated group. So, for example, you can kind of look at these actual use studies in two parts, the self-selection assessment and the use assessment. If there's an individual that steps forward and says, "Yes, this drug is right for me" and, in fact, it is not, we will gather additional information about why they thought that it was important or appropriate for them to use so that we can understand why that incorrect response was made.

For those that go on to use the product, we're letting them take it home to use in an unsupervised manner so that we can understand what might happen in real life. They're gathering data in the form of a diary or other means. There may be very minimal follow-up visits in this case. We collect the paperwork

and drug at the end and rarely post approval studies are done.

In these actual use studies which are very important for us to try to project what might happen in real life, really what our focal point is is our real life experience. So if all of us left here today and we went to a retail outlet to get some type of OTC drug, we might go through these types of steps.

First of all, there has to be an awareness and I see that some of these steps parallel some of the points that some of the other speakers made. So I was pleased to see that. There has to be an awareness and an education. So in real life, we're made aware of a new drug either through advertising that occurs or through friends and family that give us information about their experience with that drug.

We have to be motivated to see it out. And if we are motivated, we will get in our car and drive to the retail location and we'll seek

it out to get more information. Generally speaking, we'll pick up the box and take a look at it and read it. We'll then make a series of decisions. The first will be "Is this right for me?" That's really the self-selection decision. The second would be "Do I want to purchase this?" which is really a value decision that's made. The third might be "Do I want to use it?"

Now we do see consumers that will purchase things, take them home and choose to use them or not use them at a later time and there are many reasons for that. They might not clearly understand something. They may be afraid to use something. The timing might be wrong. And sometimes there are just different timing elements to a particular condition having to flare before they can actually use the product itself. And the final decision will be "Will I choose to comply with the label?" Obviously, there are no study procedures in our real life experience.

In an actual use study, what we're

trying to do is use that real life experience as our reference point and we're trying to the best of our ability to emulate a real life experience within the context of a study. And so the awareness and the education is somewhat limited. It's mass media advertising that's happening and usually it's done something like this, "Do you suffer from X? Are you concerned about Y? If so, you can call this 1-800 number."

But we don't want to bias or lead them in any way. If they're motivated, they will call the 1-800 number to get more information. If they are interested in participating, they will be referred to a local research site and then what we hope to emulate are the same decisions and processes that they go through in real life which is to give them an opportunity to read and evaluate that label at their own pace in their own way in a very unstructured manner and then to make a series of decisions, "is this product right for me?" which is a pivotal self-selection question, "do I want to purchase it?" which is

the value decision, “do I want to take it home and use it?” and then “will I choose to comply with the label?”

The difference here, of course, is that we’re doing this within the context of study. So we have some clinical and regulatory framework that has to be maintained, namely, that we need a protocol, informed consent, data collection, so forth. There must be a balance between simulating the real life needs and the study needs and that is always a challenge.

Moving on now to how we apply this type of research to an adolescent population. There’s been lots of discussion over the last two days about how we define this population. At our company, we actually define it using the FDA guidance, the E-11 guidance, for clinical investigation of medicinal products in a pediatric population and that guidance states that children are defined as two to 11 years of age, adolescents 12 and up depending on the region that they’re in and adults are 18 plus.

So that's what our company uses as guidance in how to determine.

In terms of what are research goals in adolescents, many of these goals are the same as in all consumers. The primary focal point for our consumer research is always safety. It's all about safety. Whether you're doing a label comprehension study or self-selection or actual use study in any population, we're very, very interested in minimizing risks and maximizing safety.

But we're particularly interested in this with children and adolescents. So we use a research construct of working right to left instead of left to right. So we start right to left and look at that specific drug on a case-by-case basis with that population and with the contraindications that are listed on that label and we start to ask ourselves questions about any potential for harm under normal conditions with children or adolescents, any long-term effects that we might be concerned about, any adverse

events that we might be concerned about and overall the risk/benefit ratio and we start to design a research working backwards from that drug and that population.

We are particularly concerned about any kind of compliance issues that might arise that might lead to abuse or misuse and these are particularly important with the adolescent populations. And we would love to have more usage pattern information as a reference point and I was very pleased yesterday to hear that some of that is available and developing so that we can get some kind of a baseline for what type of usage is out there. But I will point out that that current data is based on purchase and sometimes adolescents find other ways to get the drugs that they need and we'll talk about what our experience with that has been.

So the question is, is research done with adolescents on OTC products, and the good news is yes, it is. But it's done on a case-by-case basis. And some examples that I can offer

to you are that with label comprehension we've seen two variations on a theme, one in which there may be a very specific warning that's on that label that we really want to test in a special population, so a focused label comprehension study that might just focus on that one label or a full label comprehension study in a special population and, in this case, in teens. Examples of that would be the Plan B product in which label comprehension was tested in teens.

For self-selection studies, we do many of these standalone self-selection studies particularly in populations that are special populations that maybe should not be using the drug so that we can answer the core question, "do these individuals understand that they should not be using the drug and can they make that decision appropriately?" A good example of that is the study that was discussed yesterday on the Alli product that was tested in teens for a self-selection study.

For actual use, studies have been done

with adolescents. They are somewhat limited, not large groups, but they are within the entire population. Alli again is a good example. And I can tell you that there are several switches that are in development right now in which the sponsors are including an adolescent population.

Again, as I mentioned earlier, we have an option for post approval work. It's not largely used, but we do have that option.

I was asked to speak a little bit about what the procedures are for IRB submission for these types of studies with adolescents as well as the consenting process. In terms of an IRB, if you're working with an IRB and you're submitting a pediatric or adolescent proposal or protocol, it's really important that some member on that IRB or experts that are brought in have pediatric or adolescent experience. This is very important. We take it very seriously. At our company we have our own IRB and the chairman of that IRB is actually a Board-certified pediatrician.

During the IRB meeting, what is reviewed for that study is the protocol, the advertising, usually the screening tools that will be used and the informed consent and the assent. That's really important for these IRBs to really take a look at the way that patients will be recruited and particularly they look at whether the recruitment method is going to be free of inappropriate inducements to either the parent or the child.

In terms of the consenting process, I'd like to divide this into two parts, the market research type of work as well as the clinical work that's done and that spans the consumer health care research spectrum here a bit. When we're talking about market research, we're talking about interviews, we're talking about questionnaires and opinions and the types of consumer studies that relate to this work is label comprehension work and also self-selection studies in which there are not procedures or examinations that are done, so fairly

straightforward self-selection studies.

The consenting guidelines that we follow in our company are the MRA guidelines which are the Marketing Research Association guidelines which state that parental permission and an informed consent should be obtained if the subject is less than 13 years of age and that the consent should be in a straightforward manner clear and simple and should be signed by that individual.

And certainly I want to point out that you can always be more conservative and we have taken that path many times. We always err to the more conservative side. But if we have an interview, for example, that's on a sensitive topic such as birth control or HIV or something of that nature, we will go ahead and get parental consent.

When we're dealing with a clinical marketing type of study like an actual use study or clinical trials, the types of studies that we're talking about here would be a more

complicated self-diagnosis or self-selection study in which we might be conducting physical exams or doing some type of medical procedure or so forth or getting an extensive medical history, an actual use study in which exams or tests might be done but that the drug is actually used and clinical trials where the same applies where the drug is used.

In this particular instance, we follow the E-11 guidance for industry which gives a framework but not specifics. It really states that parents or the guardian are to provide consent and the quote is “participants of appropriate intellectual maturity should provide assent, sign and date.” And I think that speaks to some of the speakers that we’ve heard already talk to the spectrum of intellectual maturity.

So the question then is how do you know. Because we don’t know and we can’t answer that question internally right now, we err to the more conservative side. So in our company, we go ahead and we get assent and consent for everyone

up to the age of 18 and then at that point they're 18 and over and they get informed consent.

The American Academy of Pediatrics advocates that assent in children and adolescents should be done and they also advocate telling the patient, the child or the adolescent, what he or she can expect in terms of the tests and the treatments and we agree with this. So we spend time talking about what will be involved. The assessment of the patient's understanding is important, having a dialogue, "do you understand," "do you have any questions," assessing their willingness to participate and specifically pointing out and emphasizing the fact that this is a voluntary process and they can withdraw at any time.

I might just share just some of our learnings over the last 20 years in doing consumer research. Not a lot of studies have been done in adolescents. I'll be clear about that, but certainly there have been a number of

studies that have included adolescents and the nature of the research that we do includes probing and asking why and why did you say that and getting into that rich information about why people think the way they do, why they do what they do which is always fascinating.

But I'd like to share two types of learnings, learnings about purchase behaviors that we've gleaned from those probing comments and also learnings from usage behaviors. What we've learned and what adolescents have told us is that the parent usually purchases from the time they're born to about the age of 15 generally speaking. I think this is consistent with what we've all been talking about here in the last two days. The adolescents begin purchasing occasionally in the 16 to 18 years of age time frame.

We've all talked about how do you parse these various age groups. We all have many questions about this. We have another viewpoint to offer and this has been very interesting in

just sitting and having many conversations with adolescents. There's quite a change that happens at the point that they get their driver's permit. Right in there at that time when they're 15 and a half to 16, we see that the world is basically giving them more freedom. They are now able to have a motorized vehicle under their control. Given that, that's signal to them that they are taking on this increased independence, there are other things that come along with it.

So we start to see that adolescents will occasionally purchase. But when you talk to them about what they purchase, why they purchase, and so forth, what they'll say is they don't necessarily want to spend their money on OTC drugs. They would much rather spend it on gas and clothes and entertainment. What this speaks to is they're probably getting it from home and I was very, very pleased to hear this morning the comments about the parental interactions here because that is very, very consistent with what we've seen in our research about the examples

that are set from the time the child can start to observe parents taking OTC medications. It's very important that footprint is already set. So they don't want to necessarily spend their money on OTC drugs.

We do see that they start to purchase OTC drugs at the time that they start to head towards college or leave home and that tends to be in the 16 plus time frame but generally closer to 18. And occasionally too often, they will tell us that they will purchase if they have to. They don't like again spending their money on those OTC drugs. They would much rather take them from the home stores when they make a visit home and I can tell you that I have a freshman in college. This is new ground for me and I had no clue that I needed to be very, very ready for what was going to happen every single weekend when she came home. I thought it was just tuition I needed to worry about.

Our learnings in terms of usage behaviors in adolescents, again if you talk to

adolescents about who tells you how to use this drug, do you make these decisions, where do these decisions come from, they'll usually tell us that from the time they're born up to about that 15 which is again that semi-driving age there that usually the parent is making the decision and then they'll tell us that around the 16 to 18 time frame depending on their family and their value system and their methods in their own household, that maybe they'll start to make some of their own decisions or that the parent will be told that the parent will lay out the drug for them to take so that they get a little bit of guidance or the parent will give them how much they can take between now and the time they come home from school, for example.

But they will also borrow from the household stores or from friends and usually they will follow guidelines for usage that have been taught or observed and I think that's very important to point out and it emulates some of the comments that were made this morning that

there at least starting with what they observed and have been taught. If mom or dad takes two or four of a drug when they should be taking one, that footprint is set. That example has been set.

And then as they start to move out of the house, they will start to purchase these drugs but in terms of usage, when you ask them how they make a decision about when to take these drugs and so forth, they'll tell you, "Well, that's what mom did" or "That's what dad did." So again, we're getting that influence of what they've been taught or observed. But then as that time away from home increases we see that the influence starts to move a little bit more from family to friends and co-workers and to the points that were made in the last two days about nothing bad happens, I think that's a very important piece as well.

There are some inherent research challenges with this type of research. In terms of the label, any sponsor will tell you that the

amount of real estate on that OTC Drug Facts Label is a continuous challenge. There is so much that we need to say but we have such little room to do it and then we need to do it in a very clear way. The Drug Facts format, we need to fit things into various categories and so forth. It can be a challenge sometimes.

And we ask the question, "are we clear enough about the benefits and the consequences?" One of the questions that we have and we have talked about internally quite a bit is when we look at these label comprehension studies, in particular, "are we being clear enough about linking the consequences to a warning?" In these studies or these Drug Facts Labels, you will see there is a list of "do not use" and so forth.

And when you talk to adolescents about do they look at those, what do they look at on these labels, they'll say, "Oh, that's just a bunch of stuff that attorneys put on there." Well, no. That's really important information that there's for your health. So how do we

bridge that gap between stuff that's on the label and meaningful information that an adolescent really needs to take seriously?

In label and self-selection work, we've already discussed that verbal answers don't always coincide with behavior. So what I say may not necessarily always coincide with what I do and so we have to keep that in mind.

And then assessing misuse and abuse in the context of a study is a challenge because the study is an artificial, time-limited vehicle. So are we going to see the full scope of any possibility of misuse or abuse? We might get some glimmers and some insights and that would be helpful. But we may not get the full picture until we're more in a post approval or an observational type of situation.

In terms of observation and peer experience, adolescents are strongly persuaded by peer experiences and suggestions as well as parental and other examples. So they're getting information from all of these areas.

In terms of potential solutions, if we just start by looking at the label, clarity and consumer-friendly language and this is a challenge because when we start these OTC programs, what we are working from is the Rx information that we had in the package insert and we all know that that has a lot of techno-speak in there for a lot of different types of people. It's a lot of information.

But now we're trying to take that information and really pull out what's really most important for the OTC population to really understand and we have limited space in which to do it. So it's very important. When we work with sponsors, we really try to work with "chunking" of key information so that key concepts are put together. We're trying to be extremely clear about what the purpose for the drug is so that it's not misunderstood what the drug will or will not do and very simply, clear instructions.

Clarity about the benefits and risks

and again we'll pose the question, "Are we clear enough about the benefits and the consequences that are associated with those warnings?" We have some sponsors that we work with that have taken the next step in warnings that are on the label to give a little bit more information about what might happen or the reason for that warning and we have found that comprehension increases when there's a little bit more information given about the reason or the consequence.

Clarity about the warnings, in an OTC Drug Facts Label, there are three main areas for warnings and they all need to be very clear and straightforward. The "do not use" area is certainly for those individuals who should never be using this drug. The "ask a doctor or health care provider if it is a conditional warning" that gives you an opportunity to use the drug but only after speaking with a doctor or health care professional first. And then after using the drug, there is another area on the label that really speaks to "stop use and ask a doctor if."

So this is really instructions about when you should stop using the drug.

And then clarity about directions, the dosing in terms of the amount and the frequency of dosing.

If we look beyond the label for potential solutions in terms of label and self-selection testing, we certainly advocate testing in adults when applicable and it may not always be applicable. Testing literacy in adolescents and we've talked about some tools that are available for that and are evolving as we speak. Consider testing that has behavioral elements. This has been something we started to talk about internally and we wonder about it. We wonder what would happen in a label comprehension study, for example, if after asking questions on dosing we said, "Here is the bottle. Why don't you lay out for me the amount of drug you would take today," actually showing me instead of just telling me. Takes that next little bridge to behavior and give us some insight into whether or

not they truly understand or they're parroting back simply what's on the label.

Continued open-ended and use of open-ended scenarios. When we ask open-ended questions, really that's the hardest type of question because we're not leading them in any way. We're asking it in open-ended sense and then if we're given the opportunity to probe afterwards and get more information and certainly getting the whys behind incorrect responses. That gives us great depth of understanding and adjusting the labeling based on learnings and creating research programs that allow for time in between each of those steps, in between label and self-selection and actual use, so that those learnings can be incorporated.

In terms of the education and this has been fascinating to hear in the last couple of days, can we leverage adolescent's ability with technology more than we have up to this point and can we educate adults as well as adolescents about the benefits of appropriate use and the

consequences of inappropriate use? This is really important because we even find with adults in which we're doing comprehension or we'll see it in actual use studies they really didn't think anything bad was going to happen or didn't really understand fully what the consequences might be.

We've talked about some of these examples of how we might be able to do additional education and then terms of misuse and abuse and adverse events, going beyond the actual use study, we may want to consider some post approval studies and surveillance that goes beyond just the context of an actual use study. And then getting information about purchase of drugs and use of drugs, how they're obtaining these drugs, either from home or from friends as well as from purchase would be very useful.

So that concludes my comments this morning. I'm delighted to be here and look forward to the question and answer session that's to follow. Thank you.

(Applause.)

DR. BOSCO: Can the panel come up here? So we ate into a lot of our discussion time and we'll try to get a little bit more on schedule. But I leave it to Dr. Brass as to how we want to proceed. You guys can sit down for your questions, but in terms of how much time we should take for the discussion.

(Off the microphone comment.)

DR. BOSCO: Okay. So we just have really a very few minutes for questions and answers. But we will have time with the roundtable. So we're going to quick, move to the microphones and we'll take some questions. Up there.

MS. O'DONOGHUE: Amie O'Donoghue from FDA. Connie, I have a question for you. You mentioned that there are two groups, you found two groups of adolescents, one group that tends to respond to security and safety messages and one group that tends to respond to reward messages. I was wondering if you have any data on what are the numbers. What are the

proportions of adolescents that fall into each category?

DR. PECHMANN: No, this is based on regulatory focus theory and it's fairly new and up until now, we basically just do a split of adolescents based on their scale. But it does appear that there's a sizable group in each. It might not be 50/50. And I thought that maybe there would be a correlation with drug use, say, like smokers maybe were more what they call promotion focused, but more focused on goals and aspirations, though that wasn't the case. There were smokers in both groups. In any event, it may not be 50/50, but it's very sizable.

MS. O'DONOGHUE: Thank you.

MR. SILBER: Hi. Tom Silber for Society for Adolescent Medicine. It was a very, very illuminating presentation, everybody, and it can be well integrated together. I have a specific question proceeded by a brief comment.

There seems to be clearly from the presentations two groups of adolescents,

adolescents who need symptomatic relief from over-the-counter medication and don't spend one penny on it, just get it from their parents' cabinet or ask them to buy it and then adolescents who deliberately purchase products with specific high-risk purposes such as self-inducing vomiting or diarrhea or abuse.

So my clinical experience is, of course, confirming that and what I have seen is that actually large numbers don't purchase the product. They just shoplift it. So my question is has there been any studies done about shoplifting behavior of over-the-counter medications that are so accessible to teenagers and fits within the risk-taking category, the fun of actually, you know, going against a big organization that sells it and the self-defying things. Thank you.

DR. PECHMANN: There's been a lot of work on shoplifting with tobacco that's -- There were at least allegations that marketing companies were encouraging shoplifting to get

adolescents hooked and that in any event they were reimbursing the retailers no matter how large the shoplifting was and so then people were trying to crack down on it. But I'm not aware of anything in over-the-counter.

DR. SCHNEIDER: Heinz Schneider, Consumer Health Care Products Association. Actually, I have three questions to Dr. Cornelia Pechmann. One is, in my job, I focus on OTC medicines. You gave us examples from tobacco products. Are you aware of OTC medicines which are marketed towards teens in that way to base your assumptions on?

DR. PECHMANN: I'm sorry. I didn't quite hear the question. Maybe you could speak a little louder.

DR. SCHNEIDER: Yes. Focusing in my job on OTC medicines, you provided examples from tobacco products how they are marketed, how effectively they can be marketed towards teenagers. Are you aware of OTC medicines which are marketed in that way and have that effect?

DR. PECHMANN: No, I don't think there's -- There's not been any research because there's not been concern about abuse. So then that -- Usually, it's some kind of problem that will stimulate marketers or researchers in general to look at the problem. No one has identified a problem. No one has looked at it.

DR. SCHNEIDER: Okay.

DR. PECHMANN: So I'm just assuming that programs would be similar because there's a general approach to dealing with teens that ad agencies know about and they apply it no matter what product category, but I don't have any firm evidence whatsoever and I'm not aware of any studies.

DR. SCHNEIDER: My second question, I get that you touched on potential health effects of marketing certain product categories to teenagers and I want you to elaborate on that. I just was -- As a father of two, I'm like when they watch that TV channels religious I'm happy about every dental care TV ad which is appealing

to them. Could you comment on that?

DR. PECHMANN: On whether the ads actually do --

DR. SCHNEIDER: No. I mean, the potential health benefits of marketing which is appealing to teenagers.

DR. PECHMANN: There are, for example, in California -- You mean, public service announcements that have health benefits?

DR. SCHNEIDER: The potential health effects advertised content to teenagers.

DR. PECHMANN: Well, so I think -- I'm not sure I understand the question, but I think there is some research that shows, for example, that public service announcements if done well can have health benefits to teens that can avoid these adverse effects or what we call boomerang effects. But in terms of over-the-counter medicines having positive effects on teens, again there's no research on how they could actually be extremely beneficial.

DR. SCHNEIDER: Thank you and my third

and then I'm gone. You mentioned placebo effects being specific to OTC medicines. I'm not aware of placebo effects specific to OTC medicines. I'm aware of various grades of placebo effects for a vast variety of prescription and OTC medicines. Could you comment on that?

DR. PECHMANN: Well, that's the only study that -- I think marketing researchers have just recently turned to over-the-counter medicines I think because of the interest in prescription over-the-counter for prescription drugs. The whole area of drug advertising has, I guess, come on the radar screen and so that study was -- You could even argue that the Sobe -- it was about energy drinks. So you could argue that's not really an over-the-counter. That's just a food product.

So that is the first study that I know in that context that shows these behavioral effects and they did several studies with several different products in several different contexts and kept showing the marketing. So basically

those are pure marketing effects. That's what's unusual. It's price and it's advertising and it's not brand. So it's not like you give me beer and they could all taste the same. But then you tell me this is Budweiser. That's my favorite. All of a sudden it tastes better because I know it's Budweiser. That's been established for years.

But the idea that just to peer marketing like price or advertising can not only -- can actually enhance performance is something that's fairly recently documented.

DR. SCHNEIDER: Thank you.

DR. BOSCO: We have two more questions and then we're going to finish.

MS. LEMAH: Kristin Lemah with the National Safety Council and my question is for Dr. Jaccard. I found your presentation on parental communication fascinating. I was wondering if there are any studies that have been done sibling communications especially older siblings and whether or not it's effective or

detrimental to have adolescents get any of their health information from older siblings.

DR. JACCARD: Okay. I don't know about sibling effects in terms of over-the-counter drugs, but I do know that there is quite a bit of work on sibling effects in general within families and that there tended to be associations with sibling behaviors. But I'm not aware too much of sibling communication studies and studies that have looked at communication in depth with respect to that, that has probed that in depth.

So there are studies that clearly find sibling effects. There is controversy about the bases of those sibling effects and what underlies them. So some people argue that there are some common family variable that is just impacting both siblings or that there is some kind of genetic mechanism that might be operating. There is a great deal of controversy about that. But I'm not aware of any in-depth communication studies with siblings and I think that's really a fascinating thing to explore.

MS. LEMAH: Thank you.

DR. BOSCO: Last question.

MS. LEONARD-SEGAL: Andrea Leonard-Segal, FDA. I was interested in the numeracy, I think that's what you call it, issue that you brought up about how people have difficulty understanding what the directions are in terms of numbers and measuring of things and I'm wondering if you have a sense of if there's a difference in that numeracy literacy between adolescents and adults and if you have ideas about how one could enhance the education of the public in terms of understanding measurements of things.

DR. SANDERS: Yes. We were also somewhat surprised by this finding, although it's coming up more and more, the relationship between numeracy and health behaviors. There's another study I didn't mention we're working on right now with kids with Type 1 Diabetes and finding that parent numeracy has a lot to do with health outcomes such as their glycemic index and so forth.

It seems also as you mention to be an area for intervention and those studies that I'm aware, both the ones that we're conducting and others, are still in their earlier stages. But I certainly think that any attention to labeling should take into account the general lower level of math skills and numeracy out there from both ends, both in terms of adapting messages in the health care environment on labels and so forth and then also turning our attention to health education efforts for the public. So I agree with that. Did that answer your question?

MS. LEONARD-SEGAL: It sort of does. I mean, I'm wondering if you think that an extension of the research would be to provide better unit dosing or do you think it would not matter because people can't understand one versus two versus --

DR. SANDERS: One of my colleagues at NYU is developing unit dosing materials to go with prescriptions that are delivered in the emergency room or in some specialty clinics and

looking at precisely that question. So, yes, I surmise that that will continue to have some beneficial effects for the patients. They've shown that out of the emergency departments.

MS. LEONARD-SEGAL: Thank you.

DR. JACCARD: I'd add also that there is quite a bit of work in cognitive psychology that looks at numerical ways of presenting probability information and risk information through probability. Do you say that a risk is one in ten people get it, ten in 100 people get it, 100 in 1,000 people get it and you'll get very different inferences based upon the numerical base that's being used and then there's also research going on that is looking at numerical and verbal counterparts. When you say something is slightly likely or there's a moderate chance and you start putting these different adverb qualifiers, how does that translate into numerical indices? And there's quite a bit of work exploring ways of presenting risk information in that way.

DR. BOSCO: So, yes, and I'm aware of -- there is a certain amount of research of graphical presentations and people have a real difficult time in this country, in particular, in understanding graphs which is a little challenging when you think about it because we really depend heavily on using graphical information and yet people don't really understand graphs.

Thank you very much. It's been a fun panel and that was just a tremendous amount of information and everybody will have a second chance at this at the roundtable which will be in an hour.

(Off the microphone comment.)

DR. BOSCO: All right. We'll split the difference. So 12:45 p.m. we're going reconvene. Thank you.

(Off the microphone comment.)

DR. BOSCO: Off the record.

(Whereupon, at 11:35 a.m., the above-entitled matter recessed to reconvene at 12:48

p.m. the same day.)

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

12:48 p.m.

DR. BRASS: Good afternoon. I am sure there will be some stragglers coming in as we go along, but I do want to get started particularly while we have the advantage of outnumbering you.

I view what we're going to do over the next couple of hours as an extremely important exercise. Over the past day and a half we've heard a variety of extraordinarily interesting and useful perspectives on adolescents and how they interface with health care delivery and specifically OTC drugs. Now is our opportunity to take these varied perspectives and begin to integrate them into a more forward looking agenda and to say how can we apply what we have heard to improve the public health going forward.

There's been a lot of discussion about two spheres of behaviors among adolescents and

OTC drugs. One for convenience I will simply term “abuse” and the other “misuse” when they are using the products for some therapeutic intent.

Because of the agenda of this workshop, our focus this afternoon is going to be much more on the issues of misuse with therapeutic intent or, stating it positively, ensuring proper use when the drugs are used for therapeutic intent. To do that, we’ve brought back many of the speakers you’ve heard earlier to form a panel to discuss a number of issues on a forward-looking agenda and while you have met all these people before, I think I’ll just ask them to go -- most of them before, I think we’ll just go around very quickly and let the panelists introduce themselves which will also teach them how to turn on their microphones.

(Laughter.)

DR. BRASS: David, would you like to begin? See.

MR. SPANGLER: I need the practice. I’m David Spangler with the Consumer Health Care

Products Association.

DR. KWEDER: I'm Sandra Kweder with Food and Drug Administration, Center for Drug Evaluation and Research.

DR. BOSCO: Lynn Bosco, NIH, Office of Behavioral and Social Sciences Research in the Office of the Director.

MR. CLELAND: Richard Cleland, Associate Director, Division of Advertising Practices, Federal Trade Commission.

(Off the record comment.)

MR. SILBER: Tomas Silber, Director of Adolescent Medicine Fellowship, Children's Hospital representing the Society for Adolescent Medicine.

DR. HUSZTI: Heather Huszti. I'm with Children's Hospital of Orange County.

DR. KOKOTAILO: I'm Pat Kokotailo. I'm the Director of Adolescent Medicine and a pediatrician at the University of Wisconsin in Madison. I'm representing the AAP. I also belong to the APA and also to the Society for

Adolescent Medicine. But I am representing the American Academy of Pediatrics and I'm a member of the Committee on Substance Abuse for the AAP.

DR. SANDERS: I'm Lee Sanders. I'm Associate Professor of Pediatrics at the University of Miami, also representing the Health Literacy PAC of the AAP.

DR. JACCARD: Jim Jaccard. I'm in the Psychology Department at Florida International University in Miami.

DR. PECHMANN: I'm Connie Pechmann. I'm a Marketing Professor in the Business School at the University of California Irvine.

MS. AKER: Julie Aker from Concentrics Research.

DR. BRUINE de BRUIN: Wändi Bruine de Bruin. I'm a Psychologist in the Department of Social and Decision Sciences in Carnegie Mellon University.

MR. DENNISTON: Bob Denniston, the Office of National Drug Control Policy.

DR. BRASS: Thank you. Now we have

segregated this panel by seating order in roughly two groups and labels may be deceiving. But if we begin with Tom and move to the right, we have a group of people I have designated as Persons of No Influence.

(Laughter.)

DR. BRASS: In contrast, the four people on this end of the table -- to Tom's right. Yes. Whereas the people on my end of the table, these four distinguished individuals we will term Persons of Influence.

(Laughter.)

DR. BRASS: And usually the People of No Influence get lectured at by the People with Influence. Today we're going to turn that around and what we're going to do is use the expertise on our panel to discuss what the agenda of the People of Influence should be and I have challenged the group that -- this is organized around certain themes, but what we want to talk about is how we can identify future looking initiatives that have the potential to have a

positive public health influence on the problem of how adolescents interface with OTC drugs and improve the public health.

And the charge will be to identify those initiatives and what might be implementation strategies for those initiatives that will have this greatest influence and therefore needs to be justified whether it's a research initiative or an interventional initiative that, in fact, the outcome of this is going to be that level of improvement.

Our four Persons of Influence will serve as a sounding board to reality tests, provide factual information during that discussion and then will also comment on what they have heard. We'll also invite you after a little bit of the discussion on each issue by the panel to also participate by providing your own perspectives or challenging the panelists about what they have said.

With that framework, we're first going to discuss issues centered around regulation

broadly defined and specifically what are the opportunities for the regulators, the FDA, the FTC, for enhancing the safe and effective use of OTC drugs by adolescents and what are the challenges facing those regulators in trying to implement those strategies. And as those of you who know me if nobody talks, I will not be shy about calling on people or making it up myself which is even worse.

The floor is open. Somebody raise their hand and they get recognized. Lee.

DR. SANDERS: I mean, I think certainly from my perspective in health literacy and health numeracy as I mentioned before we need to look at improved standards for both drug labeling and advertising and perhaps to integrate those as shared standards that take into account as I mentioned the limited numeracy skills of the general population, so to have rather than just words, clearly tested iconographic images on each packages that are a part of sort of the new generation of drug facts.

As I was mentioning before, I think these should be integrated with an electronic place on the web to go. Increasingly teens and adults will be able to access this on their cell phone when they're at the point of care.

DR. BRASS: So let's separate for a moment issues around labeling and advertising.

DR. SANDERS: Okay.

DR. BRASS: And let me just ask the panel to follow up on some of the things you raised. Does anybody have any data about the effectiveness of icon or pictorial communication to relate with respect to comprehension key messages versus syntax and I can tell you that what we have seen to a very limited degree is not encouraging about pictures. So there is alternative information.

DR. SANDERS: Since I raised that, let me just raise it. A colleague of mine, Shawna Yin I mentioned I alluded to her before at New York University has demonstrated reduced error rates in dosing of over-the-counter products for

young children, so where it's liquid medication by use of iconographic handouts.

DR. BRASS: So that purports the parent illustrating the specific task of dosing.

DR. SANDERS: That's correct.

DR. BRASS: Julie.

MS. AKER: Yes. We've done some of this research and I think maybe similar to what you're referring to, Eric, that we see that it doesn't necessarily help or hurt. It's somewhat neutral. But in cases in which it's applied in a good manner and the only way I can say that is that we aren't overdoing the label. I think one of the things that becomes a problem when we start adding icons to the label is that now we're loading that label that already had very limited real estate. So to the extent that we can use these properly and not confuse or distract, I think that becomes very important.

DR. BRASS: One of the issues that came up historically was cultural diversity is a much greater impairment for understanding pictures and

icons than it is for, believe it or not, English and that there were examples anecdotal where a pregnant woman with a red X on the label intended to “do not use if you’re pregnant” was interpreted as meaning this was a birth control method. So one has to be very careful when one talks about the diversity of the population in trying to get that across.

DR. JACCARD: I just have a question for the regulation of advertising. How does the internet fit in all of this? Is there any regulation at all in advertising on the internet and what does the FTC do with respect to that and kind of what are the prospects for that?

MR. CLELAND: Well, maybe perhaps you can’t tell it from looking at it necessarily but the internet is just another form of advertising. The regulations that apply to print ads or TV ads also apply to internet ads. The unique thing about the internet though is it’s become one of the -- it’s sort of the classic example of a type of promotion where there’s overlapping

jurisdiction between the Federal Trade Commission and the FDA.

If you look at an internet site, for example, where you can order a product, it's our view that that's promotional. It's advertising. It's subject to our jurisdiction. But because you can order the product off of the internet site, the representations on that internet site may constitute labeling which would be directly subject to the jurisdiction of the Food and Drug Administration.

DR. BRASS: And, of course, not all content on the internet is advertising and there's a whole lot of content that doesn't fall under anybody's review.

So let's come back to this -- I want to come back to the labeling point a little bit more and underlying your comment has to have been a premise that what we're doing now isn't good enough and I'd like to challenge that premise. Is what we're doing today by hypothesis inadequate or demonstrably inadequate or how do

we feel about how we're developing labels now? Please.

DR. KOKOTAILO: I do think that the labeling can be clearer and especially in terms of some of the things that are the age and the weight range. I've had really overdose situations with 12 years old who have been small 12 years old because when you look at the adolescent development part of it you can have a 65 pound 12 year old who is very normal and that an adult dose can be an overdose in terms of a number of things especially in these multi-component things like in terms of the multi-drug cold preparations or some of the things with that.

And then also I think the whole issue that had come up earlier about the as-needed and what the issues like that with the indications that are not clear in terms of what does that really mean. Even the kinds of things like that, three times a day, as opposed to every eight hours can be confusing for a number of people.

But those things especially I think are ones that are difficult in looking at the weight and age ranges and as well as the clarity of the labeling and how you take it.

DR. BRASS: So, again, let me probe that. Are you talking about adolescents who are self-administrating, parents or all consumers?

DR. KOKOTAILO: All consumers.

DR. BRASS: And is that based on data or anecdote?

DR. KOKOTAILO: It's based on from my end in terms of the pediatric part of it in terms of the pediatric part of it in terms of the weight ranges are something that's very well established.

DR. BRASS: That I can accept. Yes.

DR. KOKOTAILO: And in my experience in 20 years of working with adolescents has been that adolescents come in various sizes and shapes and that's very well documented also that people can be a normal adolescent at a different size and I think also in terms of both with the

adolescents administering it or with the parent administering it and adults themselves because I've certainly seen parents mess up with medications as well.

DR. BRASS: Of course. And two points I think it's important to keep in context, first of all, even if we identify a problem with not often following the directions, it doesn't mean an attempt to improve it will improve it instead of making it worse, and that the current standard involved actual testing of what is on the label, and many times that involved comparative testing to see which formulation of the syntax or way to describe this actually works better. So what is on the label is not simply what people think works best but what the available data says works best.

And I make that explicit because if we have research needs or research opportunities, we have to do better than what we're doing and I don't want to allow the anecdote to undermine 20 years of research that has gotten us to where we

are today. Please.

DR. BRUINE de BRUIN: Even if what is currently being done is effective and even if the choice of wording or presentation of information is better than something else, it doesn't mean it can't be even better and so I think that that's a research question. So maybe I'm running ahead of the agenda, but I'll try to stick with the regulators.

I think that if we think of the label as the only way to communicate, we're really limiting ourselves and, of course, we should examine what is the best way to present the information on the label so that it's useful for adolescents and adults and people of different cultures who live in the United States. But we don't have to be limited to the label, and I'm not talking about advertising. I'm thinking about technologies that are developing that will allow us, maybe not now, but sometime in the future and maybe even the near future, to provide more communication and more tailored

communication to users of over-the-counter medication.

And it's hard to predict exactly where technology will take us, but I know that the engineers are working on ways to monitor how much medication people are taking. But you could take it even further where people will have to enter their information on a website or in a kiosk or on a DVD that they get with the medication and based on that they receive information that could be textual, it could be pictorial, it could be video that is tailored to their needs, to their group, about what we know about what they need and before they can take the medication and maybe even the bottle interacts with them if they're doing something wrong.

DR. BRASS: I think these are very interesting points that have actually been discussed a great deal. So let me push you a little bit on that. When we think about these types of material in a regulatory context, they tend to be, and I apologize if I use sloppy

wording, into two categories, one which is the core labeling which may not be simply print on text but could be broader than that which is required for the consumer to have for the safe and effective use of the product and that becomes under strict regulatory control and it's defined as a condition of the approval.

Then there's opportunities for supplemental information which consumers can elect to access. Is that fair, Dr. Kweder?

DR. KWEDER: Yes.

DR. BRASS: And that differentiation is important when we develop recommendations because, if we feel there is a need for more sophisticated labeling tools, that may fall directly under the purview of the regulators and so I just wanted to clarify it as we discussed. Please.

DR. PECHMANN: I think it's important to look at how over-the-counter drug packaging compares to some other consumer product that people have to use like a frozen dinner and in a

frozen dinner, that usage information, how you cook it, how long you should keep it in the box, take it out of the box, is huge, in big, huge, prominent, right on the back of the packaging and it's much bigger than the nutritional information or anything, ingredients, or anything else and it's easy to find and easy to follow and often has a graphic which in marketing we found that the graphic if it's not a graphic -- you think graphic in medical it's like graph or figure. Well, we think like a picture of the product with the way it's supposed to look in the microwave and that has been shown in marketing to help, not as a replacement for the word but along with the words. So it's dual-encoded.

Anyway, so those products are labeled in such a way that pretty much it's almost impossible not to know how to use it and I think there's a striking difference with the over-the-counter because everything is the same size print. Nothing is more prominent than anything else. There is no picture and it takes me

forever to figure out what the dose is and you're saying that the one I see is the one that's been tested that's the best but the best of the ones that were tested and none of them that were tested were anything like the microwave instructions.

DR. BRASS: Actually, that's not true because -- And again this has a 20-year history. The Drug Facts Label which was 2001.

DR. PECHMANN: 1999.

DR. BRASS: Time flies when you're having a good time. 1999 was the result of a 15-year effort to standardize for consumers the layout of the label so that, for any OTC drug they picked up the organization of the information would be identical. So they would always know where to look.

DR. PECHMANN: That's the same as the nutritional and I'm not counting those as the usage. Yes.

DR. BRASS: But please. Point two is that, because there's clear hierarchical

information on a TV dinner, where if they ignore three-quarters of the label and get the direction right, the world doesn't end. That's not true on a drug label and, in fact, the data showed that as you highlighted certain areas, understanding of other areas which were critical for safe use diminished. So I don't want to discount the opportunity for improvement, but I don't want people to be left with the impression that this is an arbitrary sequence of events driven by marketing from drug companies because this has, in fact, been a struggle of evolution.

Tom, you had your hand up before.

MR. SILBER: Yes. I'm sorry. I have to leave in a few moments. I just got two emergency calls, but I'll come back. But I want to have this opportunity in case I cannot come back and that is perhaps you're putting the cart in front of the horse simply in the sense that it has not yet been determined a) whether there's a difference between how adolescents and adults relate to this issue. So that would be one issue

to research and b) also the issue of the trajectory in the use of the over-the-counter medications. I know that we cannot treat now or at least not mainly, the issue of abuse, but it needs to be investigated whether there may not be two different populations of teens that have to be studied, one the population of teens that wants to use OTC medication the same as any other adult and others who are not intending to use the OTC products as such, but deliberately intend it for abuse and it's possible that there are two different populations that require different studies and in that case the labeling may really be very germane to the first group but not at all to the second.

And then finally since this is for regulators and we're talking about safety and effectiveness, there may be or there should be a step before one does this which is to a) really make sure that the products that are over the counter not be excessively dangerous for the entire population but especially for adolescents.

As an example, I will mention Ipecac which has been abandoned in Europe ten years ago as obsolete and is no longer in use. The American Academy of Pediatrics has eliminated it from households. No longer is it recommended for intoxications that babies may get into and the FDA has had publication with adverse events including 14 deaths. So this is something that is mostly used for abuse by adolescents and young women who want to self-induce vomiting. It has mortality and morbidity and a panel of the FDA has recommended a couple of years ago that the over-the-counter status be revoked. That is much more important than the labeling.

On the other hand, things that are effective that teenagers have used or need to use such as the emergency contraceptive pill are not available and there is no safety issue there. So perhaps one of the advantages of doing these studies would be to actually have a baseline that can demonstrate the way that adolescents can use this medication.

So sorry. I'll listen to the answer, but then I have to go to the phone and run back here.

DR. BRASS: I think there's no question there will be no answer. But let me expand on some things that were a little bit implicit in what you said and try to elicit a little bit more focused discussion and let's start with something very basic.

If we view OTC drugs as self-use medication, forget about who purchases it, who picks up the box, decides they have the indication and decides whether to use it and how to use it, is there any doubt in anybody's mind that adolescents have the capability, cognitively, maturely, just above some threshold that they could engage in that type of behavior appropriately? Does anybody question the ability of an adolescent to do that?

MR. SILBER: No, not at all.

DR. BRASS: Good. Okay. Now did you want to --

DR. BRUINE de BRUIN: I don't question adolescents' ability. But we do have to give them information that they can work with.

DR. BRASS: That's correct. That's where we're trying to build to. Now there's currently a, this you may need to correct me on, a relative default that because of the way OTC drugs are labeled there is a tendency to default that unless it's absolutely clear the indication is not relevant to adolescents to default the labeling to 12 and older. Does that as a default label make sense, or if you had to pick a default would you challenge that as appropriate and suggest something else? Please.

DR. HUSZTI: I was actually going to mention something about that a little bit earlier. I do think there is likely a difference in that 12 to 17 year old age range that I don't know that we understand well enough from a regulatory standpoint and I know we've talked some about the information on labels and, is that sufficient, and there's been a lot of research

showing how people use that.

But I'm a little uncertain about how much research there's been in the 12 to 17 year old category understanding how they really work with that information and, in particular, adults tend to be pretty even across the board. Right. I mean, what they show in the --

DR. BRASS: No.

DR. HUSZTI: Okay. They don't, but you're going to get them a little more likely to be what they're telling you in the study may well be what they're doing outside of it. I think adolescents what we saw from the research yesterday when they're in the presence of peers, when they're in the midst of emotional turmoil they may use that information differently. So I think there's an opportunity from a regulatory standpoint to say perhaps we need from -- and again, I'm just a researcher so I don't know if this is possible, but perhaps we need a little more in-depth work from the folks bringing forward OTC medications on if you're going to

label it 12 and above that you understand 12 and above reads that and understands that information the same way that 17 and above does. We may need some more numbers in there to understand that.

DR. BRASS: Other thoughts on the 12?

DR. BRUINE de BRUIN: Yes. I just want to repeat something I said yesterday and that is if that is done well than we may be able. If we can only write one label and we make sure that that label is understood by 12 to 17 years olds, we may find that we are educating adults better as well.

DR. BRASS: So let’s take that and pick up on something.

DR. KWEDER: I have a question.

DR. BRASS: Please.

DR. KWEDER: I’m trying to understand what you’re getting at. Let’s see if I can articulate this. Are you saying that you shouldn’t -- just assuming for the moment that there is data on the clinical use of the product in an age group, say, 12 to 18, just to make it

easy. Are you saying that for an OTC product, a new product, unless the testing shows that 12 to 18 years olds can understand the label it should not have dosing information or an indication for use under the age of 18? Is that what you're -- I'm trying to understand the practical implications of what you're saying.

DR. HUSZTI: And I think what I'm trying to say is that there should be an explicit inclusion of data from 12 to 18 year olds and also to Dr. Bruine de Bruin's point of truly if it's understandable for those 12 to 18 year olds we may indeed have a better label for adults as well.

DR. KWEDER: Okay. Let me follow that up then. Is there is a difference in testing by numeric age and education level?

DR. HUSZTI: And that I'm not quite sure what that means.

DR. BRASS: Lee.

DR. SANDERS: I think I can answer that. I think there is and that's what a lot of

literature on health literacy is indicating and it fits into that. Again, I didn't present this quite explicitly but the median reading level of the U.S. population is around the 8th grade level and probably the median numeracy skills are lower still than that. So it comports with the other advice being given, that there is a disconnect between age and educational level. I think probably a better way to do that is just to bring the literacy level as low as possible across the board. Yes.

DR. BRASS: Please.

DR. PECHMANN: But if we're going to do testing, which I agree should be done, of the adolescent group as well as the adults, then what the research shows is that as was pointed out, when under some kind of stress the adolescents -- when they are not under stress, the adolescents and adults perform the same. So you're not going to learn anything new unless you add some level of complexity to the task where they're under the type of stress they would be when they're using

the product and I honestly think that would be good to test with adults, too, because in a clinical setting you have a lot of time to review the label. But if it's night and your kid is sick and you have to read the label and it's dark -- so if you can simulate a more realistic or high-stress environment, I think you would learn. Otherwise it may not even make sense to study the adolescents because they're going to perform the same as adults, but I think you would also learn about adults in those contexts, too.

DR. BRASS: Okay. So let me just try to summarize and comment on a couple things. First of all, as I tried to allude to, adults aren't homogenous. So when you say, adolescents behave like adults, adults don't behave like adults. So it's hard to say what that extrapolation means. Second, that is the effort in the consumer research to the degree we can under a research protocol to allow an actual use, home environment for the use so as many of those environmental stressors could be brought to bear.

But what I'm hearing is that if a drug is going to -- as you heard from the consumer research, there's already an effort to ensure that the population study reflects the diversity of the potential user population, that it includes low literacy. It includes at-risk populations. It includes tests already being done with potentially one exception: that adolescents are typically not included.

So am I hearing a relative consensus that if a drug is going to be labeled for 12 or above adolescents should not be excluded from the testing and would be a subgroup of special interest? Is that fair?

(A chorus of yeses.)

DR. BRASS: I'm getting a no or -- okay. Maybe I'll ask you specifically, Julie. Are there any -- from a -- and we're crossing over a little bit, but from an industry/research perspective, are there any barriers that are preventing us from incorporating adolescents in our current trial designs or will it always

require a separate trial or are we able to really implement such a strategy ethically and rigorously?

MS. AKER: That's a good question. For comprehensive research, I would say that that's a fairly straightforward thing to do in terms of recruitment and bringing them in. We've talked about the consenting guidelines. That's pretty straightforward and some of the things that have been brought up here about simulating stress and those types of things could probably -- we can change lighting conditions. We can change the scenarios the way that they're put, and just to build on one more thing, the comments that have been made about trying to interpret these labels is very important and you can't get good comprehension if you can't interpret what the information is.

I think those two words, maybe we need to separate a little bit, interpretation from comprehension, because what we see in our research is that I think I'm doing it just fine,

but I'm interpreting it this way. You're interpreting it that way.

And some of the wording that we do see on the label is vague sometimes. Regularly, as needed, the three times a day, all of these examples are really germane to some of the problems that we see because you're asking someone to interpret. It also happens with the icons or the pictures that are put on. So if we're going to go down this path, there is simplification that we really should be thinking about, to get it down to that more 7th to 8th grade level which is going to help both our adolescent population as well as our low-literate adults.

Now I will add that, in terms of trying to bring adolescents into actual use studies, I think that is harder because, where do you draw the ethical line there, in terms of giving an adolescent that drug to take home and use it if they normally would? Maybe they wouldn't be taking it home to use if they normally would.

Maybe mom or dad would be giving it to them. So I think that's a little bit more of a complicated issue that we need to talk about a little further.

DR. BRASS: Does anybody think that any IRB, state law, parental oversight committee would ever allow an adolescent to be dispensed a drug without parental permission, except in Holland?

DR. BRUINE de BRUIN: No. I mean, I may have incorrect information, but I believe that Melanie Gold study where she gave adolescents emergency contraception to take home was conducted without parental consent, and kids were 15 to 20 years old. But I don't -- we should ask her to convey the details because I don't --

DR. BRASS: Because it seems to me this -- yes.

DR. PECHMANN: Why would it have to be without parental consent? Why couldn't you get parental consent?

DR. BRASS: Maybe you have to.

DR. PECHMANN: Yes. I think you'd want to.

DR. BRASS: But if the marketplace -- this goes back to your point of if you're trying to simulate the real world where a 15 year old can walk into CVS, buy the drug and take it without any parental interaction, no matter how desirable the parental interaction, then, by requiring the parental interaction in the research study it may be better than nothing, but it's clearly a compromise. So the question is, is that an essential compromise to get us better than nothing or are there strategies that would allow particularly what is so essential from a public health perspective to do it.

DR. PECHMANN: I think we're hearing that it's rare for an adolescent to -- that the parents often are involved anyway in these decisions up to about age 16. So having parental consent wouldn't necessarily deviate from the real world.

DR. BRASS: I didn't hear that and maybe this is subtly worded different. What I hear was up to age 16, the parents were buying it and buying it is not the same as the kid getting up in the middle of the night, walking into the medicine cabinet, picking out the drug they want to take and taking it.

MS. AKER: Yes. I mean, the comments that I was making from our probing comments really are that as they approach the driving age they start to make a few more independent decisions and then as they get into the 16 to 18 range we noticed that they are starting to take more control over that. But they're taking -- what we're hearing from adolescents is that they're taking it from home because they don't want to hear their own funds for that.

DR. BRASS: Okay. Please.

DR. JACCARD: I'm just saying it's a whole different ball game though when you move into something like Plan B.

MS. AKER: Exactly.

DR. JACCARD: And there the whole issue of parental consent, it's a whole different ball game.

DR. BRASS: Absolutely. Tom, you have a quick comment and then Dr. Kweder. But, Tom, did you have a comment on this point?

MR. SILBER: Yes. I simply wanted to comment on the point of IRB because that is so variable. If the medication is not given out and it is a survey, that usually gets approved and it's not a problem. If the IRB considers that the medication has to do with something for which the adolescent would be exempt from parental consent, they may consider this like they did in the Gold study and approve of it, but that would never be under an FDA research because the FDA does not recognize that particular possibility for adolescents to consent in situations where the law excludes parental notification. Am I right? It's not allowed to do to see adolescents without parental consent.

DR. KWEDER: Andrea or --

MS. SHAY: I might be able to clarify. I think what happened with the Plan B. In some states if an underage female goes into a family planning clinic, they're considered emancipated minors and under the legal jurisdiction of an emancipated minor, they can consent as an adult. So that's how informed consent was obtained in certain states in that type of clinic for them to conduct the Plan B study. That might help.

DR. KWEDER: So in some sense, Plan B was easy.

DR. BRASS: Did you have another question?

DR. SANDERS: Can I just add that, also in some states including Florida in certain institutions, there are different rules applied for treatment than for research. So, for example, at my institution to do research on teenage mothers, we need the grandmother's consent right now. So there are complications and that does not apply to treatment.

DR. BRASS: Sandy, did you have another

question?

DR. KWEDER: Yes, I have a question. I want to probe the recommendations about doing these types of studies in adolescents and we just heard a little bit about some of the potential barriers. I mean, once you get into the parental consent you suddenly don't have an actual use, you don't have much an actual use, study or at least the type of actual use that we really want to get at is what happens when they're on their own. That's what we really want to know is what happens when they're on their own.

So the general comment was made to not exclude adolescents from these studies. Okay. Let's say we say that. Is this important enough or when it is important enough that adolescents not just be in the mix of the heterogeneous population in an actual use study and they need their own study because that was one of the issues with Plan B as a good example where there were some in the general study and the concern was that there weren't enough. We needed unique

studies in adolescents. So under what circumstances would we need to be thinking about asking for a specific study?

DR. BRASS: Please.

DR. HUSZTI: Okay. I'm going to go back a little bit to what we don't know, I think, and you guys can correct me if we do know it. But I think what we don't know is what are the particular areas. I mean I think we have some sense of something like Plan B, contraceptive kinds of uses, those sorts of things, reproductive health. Adolescents are going to be more private and probably, really, we do need separate studies.

In terms of other kinds of over-the-counter medications, I'm not sure we have the evidence to know what's most likely to be misused, abused or that adolescents just aren't going to get it right and will need their own separate study. So I may be jumping to the next one, but we may need some research to understand.

DR. BRASS: Well, the assumption from a

regulatory perspective for OTC drugs is nobody can use the label until you demonstrate they can and that's the standard we have for adults that we have to demonstrate that the cohort can do it and it seems to me, Sandy, that goes to some of the basic trial design issues that we talked about, that the full committee talked about, in September, because it has to be robust. And either you pre-specify a subgroup that's sufficiently powered in the actual use trial to draw adequate conclusions about that subpopulation or if you want to know what that subpopulation does you have to do another study and that's what orlistat decided to split it.

DR. KWEDER: Right. So my question is how can this group then help us think about when should it be required? Is it for everything? And that's a lot. You know, orlistat's a good example. What about statin drugs? What about anti-hypertensives? What about drugs to treat allergies?

DR. BRASS: Well, I don't think even

Merck wants to label statins down to 12.

DR. KWEDER: No. But I'm just pulling that one out.

DR. BRASS: Because the recommendation is specifically when the drug is labeled.

DR. KWEDER: Is that what the recommendation is?

DR. BRASS: Well, the way I posed it. One step at a time. Because I was trying to do the simple one first, that if a drug is labeled for adolescents then understanding their behavior becomes central to saying it's going to be safe and effective in the marketplace as labeled.

Now orlistat is the opposite example because orlistat truly was an abuse question, because the product is labeled for 18.

DR. KWEDER: Right.

DR. BRASS: So the question for orlistat was not the actual use study per se, but whether, when adolescents had access to it, would they ignore the age limitation and use it? So orlistat was a very different framework than the

one we started off. Please.

DR. PECHMANN: I don't know a lot about drug trials. But could it be the case that if data are collected on adolescents in home use and it's analyzed separately and you see a problem, then you can do the subsequent study so that then it would just --

DR. KWEDER: That's one way to look at it.

DR. PECHMANN: And another comment, it strikes me it's so different how the perspective is of a regulatory person versus an academic because I always get parental consent for any youth study that I do and that often comes way before the study is actually conducted and I think the impact of the parent ultimately on the kid's behavior no matter where I do the study or what kind of study is minimal and your assumption is if you get the parental consent it's going to screw up the whole study and it's not going to be realistic. And we have exactly the opposite assumption and probably don't have data either

way.

But I just wonder if a parent just says, “Okay, I’m going to give consent to my kid to get this over-the-counter medicine and have it at home,” that if the kid wakes up in the middle of the night and needs it the parent is not going to go running downstairs to supervise because they signed the consent form. It’s just funny. I don’t know what is correct, but I think we both have to look at our assumptions because they are opposing.

DR. BRASS: Julie, did you?

MS. AKER: Yes. When we designed -- welcome to our world. These are very difficult questions and I think we’re all glad we’re having this opportunity to discuss it. But when we design these studies, one of the things that we start with is, what’s the target population, and I think that’s central to the discussion that we’re having here because we should ask who is the target population.

In a Plan B situation, the target

population is very different than for an allergy drug, for example. It doesn't mean that a teen can't use it, but they're not necessarily the target population. People who suffer from allergies are the target population. So we need to kind of think about that versus applying generalities across all drug categories and I think that's really the approach that many of us have been struggling with is we hear case-by-case approach and right now that really is the right way to go, case-by-case.

But the target population becomes the core question. The secondary question is do we feel that there is a potential for abuse or misuse and the two examples that Eric gave are perfect for demonstrating both of these. If we ask those of each program, it's going to get us a little further down the road.

The last point about introducing informed consent to these situations, that is the ongoing conundrum of these actual use studies is, it's a study. We all know it's the framework of

a study with regulatory and clinical controls. At the same time, we are trying very hard to understand and project based on this study what's going to happen in real life. So I think these continue to be challenges.

DR. BRASS: There is one other label issue I'd like to pose to the committee and then shift a little bit to regular day advertising and the one other issue I want to put on the table is, it was hinted about this, about the effectiveness of communicating warnings and those of you in the pediatric community know the concern about the current labeling paradigms, specifically what information is conveyed by the "ask a doctor before use" type of warning and I don't know who showed it, but generally warnings are split between "do not use," a very absolute contraindication and what appears to be a weaker one, "ask a doctor before use."

The difference being if in fact you had a doctor's permission to go buy it, it would be a totally safe and appropriate thing to do, based

on your own personal health history. But that whether or not that is being construed that way by consumers and, in particular, what would an adolescent think if there seems to be a partial endorsement as opposed to an absolute warning. Any thoughts about how warnings are communicated on these labels and how, in particular, that impacts how adolescents perceive them?

Lee.

DR. SANDERS: Yes. I'll just say from our study indicating that they don't seem to be heeded very well, at least, in the cough and cold over-the-counter medications. So that's true empirically and it certainly comports with my own clinical experience that you just alluded to, that these are individuals, both parents and adolescents, who are used to coming to the doctor when they need to and otherwise if it's available they assume the doctor or another consulting individual doesn't need to be involved. So I think it makes sense --

DR. BRASS: Again, based on experience

with communication with adolescents, alternative strategies that might be, if required, more effective in getting across what is really the intent that based on your own health history if you use this in an unsupervised way you're exposing yourself to risk. Julie.

MS. AKER: It's that issue again of trying to link the warning to a consequence. Most of us understand and take seriously any kind of direction if we understand the reason why and adolescents are certainly no different than that. They're going to maybe breeze past some of these things even more than an adult would. So linking the warning to a consequence even if it's three more words has been very, very useful in gaining their attention.

DR. BRASS: Okay. Please.

DR. KOKOTAILO: And I think that the whole issue of "ask the doctor" somehow legitimizes that this is something that could be used and you just need to ask the doctor and when you think about the access to care in terms of

how easily it is to be able to ask the doctor, I think many people are going to breeze by that whether they're an adolescent or an adult to be able to use it and somehow that they feel that this is still something that they can use.

DR. HUSZTI: I think the other issue that we may not understand as well as perhaps we should is for an adolescent just like they sort of believe anything that's printed must be true, I think, there's also a sense of if it's sold over the counter, it must be safe and that sense of "Oh, something can be safe to this point but not this point," I think is a hard concept for adolescents to work with.

DR. BRASS: That's a good segue to advertising because let's talk a little bit about the regulation of advertising. Obviously, the purpose of advertising is to sell drugs and that's the purpose and that's all fine and good and the purposes of regulation as perceived by many people is to make sure some extreme line isn't crossed and one might wonder whether

there's opportunities some place in between to use regulation of advertising for OTC drugs to do better than not the worst possible thing. Maybe the standard should be a little bit higher than that and, in particular, whether there are messages that could be effectively communicated and should be effectively communicated.

As you know, direct-to-consumer advertising of prescription drugs has a variety of requirements in it. One might question the effectiveness of any of those. But nonetheless there are such requirements. We've talked about how, when we construct labels, we predefine a variety of key messages that are central and so I'm just interested in any thoughts about how advertising might play into improving this paradigm, recognizing that the label is the regulatory instrument, but the problem goes far beyond that. Lee.

DR. SANDERS: One comment based on some of the evidence I presented earlier and also a question. The comment is that I think packaging

needs to be included and as I understand, it is in the area of regulation so that when we think about regulation, as I understand it, it includes packaging and in the research that I've done that tends to be the strongest for this population, the strongest indicator of use, that and their experience.

The question I have is related to what we just left which was the Drug Facts Label and what the authority is of the FTC to require something similar to the Drug Facts Label to be applied to, for example, magazine ads of both over-the-counter and prescription medications.

MR. CLELAND: A very complex question. To some extent, the sensitivities for requiring that kind of information for OTC products, particularly since the presumption is going to be that they're safe and effective because they've been approved by FDA, that --

DR. BRASS: When used as indicated.

MR. CLELAND: Well, you know, you may understand that, but I'm telling you the public

doesn't. There is an assumption out there --

DR. BRASS: That's exactly the point.

MR. CLELAND: -- that safe means safe.

DR. BRASS: That's exactly our point, yes.

MR. CLELAND: But the point that I was going to make is that we are more restricted in terms of 1st Amendment issues of what we can require that advertisers put in their advertising. The exceptions would be, and I talked about some of them yesterday with regard to -- if it is a material omission that is a statement or a disclosure that's required to correct a misimpression that is being communicated through "truthful statements in an ad," then maybe we can require something along those lines.

But again, safety is probably the easiest area for us to do something like that in but it's going to be a limited-type disclosure and my concern is based on the research that I have seen that we've conducted that disclosures

are not very effective when it comes to advertising. For a whole host of reasons in all kinds of context, we've never met a disclosure, well, that was particularly effective.

So I don't know that conveying this additional -- using the advertising as a method of conveying this information is going to be the solution that's -- what we probably need to focus on in the advertising is making sure that what is being said is accurate and that's where we're on the strongest ground.

DR. BRASS: David, did you want to comment?

MR. SPANGLER: Yes, I wanted to make three points on your question. One, back in the '70s and into the '80s, the FTC did have what's called a trade regulation rule which wanted to require that the claims all be based on FDA's approved language for the claim. So, for example, you would have to say "anti-tussive." You couldn't say "treat cough." It took the FTC about seven or eight years to come around to

thinking, deciding, “You know what, that’s kind of silly. We want to communicate in clear, direct consumer terms. That’s who we’re talking to.”

Similarly in that same era, they had a trade regulation proposal for warnings in advertising. Now this was before about 20 or 35 years worth of 1st Amendment commercial speech law development, but nonetheless they did go through the same exercise and ultimately concluded, “You know what, for the reasons he just said, this isn’t a good way to go across that. That’s the label’s job to convey that important information about the safe use.”

About the best you can do in an advertisement is get attention and maybe get across a message. There was a good study done in the U.K. probably a dozen years or so ago that showed people a bunch of ads, what do you take from the ads, 1.8 messages. That’s a good ad, 1.8. So if you get across the name of the product, there’s one. We only have four-fifths

of a message left.

(Laughter.)

MR. SPANGLER: Headache maybe. That's about it.

DR. BRUINE de BRUIN: So when I talk about risk communication, I often point out, like I did yesterday, that a lot of existing risk communications are not effective. They don't change behavior when they intend to. One example that I didn't give yesterday, sometimes risk messages try to change behavior one way and then they try to make a behavior safer and then they unintentionally make behavior unsafe.

I'll skip the example. What I then try to argue is that risk messages should be tested to make sure that they have the intended effect, that they make behavior safer and that they don't make people accidentally take risks because they misunderstand what you're trying to say.

I don't know whether this standard can be applied to drug ads but maybe we should think about whether advertisers need to show for over-

the-counter drugs that their message is not leading to unsafe behavior, just the standard we have for risk messages in general as well.

MR. DENNISTON: Or at least no misinformation. We do a lot of our research to make sure that first we have no counterproductive results as in unwittingly and unintentionally increasing perception of benefits of illicit drug use. We have a pretty good methodology for that. So not just behavior but I think the antecedent of misunderstanding could be important.

DR. BRASS: And as he has noted, particularly unintentional misunderstanding which might pass face validity at an FTC review but in practice have a different impact. Before we move on to to research --

MR. CLELAND: This does lead to an interesting sort of result and sometimes we're sort of caught in a paradigm of because of -- because these products go into an FTC review with the presumption that they're safe and effective based on their approval, it does become

interesting when they start playing with the advertising claims where they can say it's safe, but they can't say it's safer without some type of disclosure and all of which at the end of the day is probably going to be lost on consumers.

DR. PECHMANN: From a marketing perspective what we've learned about advertising versus labeling is just what's kind of said here that advertising gives just a very simple message like the brand and maybe the benefit. But very specific things like dosage or who shouldn't use or contraindications, people are very confused. They have no idea which brand said that or which product and they know or they heard it somewhere but they have absolutely no idea of what they heard it about.

So even if you were to have it in the ad, you have to have it clear on the label. So you might as well just have it on the label. But it does help, to some extent, to have it in the ad so that they are prompted to look at the label.

MR. DENNISTON: To the effect, is there any interest in discouraging if not regulating exposure of OTC advertising to youth? Certainly in the alcohol area, I think FTC has given some guidelines to the alcohol industry, knowing that despite the best of intentions the alcohol industry reach underage youth with a huge advertising and I think the intent there was to discourage that as opposed to ban it, if I have that right, on the grounds you can get only get so much information that tends to tout the benefits and some of the risks.

MR. CLELAND: You know, I can't think of a -- off the top of my head, I can't think of an OTC drug where I think that would be an appropriate --

DR. BRASS: Certainly, if there was a drug, since this is not going to happen, I'll pick this example. So if anabolic steroids were OTC for over 18 but reviewed as too dangerous for adolescents to use because of growth effects and then it was advertised in teen magazines, that

would seem to be a situation that would be quite analogous.

MR. DENNISTON: Or maybe there's evidence of spill. Despite the intentions to advertise to adults only, we know that we can get metrics on spill and I think there are probably some statistics out there about OTC advertising spill to younger teens. I don't know if anybody has that, but it's certainly available from Ad Views and elsewhere.

DR. BRASS: David.

MR. SPANGLER: I was just going to say as we talked a little bit about it yesterday, and as Julie was alluding to on the label comp studies, it's who is the target market because that's who we advertise to. So let's face it. We mostly advertise on the news because that's when old people watch. So other than maybe acne and period pain, those might skew younger. Most OTC categories skew significantly older. So that's where we advertise and that's what we advertise about. So just look at some ads when

you're home tonight and you'll find them on the news.

But even in print, it's not -- you see a lot of things in *Parade* and *Time* and *Newsweek* and those sorts of places. You don't -- flip through a *People* magazine in a grocery store and you're not going to see a lot of OTC ads. I never seen OTC -- well, hardly do I ever seen OTC ads in *Sports Illustrated*.

MR. DENNISTON: It seems to me the empirical question is to what degree is there spill to teens and, second, what the net effect of that is in the sense of the metamessage being there are more and more products out there which will solve your problems and yet the risk side of the equation is not likely to be either (1) presented or (2) understood.

DR. BRASS: So we're going to move on in a second to the potential research agenda. But I wanted to give the audience an opportunity to raise any issues or anything they've heard about the regulatory discussion if anybody would

like to comment on anything. Please. Go to a mike or ask the panel anything.

DR. MATHIS: If I just could bring up, there were a couple of issues raised about the complexity of studies and I know when we have looked at some of the data and tried to assess whether or not we can actually approve a drug down to a certain age, one of the concerns that we've always had is that perhaps actual use or even label comprehension studies aren't telling us the whole story. We won't know what that patient is going to do when they're actually using that medication under the stress of real life or the stress of the condition at the time that they're taking that medication.

And I'm just wondering, first of all, if people think this might be a place for post-marketing studies to be done because some people have talked about that. And then, just another point, people have talked about doing separate adolescent studies and one of the things that we've actually been able to do for pediatric

studies in -- especially Rx drugs -- is to require a certain percentage of children within each age category. So, for example, we would say this study must include 15 percent patients between the age of 12 and 13 and 30 percent between the age of 13 and -- so that's one way that we can get to making sure there's adequate representation of adolescents of different age groups.

DR. BRASS: Any comment? I think that's right and that goes back to the robustness of the study, design kind of thing, and I don't know if you want to talk about post-marketing studies in the context of regulatory. I was saving it for research is where I was going to put it as a research opportunity, rather than a regulatory thing. Dan.

MR. KERAVICH: Yes. Hi. Dan Keravich from GlaxoSmithKline. This is an FTC question that might border on 1st Amendment rights. But has the FTC ever looked at the issue of holding commercial artists responsible for messaging in

terms of product claims or abuse claims? The example comes to mind of -- we've seen OTC products being brought up in -- promoting abuse potential on website and in songs and actually in commercial songs and I was wondering if the FTC has any position on that at all.

MR. CLELAND: Let me try to -- don't go away from the mike because I want to make sure I understand the question. Do we have any jurisdiction over the promotion by, I'm assuming that it's being promoted by people who aren't actually selling the products, in songs or in movies or things like that.

MR. KERAVICH: Correct.

MR. CLELAND: Well, if we throw in the assumption that the company that is marketing the product isn't paying to have its name or its product mentioned in the song or in the movies and if that's the case, then we don't have any jurisdiction over that. You're free to go out and promote as much abuse that you want to. That's what the 1st Amendment says, I guess.

Where it draws the line, of course, is you can't be doing that in the context of a commercial to sell that product. So if I am the manufacturer of a drug or an OTC drug and I'm actually paying the entertainer to tout the hallucinary effects of my product, then, yes, that's something that we could take action, and it probably would amount to unfair conduct at that point.

DR. KWEDER: I have a question for the questioner. Have you guys ever tried to pursue yourselves a product that perhaps was appearing and it's your product and somebody else is promoting it for uses that you think are inappropriate or potentially put you at risk? Has the industry looked at pursuing that?

MR. KERAVICH: Sandy, I can't comment on that. GSK has done that -- because I don't think I have an example I can think of. But I worry that the next round of drug or any drug that might be OTC or currently OTC or we do a new formulation or a new product line segment all of

a sudden has abuse potential and we find it with some rapper promoting it on YouTube as far as an abusive use potential. We worry about that, I think. I just didn't know whether FTC has tried to look at that or deal with that issue. It's a concern for the industry, I'm sure.

DR. BRASS: David, do you want to comment?

MR. SPANGLER: We're getting off from adolescents here. Sorry. But I can't think of any examples in the OTC world. But you could bring a trademark action of unfair disparagement and those are fairly common. I can't think of any in the OTC world.

MR. CLELAND: That would be the private party.

MR. SPANGLER: Yes.

DR. PECHMANN: So tobacco has done that when they -- like Philip Morris doesn't want -- it has the right to its brand and so if it's being used in a movie and they don't want it used and they hear about it, they can stop it. So the

industry can do something and has, but not OTC.

DR. BRASS: Thank you. Another question.

MS. NADORFF: My name is Gail Nadorff. I'm from the Center for Health Communication and Marketing at the University of Connecticut. I just wanted to provide the panel with one example of marketing which is to parents, but maybe implicitly to children as well and one example is for cough syrup which tastes good, or better than the competitor. Children don't want to taste nasty cough syrup. So one of the implicit implications of that is that kids are going to tell mommy or daddy that they want to go to the store and get the cough syrup that doesn't taste bad and maybe that's something that you can think about in terms of regulation.

But I also wanted to make a comment for clarification. There have been studies done in PSAs about advertising in sports because that was one of the comments made up here and very, very little advertising from PSAs are in sports,

period. It was less than two percent and the same is true we found with other types of drug advertising.

DR. BRASS: Yes. Save those. Those will be for the industry part, because those are -- do you have another question, Dan?

MR. KERAVICH: Yes, I do, Eric. Just one question on recall. Has there been any studies done about us being able to read confirmation that was verbally presented versus in print? Any strong differences in recall?

DR. BRASS: So this goes to the potential talking bottle kind of thing. Do we have data that verbal instructions are understood or heeded differentially than written instructions?

(No audible response.)

DR. BRASS: I guess not.

MR. KERAVICH: And the last question, Eric, is any information, anybody aware of using information posted on a separate site like, I guess the term was used today, a kiosk for

adolescents in terms of understanding, but understanding of product labels?

MR. CLELAND: I think that -- was the question is there any data on that or has anybody done anything?

MR. KERAVICH: I mean, I'm curious to see has there been any research showing that if you go to a neutral site or an offsite with information either verbally or written that that information is better understood and recalled?

MR. CLELAND: Not that I'm aware of.

DR. SANDERS: I was going to say, not specific to medication use. I think for other health promotion messaging in the adolescent age group there is some work being done.

MR. KERAVICH: What were you thinking of specifically?

DR. SANDERS: Well, among adolescents, I think this was in the Seattle area, looking at risk behaviors and around -- I'm trying to remember what the outcomes were. There's smoking, eating behaviors, physical activity and

giving some messaging around that, was received positively.

DR. BRASS: I'm sorry. I don't understand. How was the messaging delivered?

DR. SANDERS: The messaging was delivered in interactive, electronic kiosk with touch screen technology.

DR. JACCARD: On the previous question, again I haven't seen this in the OTC context, but I do know that psychologists have looked at people's understanding of verbal versus written information and that it's a pretty complex phenomenon that often you find that people with low reading skills actually can retain and understand written information better than verbally presented information which seems counterintuitive. But the dynamics are is that when you present information through verbal instructions, then there's a certain memory demand and there's a certain rate of processing that gets imposed on you; whereas with written materials you can reread it and you can go at

your own pace and even though it might take someone with low literacy skills longer because they can control the rate of the flow of the information, they actually in the long run end up retaining more information and better than the verbally presented stimuli and there's a whole series of studies that kind of look at the interplay between that. I've never seen it applied to OTC stuff.

DR. BRASS: Please.

MS. YASS: Hi. Alicia Yass from the Society of Women's Health Research. A lot of the misuse discussion seems to be stemming from misunderstanding or not fully understanding labels. But I was just wondering how much has it been looked into about people not even reading the label or just thinking "I've taken a similar drug to this before. I know how much to take." Or then also comparing drugs that come in either liquid form in a bottle or a bottle of pills where you have to dose it out compared to drugs that may come in a package where you have two

that you punch out. So you know you take those two pills because they are packaged together.

DR. BRASS: That's very important. I'm going to ask you -- I promise we'll get to it in the research discussion.

MS. YASS: Okay.

DR. BRASS: But I don't think that's regulatory. Andrea.

MS. LEONARD-SEGAL: Yes. I have a couple of questions actually also related to the label. I've heard a discussion about the problem with the "ask a doctor" phrase because it implicitly says that it's really okay under a certain condition to use the product. But internally we've been doing a lot of grappling over the "do not use" phrase and because the "do not use" phrase says don't use it. But then if you go to your doctor and your doctors says, "Okay, you can use it" then you're giving a whole different message and you're putting the physician in a very complicated place because you're creating an environment for a physician

where FDA has labeled something and says, “do not use it” when, in fact, it could be okay to prescribe under certain circumstances and then you’re no longer in the OTC framework. You’re in the prescription framework.

So I’m wondering what kind of messages you think that might actually be giving to a kid in terms of the trust factor that we were talking about before. I’d be interested to hear a discussion about that.

And I also just -- Well, I can stop and ask the second one afterwards. Maybe I should do that.

DR. BRASS: That way there is some chance that I’ll remember it.

MS. LEONARD-SEGAL: Okay.

DR. BRASS: Some reactions to that because this has been an area that’s been discussed a lot lately.

DR. SANDERS: I agree with that. As a matter of fact in follow-up to our study of OTC use among parents, one of the conversations we

had was we couldn't find any good data on what physicians do when they are asked by parents based on the label whether or not this medication is indicated for their child and I'm sure that there's no standard training for physicians in that. It's certainly an area open for research and exploration. So I agree it's a concern.

DR. BRASS: Other thoughts? To me, it always seemed like a little bit of a false argument. Philosophically, there's absolute symmetry that you're going to violate one or the other and what difference does it make. But it seems to me like from a public health and practical standpoint it's asymmetric that if something said, "do not use" and a doctor said, "Go ahead and use it," that would seem to be a higher level input that would trump the label and that's part of our hierarchal lives; whereas the current construct is clearly -- or the suggestion is the current construct is ineffectively protecting the public health. So even if it worked the opposite way and people didn't use

when they were told by their doctor, at least, there would be no adverse consequence. So it seems asymmetric to me and I agree we clearly need data. But I'm a little less concerned about the "it says 'do not use' and I'm going to do it just because my doctor told me."

DR. KWEDER: I'm going to disagree with you there. I think we need data on this.

DR. BRASS: I know that.

DR. KWEDER: Because I will tell you my experience as a physician and as a daughter in trying to tell my parents who couldn't reach their doctor that it was okay, and I've had as many other settings, to take two of something. Okay. To take two. "No, it says right here do not take." I said, "I know that. But I'm trying to tell you that the prescription dose is this and if you could reach your doctor, they would surely give you a prescription for the same thing." And these are parents who routinely consult me to double-check what their physicians says. So I think they're really --

DR. BRASS: I think this is a much deeper issue.

DR. KWEDER: It's a much deeper issue.

(Laughter.)

DR. BRASS: I think clearly how you are perceived in the hierarchy by your parents.

DR. KWEDER: But I see it in patients, too, where I precept a clinic and I see residents. I told a patient that probably it's easier for them to just take two or to do this or do that. They already had it at home. They had it available and they were worried because the package says this.

DR. BRASS: I think we absolutely agree that we need the answer to these types of questions and that's where the research comes in. The second question.

MS. LEONARD-SEGAL: Okay. Actually, there are two more. I hope it's all right. One of them is about the willingness of adolescents to read and we know -- we always worry in our group about how much information we're putting on

a product label. We have been listening to experts. We have learned that if you don't have white space -- and this is for adults now, and Julie have been very helpful in educating us along these lines. If you put too much on, people don't see anything.

So sometimes we want to give warnings and we have to decide what the hierarchy of those warnings are because we worry that we will not -- If we give too much, the important stuff won't be seen. But what really is important and what isn't important and that comes to the hierarchy questions that we all just go dizzy over.

What degree of information do you think kids actually would read? And do you think that there is an opportunity for research into more interactive labels where it's not something speaking or not necessarily something even electronic but something that relates to opening and closing things and popping things up or down? I mean, could it be simple that encourages? Could there be a way of playing through a label?

I guess that's what I'm asking you. And has anyone ever looked at this kind of thing? What makes kids read something?

DR. BRASS: Julie, did you want to?

MS. AKER: It's a great question and we ask a lot of these questions internally as well. I like the idea of playing through the label or having something interactive because kids they like tactile things and they learn that way. Probably we could learn an awful lot today if we had a panel of teenagers sitting up here because one of the things that we learn so much through the early work even as we're trying to develop that first label or the first three labels is that people are very willing to talk and we may not leverage that quite enough in the early stages.

We may get so far down the road that we have self-fulfilling prophecies start to occur and I'm wondering if -- I'm sitting here thinking we really should talk more to these special populations up front when we're developing these

labels because a teenager might very well tell us that they don't read any of it. We've had some teenagers tell us in the "do not use" which are extremely important that they just feel that an attorney wrote those and they kind of glaze past it to how much are they supposed to take. It speaks back a little bit to what I was talking to earlier about trying to link consequences and I've wondered as I've sat through this good meeting in the last couple of days if there's not some way to prioritize.

You almost think of a traffic light with red, yellow and green and I know we get into all the color blindness issues and everything but just that premise for a minute, it would be nice if there was some way on a label to say "These are the things we really, really mean" and they are designated in some way and "These are the things that you should be cautious about" and "This is the way we really intend you to use it.' And we don't really for any consumer, an adult or a child, discriminate between the list. So we

may be going past really causing folks to move right past it to “My child is sick and they’re crying and I just need to get them to stop.” So maybe some hierarchy could be reviewed.

MR. DENNISTON: Some of the research from Teenage Research Unlimited and MTV we’ve seen suggest a lot of teens these days increasingly are interested in back story, particularly with entertainment, particularly with technology. We’ll spend time online really have a better understanding of what’s behind the product, what goes into, who created it, what are the potential applications, how you can leverage it to another level. So I think from the research we’ve seen if you can demonstrate to them what’s in it for them, then, in fact, they will spend time with it.

DR. BRASS: Yes. Tom.

MR. SILBER: I would like say a little bit about focus groups with teenagers which is a very important source of research because results are unexpected. Some years ago, Gail Slap did a

research in which we were interested in, the Society for Adolescent Medicine, what do teenagers look for in the qualities of a doctor that takes care of her. The number one thing that came out that blew us all away was that they washed their hands. So we may be making all kinds of suppositions, but we need to hear what the teens have to say about us because it may be that the answer we'll hear is "Well, I don't know. My mom gives them to me." And that's the end of the story. So we may be in a way researching a non-problem.

But the non-problem it may be useful to research and to demonstrate that it's a non-problem to then begin dealing with the real problem which is the teenage population and young adults that deliberately go into OTCs either to commit suicide which are the usual cases of side effects, etc. "Oh, I took eight or nine because I wanted to feel better with my headache" and then you investigate a little bit more and it was a suicide attempt or with the purpose of getting

high and I think there are different populations for --

DR. BRASS: Excuse me. In the interest of time, I'm going to cut you off.

MR. SILBER: Sure.

DR. BRASS: Because you're limited on time. Please.

DR. BRUINE de BRUIN: Every time I heard the words "focus groups" I have a response to that and that is I want to agree that it's very important to do qualitative research with teenagers to find out what they're thinking and how they approach a decision. But I'm not sure that focus groups are always the right way to go as opposed to one-to-one interviews because -- especially if we're talking about -- Well, in general in focus groups you run the risk that the most vocal teenager will share what they think and the rest will just agree.

So I guess we're moving into the research part of the agenda if you don't mind. But if we're talking about taboo topics, then

it's even more difficult for adults or teenagers to speak up about how they view the issues. So it might be better -- Yes, I agree that qualitative research is important but we might consider doing one-to-one interviews instead of focus groups.

DR. BRASS: And your last question?

MS. LEONARD-SEGAL: Okay. There was another discussion earlier on about the supposition that if adolescents understand the label and can follow the label that adults probably could, too. I think that's what I heard. So I guess what I'm wondering is is that just supposition. Is there data that actually supports that notion because people have been talking about the intellectual ability of adolescents that comes pretty close to adults as they approach 16?

But there are these other psychosocial things that are tumbling on top of it. We do a lot of discussing about extrapolation lately in our group and I'm wondering if there's any basis

for our thinking based on that discussion that we could test these labels in young people and extrapolate up from it and not have to test them in adults.

DR. BRASS: Anybody have any thoughts on that? Please.

DR. PECHMANN: All I can say it's not to older adults because there is research comparing adolescents and young adults to 65 plus and that's a different category entirely.

DR. BRASS: Yes. I would just be very hesitant. Again, I think the lesson we learn every time is the diversity and richness of the population and segmentation is dangerous has been my general thought and again I come back to what I said yesterday. If you want to understand a population, make sure you study that population.

Okay. I'd like to now shift to the research agenda and before we get to a number of specific issues that were raised which I will try to make sure we get explicitly discussed, I would like to just open it up to the panel for a

general discussion of issues from their perspective that would be the highest priority research objectives to improve public health in this area.

DR. KOKOTAILO: I think the bottom line here is that there's really the lack of data, that there's a lack of data with use, there's the lack of data with abuse and there's the lack of data with risk for everyone. With looking at some of the information especially with the dextromethorphan issue which a lot of us are concerned about the overuse potential and the abuse potential there's no good data in adults that that's an effective, safe drug also. So I think that's something that there's really a lot of potential for with bottom line for that type of research with everything and including how we're doing this with adults.

DR. BRASS: I want to be a little more explicit. Are you talking about product-specific research or more general research?

DR. KOKOTAILO: I think it's both.

DR. BRASS: Okay, and let's start with the general. So if you had to articulate a couple of specific research questions that would be highly relevant for the general use of OTC products by adolescents what issues would you articulate?

DR. KOKOTAILO: I think we've brought up a number of them that we don't really know how much adolescents are using this on their own or how much is given by a parent.

DR. BRASS: So understand the dynamics of the interaction between --

DR. KOKOTAILO: -- what age that this really happens. I think that would be one to be able to start out with. I think also then in terms of the abuse potential as well. How many children are really using this to abuse it? Now obviously they're probably not using acne medicines to abuse it, but there are some other of the over-the-counter drugs that definitely have the abuse potential that we don't really have as good information because some of it comes

from poison control data.

There's a lot of under-reporting with things like that as well as we don't -- There's a lot of ambiguity with reporting. Was it really taken as an abuse or a suicide attempt or something like that as opposed to really something that they did take? Well, if two of this tablet is good, then four must be better kind of potential.

DR. BRASS: Other opportunities to obtain --

DR. SANDERS: I agree with the primary goal of documenting patterns of use but to understand the different factors that influence that use. So certainly one of the things that we've been discussing is an adolescent's capacity to understand. Whether that's construed in the health literacy concept model or another one, I think is very important and in the context of the real family unit, not just that adolescent alone but in the context of parents and peers, trying to understand what is that, in my research I'm

calling it, collective health literacy of the adolescent and the family that surrounds them.

DR. PECHMANN: I would say that we already have a lot of knowledge that we haven't tapped into. So I think the scientists would know which of these OTC products might be misused in a way that's harmful. Where you have to do 100 times the dose to get in trouble versus six times the dose, you guys already know that. So I don't know if it's politically problematic but it seems like you could create a list of target problems that are for misuse or then abuse because like allergy might be one but not abuse. So which is the ones that where a misuse would lead to a serious hump because I loved your thing about frequency by risk, you know, that you have to think about both.

Then once you know the target, you have a manageable number of OTC products, then you can start to get data. Monitoring the Future, the survey I talked about, they just added that question just this last time about using cough to

get high. Now I don't know how they put that question in. But if you went to them and said, "We have these four products that we think, five or whatever, more than just that one that we think there's a potential for abuse. Could you add those to your survey" you might all of a sudden have data from now until eternity practically on how big the problem is, the frequency question. And then the ones that are just being misused that would require a different survey.

But some other survey, you could either tack it on or get some data that then you could start to get the prevalence numbers and then once you can focus on that, then you can say "why those" and "what about those labels or those context" or "who's buying" to help to explain and then you can narrow. Because researchers will code to the problem if you indicate there is a problem. The reason so many people work with tobacco or alcohol is because the case was made. This was a huge problem and right now we don't

have the data to prove that it's a problem because -- And like I said the basic question of who is buying it and who is using it and who is supervising the use is also related. But I think if you could just put together your list of problem OTC drugs and then ask some of these survey people you might get some data pretty quickly.

DR. BRASS: Other comments?

MR. DENNISTON: Just by way of point of information, SAMHSA from the National Survey on Drug Use and Health first captured in '06 data on misuse of OTC and by that they meant non-medical use for use to get high on cough and cold medications among persons 12 to 25. They just provided that information to the American Public Health Association Conference maybe three weeks ago. It was a special report.

But to me one of the principal research issues is the parent/child dynamic. We know a lot about that. We have encouraging reason to believe I think that youth do have a lot of

respect for, look to, their parents, perhaps even more now than even three or four years ago. So I think having a better understanding of that dynamic to alert parents to have the conversations specific to the product could be very important.

DR. HUSZTI: And I'm going to take even one step back from that. I don't think we know enough either about how adolescents approach health, think about health and think about when you would access OTCs and why you would do that. So I think even a step back to understand that part and who are you going to and who are you getting the information from may be helpful as well.

DR. BRASS: Sandy.

DR. KWEDER: I want to follow up on that point because I agree with you. I think that, first of all, some of the things that we've talked about about things that FDA could do about requiring studies in adolescents, etc., those are enormous burdens for a problem that we don't know

exists. And there are certainly where we anticipate a potential problem either because of misuse or adolescents that may have unique factors in seeking to use wisely and appropriately we need to be able to identify those and then seek specific studies in those cases.

If you look at the vast array of products that are available without prescriptions, most of them are not being abused. I think that's probably a fair statement, most of them, because there are thousands. So I think from a research -- Two things. One from a research standpoint, we do need more information on what types of products and how adolescents perceive nonprescription products as related to their health or things that we don't even consider health, their day-to-day existence that they don't think of as health which we heard yesterday.

And then from that research understand what are the factors that we as regulators or as

a society can look at to help us flag products in advance that may need to be studied specifically in that population. I really think this -- we're talking here about nonprescription medicines or nonprescription products that we think of mostly as drugs. But I think that from a public health standpoint this is much bigger than that because the area we really haven't talked about today is dietary supplements and most adults don't consider those drugs. They do not consider those drugs and they just swallow those claims and assume they're all true and they take as much as they feel like and I think that -- You know we have a population that is increasingly reliant on self care. So I think these are the kinds of questions that -- what drives people to seek different kinds of therapies are really bigger questions that will need to be addressed to help us address the more focused ones.

DR. BRASS: David.

MR. SPANGLER: I was going back to Monitoring the Future in the past questions.

They are there because we asked them to put them in there because we needed to know. And I'm not aware of any data that supports your assertion that people are that reckless with dietary supplements.

DR. BRASS: Please let's not go there. We'll spend the next hour going around the room knocking -- Yes. Please.

DR. BOSCO: So I think I would like to support the idea that the first thing that needs to be done is some kind of a prioritization exercise. We've gone round and round here about we think this is a problem, we think that is a problem and the idea that you have a list and that it's a prioritized list and that you identify how you've prioritized the list, I think that's kind of important.

And then there's the next step is getting it on somebody's agenda. So research agendas in Washington I think are often times driven by the associations, special interests, whatever you want to call them. I think that's

probably a good thing. It can be a bad thing. It can be good thing. But in the good sense if we make the case that this is an issue, it's the AAP, it's not we and government who drive the research agenda. We listen to you. We listen to Congress. We listen to the constituency and that's what drives the research agenda in Washington. So, you guys, we really are the listeners here and you are the drivers in this. I want to reiterate that.

I also want to reiterate that there are all kinds of existing surveys and other kinds of things that go on like the SAMHSA survey and some of these other government surveys that if you can make a case for it, people will collect that data. They'll add it to your survey. It won't cost that much. Sometimes you'll get a lot of feedback. "Well, we have this thing and it is more important."

And therein lies the need to prioritize things and to say "We really think this is a problem and we need to get data." And it may

well be it's one year, one off kind of data collection and nobody finds anything and then it is replaced by something else.

DR. BRASS: I'm going to -- because I want to push on that little bit.

DR. BOSCO: Okay. Sure.

DR. BRASS: I want to push on that in a couple of ways. The first thing I want to push onto is that I'm a little concerned that many of the existing survey instruments are too simplistic, that they probe the dynamic fully to understand the conditions of access, the degree of nonheeding and a variety of more subtle factors that I think are particularly germane here.

Second, I would say that the issue of assuming there is no problem because it's not identified by mechanisms like this I'm also not sanguine about because we're talking about products that are used by millions of people and many of these products if misused would have a substantial risk so that a low frequency event

might become highly relevant. So I think that I agree that it requires the data to collect it, but I think we should make sure the techniques used to collect the data are sufficient to address the underlying concern and not giving us another just broad sweep that may be misleadingly reassuring.

DR. BOSCO: Yes. That's the issue with surveys is how deep a survey goes. So along with surveys, I think you do need that kind of qualitative research. There's always that balance is that you're looking at quantity and quality and you get something like you can't get rare events with qualitative research and many of these things are very rare events and you won't get that. So you're really kind of stuck with looking at a variety of data sources. For example, if you're looking for suicides and poisonings and what have you, you have that data that comes out of the emergency room and what have you.

DR. BRASS: I'm arguing the opposite.

DR. BOSCO: Okay.

DR. BRASS: For example, if when they have a headache and adolescents use acetaminophen, if the label directions for dose frequency in cumulative amount were routinely rounded up by a certain amount, we wouldn't see that in poison control data because in point of fact they are relatively protected physiologically against the adverse event and we know from acute liver failure data that it occasionally does happen, usually in abuse kind of situations, but the pattern of misuse that would be associated with that product I think would be informative.

More so, I would need help in the future. So when the next drug comes along, we can say "Dose instructions are typically followed in the community very well" or "They're typically not and we can no longer afford this margin of safety" because you have a mandate going forward to make affirmative statements in this population about the safety and in effect you have a mandate

to make an affirmative about the safety and effectiveness and we need the tools and underlying data to look forward about new situations and have those fundamental tools.

DR. PECHMANN: In marketing, the whole issue of how you define use and misuse and what the frequency is and the amount, that's constantly a struggle and you just word the question appropriately. So the question is did you misuse painkillers or did you misuse Tylenol and you're thinking that's just not going to be at it, then state the question the way you want it. Did you take double the amount? It said two. You took four. Ask the question and then you'll get the answer you want in the sense that it will be refined enough. But I think unless you -- Once the question is in one of these surveys then you get tremendous attention to it. It goes to conferences. Researchers like me hear about it and go "That's a legitimate topic to study. That looks like there's something going on there" and then you get the ball rolling. But

I think without something about the prevalence --

DR. BRASS: Yes.

DR. PECHMANN: And I agree you have to have word the questions appropriately. But I don't know how you -- Generally, you can tell them pretty much how you want to word it. If you give a strong argument, they'll word it the way you want.

DR. BRASS: Other comments from the panel? Please.

DR. BRUINE de BRUIN: I wonder whether it would be possible to take a general approach such that we can identify what needs to be communicated about over-the-counter drugs without looking at the specific drug because we've advocating looking at drug specifically and we probably can't skip that step. But I wonder whether -- I just heard we should go back and look at whether we even know how teens generally think about over-the-counter medication.

But I wonder if we can take a step back even more. Can the experts identify what do

people generally need to know about over-the-counter drugs? What do they need to know in general and what skills do they need to understand that information?

DR. KWEDER: I think that's a great point because I think we're focusing here on adolescents and, in fact, they may be no more different than the rest of the population.

DR. BRUINE de BRUIN: Right.

DR. KWEDER: After some of the comments that have been made today that suggest that in certain areas they're just like their parents.

DR. BRUINE de BRUIN: Right. So before we run away from this to go and collect data we need to first think what the questions should be and then once we have taken a more theoretical, more expert based approach, then formulate the questions and study adolescents as well as adults to see whether there are any differences and use interdisciplinary approaches, use a combination of quantitative and qualitative approaches looking at knowledge and behavioral skills and

taking those steps, but starting with the broader question.

DR. BRASS: Lee.

DR. SANDERS: I agree with all of that. I think we also need to be mindful of special populations within adolescents and one of them that has -- We've mentioned literacy, limited English proficiency, so forth, but one other population is children with chronic illnesses. I'm thinking particularly high prevalence chronic illnesses such as asthma and ADHD where use of these medications might have a different impact and also their health belief model to throw out another context might be slightly different.

DR. HUSZTI: I think that's a great point because one of the things the research also shows is that adolescents with chronic illness develop health concepts earlier and have different health concepts than kids who don't. So that's great.

I think, Eric, you made a great point, too, of just -- I think all of this makes sense

of taking a couple of steps back and sort of looking at some of this as we think what's going forward as people are -- If the sort of push in health care you're becoming more and more self directed, that we're only going to becoming more of this, not less of this. Then again, it probably is useful to know more about how do people think about this, how do they access, how do they manage their own health care and how do they made decisions about that because that also then will hopefully guide as more and more products and things come online where people are managing their health care themselves. We have a way to direct -- We're ahead of the curve as opposed to being behind the curve which I think is kind of maybe where we're at, at the moment.

DR. BRASS: I want to bring back the question that was raised thematically about what we know about how the label which is so key to the initial communication is actually utilized and we've talked about this for a very long time about a bunch of very basic things where you can

find using just numbers what percentage look at the label, what percentage don't look at the label. You can find any number you want for any of those questions you want and it hasn't yielded definitive clarity on some of those basic things.

Even as opposed to some of the issues about label format, we don't know how eyes -- And I'm not a cognitive psychologist, so I'll mess this up too. When you first see the label, how does your eye track through the material on the label? What influences what parts of the label you look at, in what order and when? A bunch of very generic information that is central to how we're trying to communicate seems to me to not be you look it up in the book and you know the answer and that's how you go forward.

What do others think about those kinds of issues and whether they have validity moving forward or is it just going to be we already know everything is different? Does it have potential to yield utility or is it just going to tell us what we already know?

DR. PECHMANN: I think that's an excellent idea because that's extensively used in other marketing context and it leads to very valid information that usually has a theoretical basis and can be explained and it hasn't been done and I think it would help tremendously.

DR. BRASS: Other thoughts? Please.

DR. JACCARD: I was going to change the topic.

DR. BRASS: Go ahead. Please.

DR. JACCARD: I was just going to mention a few things that I think are important for research and just some things to think about and parents, of course. I have to say that. But something I think could be useful in this domain that is very rare to see in the form of RFAs or RFPs or things and that is just asking for a high quality literature review and a very thoughtful reflection by groups of scientists on where we need to go. They tend to fund empirical studies or they're fund in the form of literature reviews meta-analyses. But I'm not talking about that

right now.

If you took a group of really strong social scientists and said, “Go do a very careful literature view of all the lack of studies that are out there, and then take all the lessons learned in other areas like AIDS, application of behavioral science to AIDS and things like that and write us a great roadmap on where to go,” that kind of research, it’s almost impossible to pursue that through formal funding mechanisms. We can value from that so much. So I would emphasize that as one thing.

A second, I’ll just mention three things. Second thing that I think is really important is that we recognize how much technology is changing relative to how slow research goes. You put in for a proposal. From the time you get an idea, it takes a year and a half to two years to get funded. It takes five years to conduct it. It takes a year for it to get out from there. You’re looking at eight years.

Twenty years ago, the internet didn't exist. We are seeing huge changes in technologies now and I think it's really important for funding agencies to think outside the box, to think about where we're headed, where are we going to be ten years from now, where is technology going to be with us ten years from now and how can we start laying the groundwork for where we'll be then. That's not easy to do but it's really important given the dynamics that are involved.

I think another area related to that, there are two areas that come to mind, is that we do need to do research on the internet and kids access tons of information from the internet and it's going to be such a central tool that we have to be starting to do research on information search strategies that kids use on the internet. Right now, computers are not widely accessible. For example, I do a lot of work with very poor populations in New York City in the South Bronx and families just can't afford computers. But

there is going to come a point very soon when computers are like televisions and they're going to be in everybody's home and we need to be thinking about things like that.

I think of information and sources of information and I know that in a lot of marketing companies where I have friends who work there are huge efforts going on to the development of advertising and reaching people through avatars and the use of simulated people. And the idea is that when we get information, we like to get that information from different sources and the marketers now are creating websites where you can choose who you want to get your information from and they are all simulated people and they are amazingly real what's going on and there is so much potential with technology that way that I think we really need to thinking about ten years ahead of time and where we need to go relative to that.

I think the idea of kiosks and presentation of information through kiosks and

through new technological means is something that we really need a great deal of work on.

Then there's a whole psychology side of me, more behavioral side of me, that says and a parent side of me that we do need to look at building relationships between parents and physicians for dealing with issues of proper use of medications and adolescents. How can we get adolescents to disclose to physicians or to disclose to parents what medications they might be taking without the parents' knowledge or the physician's knowledge and issues of disclosure, I think, are also very important.

We can't assume that if a label accurately conveys information that that also means that behavior is going to follow from that. Knowledge is a necessary but not sufficient condition for accurate use and we desperately need research to understand given accurate information why aren't people using medications properly. So those are just some thoughts.

DR. BRASS: Just is there any data on

counter-programming on the internet, creating sites that will show on searches and provide counter information on the internet for people who are looking for information about substance abuse in your case?

DR. JACCARD: Yes. I think there is but I think it's really small scale and the dynamics and the metrics move so fast it's hard to read.

DR. BRASS: You can't keep up.

MR. DENNISTON: If anything, it's the other way around, pushing back against limited use or circumscribed -- but I think these ideas about the future are really important particularly what we already see now, Second Life and the avatars and basically selling billboard space if you will and personalities in the whole Second Life and that's where kids spend so much time. I don't know if that's a regulatory issue or not. Does FTC -- If you regulate product placement, what about avatars on Second Life?

DR. BRUINE de BRUIN: With regard to

the internet and the kind of information that people find there, we have a very small scale study in which we looked at parents and their decisions to vaccinate their children and where they get their information and the less informed parents use different words to describe vaccinations. So when they search for information about it on the internet, they would use different words as search words than more educated parents and, of course, the less educated parents need more information about it. But they are the ones who find the anti-vaccines websites because of the words they type in the search engine. So it's something to be aware of.

But to go back to the suggestions that were just made, I like all of them. I want to add that if we're -- I like the idea especially of encouraging an interdisciplinary literature review. Those things are often -- Literature reviews are often not funded and I wonder whether we can even ask for not just literature review but maybe the involvement of risk analysts,

people who know about risk, so that influence diagrams can be built to find out which areas would be most promising to focus research on and then in addition to that, I think in general this topic needs research as interdisciplinary and I think that one thing that often happens in the funding mechanism is that there's a call for interdisciplinary proposals, but then the reviewers come from one discipline and don't like it. So maybe that is something to address like how do we make sure that interdisciplinary proposals do indeed get funded and not just on this topic but in general.

DR. BRASS: Lynn, would you like react to some of the things that you've heard or are you just going to pass out the checks?

DR. BOSCO: Yes, there are so many. Anyway, as a disclaimer, I've only been at NIH for a year and I can't say I talk for all of NIH at all. But actually, I spent 16 years at AHRQ. So I'm going to kind of back up a little bit with people and talk a little bit about AHRQ. This is

the Agency for Healthcare Research and Quality.

So a lot of what we've been talking about here tends to be applied research and it actually does fall more within Health Services research and in AHRQ purview. On the downside, AHRQ doesn't really have an investigator-initiated research program anymore and has no money for it. So that's kind of a Catch-22 of having what ends up being a research agenda almost more as appropriate for AHRQ as it is for the NIH if not more so.

So what to do? I'd make a few suggestions about some of these things and how you might approach them. Now what AHRQ does have is a program that I started which is the Centers for Education And Research And Therapeutics, the CERTs Program, which is nowadays 14 centers at various institutions focused very much on therapeutic issues, a lot on prescription drugs and devices, but also able to deal with OTC drug issues and they have done some of that.

Now the nice thing about the CERTs

Program is that these are cooperative agreements and this is infrastructure money. So that's kind of something to listen to, I think, when you're on the edge in research is to find people who have infrastructure money. So CERTs is our infrastructure money and what that means is that they're to some extent not hooked into the investigator-initiator what we call around here the RO1 which is that you give us an idea. We give you the money and you go away for five years and do your research on that one particular topic. They are able to deal with topics that come up and have like worked on areas such as Vioxx and ACE inhibitors as issues have arisen. So they are not hooked into this project that they developed and wait eight years to get it done. They are actually able to be a little bit more nimble. There is that program.

And the other thing that AHRQ actually has is the Evidence-Based Practice Program, the EPCs, which admittedly do a lot of meta-analysis. They have a bunch of centers that they pay to do

essentially an evaluation of the literature and it isn't just a meta-analysis, although they do meta-analysis. They will look at epidemiology and they will look at other things.

So if there are topic areas, it's possible to -- I still think that they have set up on their webpage the ability to propose topic areas. I mean you have to be kind of specific about the questions that you're trying to have answered. But there is money there to do that. They do have money that's budgeted to do these evidence reports.

They'll also feed into a process that goes on at the NIH that's in the Office of Medical Applications Research which will take something into a State of the Science Report or they do -- I forget the other thing that they do, but a State of the Science Report is one of those things where they'll take everything and they'll have a bunch of experts look at issues. So there is that.

The other thing that NIH is actually

moving towards is some very large program type projects. These again, sometimes these are cooperative agreements and the one program that they're actually putting a lot into is what is called CTSAs. You guys all nod your heads because you know about these things and what these are are basically clinical research centers. There are currently, I think, 20 of them. The plan is that there would be 60 of these. These are again infrastructure programs where people get money to develop a center and then you can test the ideas as opposed to again coming in in the traditional way of "I had this idea and I want to study it. I'll be gone for eight years and get to me then." The structure is there. You propose the ideas.

Those are some opportunities, some research type opportunities. If you're in an area that is kind of on the edge, kind of not well researched, kind of difficult to research, it's to partner with organizations or academic institutions that, in fact, have the data, have

access to the data, can support, say, a fellow or a project and it doesn't end up having to go through the whole peer review process because the center has already been peer reviewed and chosen as appropriate to do this kind of research. It's certainly not a panacea for some of the issues you raise and I think that the amount of time that research takes is on everybody's screen.

DR. BRASS: But certainly if the NIH perceives a need, particularly a need that's helped defined by other sister agencies and that's consistent with mandates that have been given within the broad five year plan of the institute, saying that no existing structure exists to meet this research need, we have to do something about it is certainly something that you can do.

DR. BOSCO: Yes.

DR. BRASS: And I think that's one of the things you're hearing is that these problems have been recognized for many years. We've not been able to garner research support from the

peer review process in part because it doesn't fit into any niche, because the FDA doesn't have the money to support its own research needs and here we are after all that time. So it seems like the opportunity for a more imaginative solution if this really is perceived as integral to safe use of drug by adolescents should be there.

DR. BOSCO: Right. I mean, our office is currently working on an initiative related to adherence which some of this falls into. There is also a very active group within the NIH that works on health literacy issues. That is a topic that there are many of the institutes that are interested in health literacy issues. So those are at least on the radar screen. Some of these other issues probably not and would need to be brought to the attention of people and as I said, we're moving more towards different models and looking creatively at trying to deal with the issue of how long it takes to get research done and then once it's done, how to get it

disseminated and how to get people educated about it.

DR. BRASS: Because my last editorial on this would simply be that it's -- I mean I'm a cell biologist and that the amount of resources it would take to address many of these questions that would translate to an immediate impact on public health is trivial compared to many of the other investments that are quite legitimate but are structurally supported to get priority.

MR. DENNISTON: I would also suggest that a huge asset is the, jointly funded by NIH and the CDC, Health Communications Research Centers, UConn with Leslie Snyder, Annenberg with Bob Hornick, University of Georgia with Vicki Freimuth, because these people are really expert, top of the line and I think some of these issues that we're talking about today are really applied health communication issues and they have the expertise and already been peer reviewed and funded. So I think there's a great asset there to work on some of these issues.

DR. BRASS: We're nearly the top of the hour and I'm going to take just probably to streamline just a little bit and try to get to some issues that we've talked about and get a little bit more focus recommendation. And this is probably more in the industry barrel. What can the industry do?

We've heard that in addition to a number of the product-specific issues or these broad research issues there really may be a very broad attitudinal and knowledge misconception in the area of OTC drugs in general. The presumed safe, a variety of other labels are or aren't important and one of the things I was very impressed about in the drug abuse is the value of sustained, consistent messaging with a long-term objective of changing attitudes.

And I wonder if there's not an opportunity not to run a few PSAs for a few weeks, but really a long-term strategy to say these are attitudes and behaviors that we need to change in the general public, adolescents is one

targeted focus of that, but really this is going to require changing the perception of the U.S. population about OTC drugs and we're not going to do it at 3:00 a.m. with an ad.

Reactions?

DR. SANDERS: I guess my reaction goes back to the earliest comments which was before we do that we need to identify that there's a problem and what exactly the message would be.

DR. BRASS: Exactly.

DR. SANDERS: And I think once we get that, then we can take the expertise from the truth campaign and others to deliver it. But I think we need that prior research.

DR. BRASS: Other perspectives?

MR. CLELAND: The way you formulated that question it's not limited to adolescents.

DR. BRASS: No, that's correct.

MR. CLELAND: I think that -- I agree with it.

DR. BRASS: You might --

MR. CLELAND: And my perception is even

without our data in front of me that's exactly what we're seeing. We have a great deal of confusion about what safety means. We have a great deal of confusion about what products are actually notwithstanding the FDA disclaimer, what products are actually FDA approved and which ones haven't been reviewed by FDA. You go to the grocery store. You go to the cold and flu aisle and in the cold and flu aisle, you will find homeopathic products. You will find dietary supplements. You will find OTC drugs. And a consumer hasn't a clue what the difference is between those products.

So I think there is a problem, but it's not a problem in terms of just adolescents.

DR. BRASS: Sandy.

DR. KWEDER: Yes, I agree with you. I think that in some sense it's a challenge and I think it's a challenge to anticipate medicine and health care as we go forward and what are the messages that the experts believe need to be communicated. We have to understand something

about those who we're communicating with first and understand something about their attitudes.

But are there certain messages that are important just like in the drug abuse field? Which one will resonate because we're talking about the future of health literacy for adults really?

DR. BRASS: Please.

MR. DENNISTON: By way of a parallel, the IOM a few years ago studied the underage drinking issue and their recommendation or the top three was a parents' campaign, not a youth campaign, and frankly I believe for the drug campaign that's probably where we should go. But due to Congressional influence, etc., we really can't go there because if it's seen as a youth campaign, everything must go to youth, although it's about 60 percent youth, 40 percent parents now. But the IOM model, a terrific study, made some strong recommendations which are basically being ignored, but notwithstanding it was a good study.

DR. BRASS: Other comments about that kind of approach?

DR. PECHMANN: I would just say that there has to be something in there for the industry in terms of they have to really believe that. Because if it's just going to be "I'm going to sell less products," so people are taking double they should, but they're not really being heard and I'm selling more because they're --

DR. BRASS: I would say --

MR. SPANGLER: I'll take care of Connie so that our view gets heard. You don't need to defend.

DR. BRASS: I think nobody has more at stake in this than the industry.

MR. SPANGLER: Precisely.

PARTICIPANT: Exactly.

DR. BRASS: If you look at what the opportunities in theory are to self-management and self-treatment over the next ten years, the greatest barrier is the inability of the average

consumer to have the proper tools to take advantage of those opportunities. If regulators and the public had confidence, there would be greater access. So I think nobody has a greater stake in achieving that end than the industry whether they know it or not.

MR. SPANGLER: We know it. We want people to use the product safely and responsibly and live to be 110 using them safely and responsibly. That's our commercial interest.

DR. PECHMANN: Right. Just pushing back, but you haven't done -- I mean a lot of other industries have done public service announcements and that sort of thing and you guys haven't.

MR. SPANGLER: That's not true. That's simply not true.

DR. BRASS: That's why there's the campaign.

DR. PECHMANN: Right.

DR. BRASS: I mean, there have been a number of OTC related public service

announcements. But contrasting --

DR. PECHMANN: But not of the type we're talking about here.

DR. BRASS: Right.

DR. PECHMANN: Right. So there's --

DR. BRASS: I think that's why the contrast is so striking that the approach taken, the episodic versus the sustained, and --

DR. PECHMANN: Exactly.

DR. BRASS: One last category just to make sure the representatives of the clinicians and advocacy groups, it seems to me again -- in the interest of time, I'm just going to skip to a posit for you to criticize -- that adolescent physicians have a very broad education agenda with the teams they interact with and it's a very important, very constructive component of what the discipline does. I'm wondering where education about OTC drugs appears on that agenda and whether there's an opportunity to explicitly define it in the context of domains of education that over the teen years might be developed.

DR. KOKOTAILO: There are a number of opportunities for education in terms of faculty development, in terms of residency education and student education. I think that over-the-counter medications may not have been addressed specifically in a lot of these things. They are addressed in a number of different ways in terms of substance abuse education curricula, in that overdose potential and that comes up in that as well as some of the mental health type things and as well as pharmacology. I think this is something that hasn't been probably as addressed maybe as thoroughly as it should be in many of those areas of education, but there still are educational programs that are available with this.

I myself work a lot with faculty development and so this is something that everybody needs in terms of the updates, even in terms of what is newer or what are things that they need to have information with us and also what's out there even on the internet. What are

some of the things like that people aren't as up-to-date with perhaps in terms of the faculty and this teaching the teachers I think is especially important. That's been more difficult since some of the federal programs for that with like HRSA and Title VII have been cut or semi-cut or unexplained, not exactly knowing what the cuts are going to be. But that's something that I also think needs to be supported.

MR. SILBER: The other thing is it is introduced into the teaching models, I'm Director of an Adolescent Medicine Fellowship. in different aspect of it. When we teach adolescent suicide, we teach about acetaminophen, liver transplant, hepatic coma and so on. When we teach about transition to college health and how to prepare a young adult, it's part of it. There's not a specific area when we teach about substance abuse. That's where this is no, it was four and seven percent in the young and old adolescents. It was zero a few years ago.

So from the point of view of the

research that we clinicians are interested in, the one concern that we have when we discuss research is that to be careful that if one has a hammer it looks like everything that you want to study is a nail and the reality is that we are looking at a whole series of things that can be studied here that need to be studied simply to once and for all have the documentation. But it is not what needs to be studied more in depth. What needs to be studied more in depth is the trajectories.

DR. BRASS: We're not going to go back to abuse.

MR. SILBER: Yes.

DR. BRASS: So we're down to seconds left. Any urgent last thoughts that we haven't covered that people feel we have to get on the record? Please.

DR. BRUINE de BRUIN: We'll see how urgent you think it is. Pediatricians and clinics are not the only place we can educate. We can educate and we've talked about the

internet and whatever, but kids go to school and if there are general skills that they need to make good decisions about over-the-counter drug education those general skills may help them in other areas of their lives, too. Maybe in school, they need to be taught health literacy, decision-making skills, general skills that will help them to make those decisions.

DR. BRASS: Good. Thank you. Julie, you had one.

MS. AKER: I do. We have a lot of good ideas on how to get good information here, but I just want to restate that the best way to get good information is to go directly to the consumer and that’s going to be information right now in a relevant experience in a robust way where we can look at a variety of different age groups and so forth on a variety of different topics. So going to the source is really going to be very important to this initiative.

MR. DENNISTON: I understand that a lot of the schools require administration of

prescription and over-the-counter drugs to be done by a school nurse, whereas in the child/adolescent taking them in. I think the question would be how effective that is. We hear anecdotally that a lot of parents avoid that. They don't trust the school nurses. They don't trust the situation. So another educational moment, but how effective are the programs now working?

DR. BRASS: Yes. I think, one of the messages that I hope came across is whatever we do we can't simply implement it but we have to assess its efficacy longitudinally and a rate based on that. I agree.

I'm going to shift to concluding remarks now and I won't use my entire five minutes because they're gone already. But I first of all want to thank the organizers, all the participants and the audience for what I hope, I certainly found, and I hope you found to be a very productive discussion. But I hope it's also just the start. If what we have done ends

at 3:00 p.m. it was two pleasant days in Bethesda.

But we really need an action agenda to come out of this that involves all the stakeholders so that when we meet next it's to review what we've learned since and begin the next phase. And this should be absolutely future looking because I think whether it's in technologies, new medications, new health care dynamics, the future is going to be different and we should be trying to ride the wave, lead the wave, not watching it go by.

Again, thank you all very much and have safe trips to wherever you're off too.

(Applause.)

DR. KWEDER: I'm going to take the government mike and as someone from the FDA, we're the ones, I think, it was our staff that initially tried to get our arms around putting this workshop together and I really want to thank the other parts of HHS that worked so hard with us to put this together.

This was one of the hardest workshops that we ever put together, at least, in my experience and we do a lot of them because it really forced us to stretch. And your contributions in your respective areas, this has really been absolutely fascinating. We have so much to learn and I think we're going to be going back to do exactly what Eric has challenged us to do which is try to come up with really what is going to be the path forward so that we do continue to learn and apply that learning to meet public health needs.

Now before I let you all get up, I have to take this opportunity to do a little lesson because my experience was when Don and I walked in here, there were a lot of people who were looking at this morning like "What the heck is that. Why are you guys dressed like that?" For people who are used to being around Public Health Service, they know why we're dressed like this, but I suspect that many people here don't know what on earth this uniform is.

No, we're not going to Iraq, at least, not yet. Right, Don? You didn't sign up for that, did you? Just for people who don't know because I know a lot of you don't come to these things, this is -- You see a lot of uniforms in the room. These are Public Health Service uniforms. We're one of seven uniform services. We are not an armed service. They don't give us guns and that's a good thing. Right, Lynn?

And we actually do get deployed, however, and we get deployed in disaster situations. So every officer you see in this room makes a lot less money than you (a) and (b) has the pleasure of having a deployment role and some of us here have been deployed together. Don and I spend a couple weeks together in Louisiana during the hurricane, but we wear these uniforms on deployment. We often are deployed with Department of Defense. This is called the -- What are we calling them now? BDU?

(Off the record comment.)

DR. KWEDER: Yes. BDU, Battle Dress

Uniform. So that's your lesson for the day and it's a Public Health Service. The Surgeon General. Yes, that's Public Health Service. Thank you. That's the lesson.

(Applause.)

DR. KWEDER: Off the record.

(Whereupon, at 3:09 p.m., the above-entitled matter was concluded.)