century. So, I welcome everybody's thoughts and I look forward to the discussion that will take place. Thank you.

SCIENCE PANEL

MR. CLELAND: Good morning. My name is Richard Cleland. I'm an Assistant Director for the Division of Advertising Practices at the FTC, and I will be the moderator of the first panel this morning. With me is Walter Gross, a Senior Attorney in the Division of Enforcement, who will be assisting me and keeping track of time.

First, I would like to thank the panelists for volunteering their time to participate in today's workshop. I'm very familiar with most of the members of this panel. I have worked with them, many of them, through the Partnership for Healthy Weight Management or through their work as expert witnesses or consultants to the FTC.

This morning's panel consists of scientists, researchers and physicians with extensive experience in the study of overweight and obesity. We have a specific, narrow goal. We will be looking at eight popular diet claims. Specifically we will be considering whether such claims are scientifically feasible and the conditions that might affect the feasibility of such claims.

Before getting into the assumptions for this morning's discussion, I would like each member of the panel to take 30 to 60 seconds to introduce themselves, and if they would, at the same time, also identify any specific weight loss products or treatments in which they may have a pecuniary interest. And I'd like to start at my right, Anthony.

MR. ALMADA: My name is Anthony Almada and I'm the Chief Scientific Officer for a company called IMAGINutrition. We develop and create nutritional and dietary supplement products. We do clinical trials on them when we insert and wrap intellectual property around them. I do have a disclosure of interest in terms of having a patent pending -- an international patent pending for an agent that reduces the side effects of ephedra. I was the co-founder of a dietary supplement and sports nutrition company called EAS, and I've been working in the dietary supplement industry since 1975.

DR. BLACKBURN: I'm George Blackburn from the Division of Nutrition at the Harvard Medical School and the Director of the Laboratory for the Study of Nutrition and Medicine, and for Nutrition and Metabolism at the Beth-Israel Deaconess Hospital.

As far as disclosures, I don't have any diet products for which I have a direct benefit. I have

served as a consultant advisor and we do receive grants from a variety of federal government, industry, NIH and foundations to carry out this work, and I have provided consultations to all of these parties.

DR. GREENE: I'm Harry Greene, Medical Director at Slim Fast Foods Company, and I have a special interest in meal replacements, in particular, Slim Fast Foods. During the last six years, I've been responsible for the development of a number of clinical evaluations with Slim Fast that have been published in 16 peer review journals and am continuing to work with Slim Fast in developing programs that will prove that it's effective in special situations.

DR. HEYMSFIELD: I'm Steve Heymsfield. I'm a Professor of Medicine at Columbia University and I'm Deputy Director of the New York Obesity Research Center, a federally funded center. I'm, like Dr. Blackburn, on a number of drug company and food company advisory boards. I'm on speakers' bureaus for these companies and I also do contractual studies in addition to NIH-funded studies on weight control products.

DR. HUBBARD: I'm Van Hubbard at NIH and one of the things I can tell you is that I'm a pediatrician and Professor of Pediatrics at the Uniformed Services University of Health Sciences.

DR. STERN: I'm Judith Stern. I'm Professor of Nutrition and Internal Medicine at the University of California-Davis, and I'm also a past president of the North American Association for the Study of Obesity, which is our major research organization in the United States.

I'm co-founder and Vice President of the American Obesity Association, a lay advocacy group, and I really look to the FTC to establish leadership in the area. I hope that we can get information out to consumers that they can really use. And I don't have any conflicts at the moment.

DR. STIFLER: Hi, I'm Larry Stifler, I'm President of Health Management Resources. We currently work with several hundred hospitals and medical centers around the country establishing medically supervised treatment programs, and we currently have about, I'd say, 10 or 12 long-term research studies going with these institutions. My only conflict, I guess, is I'm President of HMR.

DR. WADDEN: Hi, I'm Tom Wadden from University of Pennsylvania in Philadelphia. I'm Professor of Psychology, Director of the Weight and Eating Disorders Program. I do research on weight loss using diet, exercise, pharmaco-therapy, surgery. I don't have any

direct financial interest in any diet products. I do serve as a consultant to a couple pharmaceutical firms and to one firm that produces a very low calorie diet.

DR. YANOVSKI: I'm Susan Yanovski. I'm Director of Obesity and Eating Disorders Program at NIDDK and I'm Executive Director of the National Task Force on Prevention and Treatment of Obesity at NIH, and I am a family physician and physician nutrition specialist. And I have no conflicts with industry.

MR. CLELAND: Thank you. As noted earlier, we'll be looking at eight specific performance claims and we'll be looking at them in the following order: One, the advertised product -- and that's a term I'll define here in just a moment -- will cause substantial weight loss for all users; the advertised product will cause permanent weight loss; three, consumers who use the advertised product can lose substantial weight while still enjoying unlimited amounts of high calorie foods; four, consumers who use the advertised product can lose weight only from those parts of the body where they wish to lose weight; five, the advertised product will cause substantial weight loss through the blockage of absorption of fat or calories; six, consumers can lose substantial weight through the use of an advertised product that is worn on the body or rubbed into the skin;

seven, consumers who use the advertised product can lose substantial weight without reducing caloric intake or increasing the level of physical activity; and eight, consumers who use the advertised product can safely lose more than three pounds a week for a time period exceeding four weeks.

These claims will be considered with regard to the following products: OTC drug products, dietary supplements, creams, wraps, devices, and patches. When we refer to products this morning, unless otherwise specified, we're going to be referring to that class of products. In other words, we're not specifically considering prescription drugs, meal replacements, low calorie foods, surgery, hypnosis, or special diets such as the Atkins Diet or VLCDs. This doesn't mean that claims for these types of products may not be false or misleading, only that each of these areas may raise specific issues that time is just not going to permit us to explore this morning.

Now for the panelists. We would like your individual opinions on the validity of these claims. We are not asking you to work out any uniform or consensus view. We will, however, ultimately ask each of you for your bottom line on each claim, whether you believe that given the current state of knowledge, such a claim is

scientifically feasible, not feasible or uncertain.

And some points to keep in mind. First, we're not looking for scientific certainty, but only your individual opinions based upon a reasonable degree of scientific and medical certainty. On each claim, we would like you to consider, first, whether the claim is theoretically plausible, and second, whether the claim's performance is scientifically feasible.

In considering these claims, pay close attention to -- or consider the mechanism -- possible mechanisms of action, as well as any available scientific evidence that is relevant to the claims. Please keep in mind that as we proceed through these claims, it may be necessary to define certain terms in order to get a better understanding of the claim.

Are there any questions at this point?

(No response.)

MR. CLELAND: I'm going to have a little bit of difficulty seeing everybody down the table here. So, if somebody's trying to get my attention, you all in between, just yell at me or throw something or whatever.

At this point, in order to provide a frame of reference for this morning's discussion, I've asked Dr. Steven Heymsfield to kind of go over with us and review for us some of the mechanics of weight loss, what's

involved, on a very general view with the hope that this is going to provide us with some basis for our discussions this morning.

Dr. Heymsfield?

DR. HEYMSFIELD: Thanks very much. Dr. Hubbard was off to a good start when he talked about energy balance. Energy balance is the ultimate determinant of weight loss or weight change, and we can think of it simplest as energy intake and energy output and the two have to balance in order to maintain your weight. So, if you've maintained your weight over the last year, that means you've been in energy balance for the last year and that everything you've burned up in your tissues in terms of energy has been replaced by food you've eaten. So, that's the simplest overall model that we work with.

We burn energy in the body to commute function, muscle strength and to keep us alive, to keep us thinking, and that heat is given off by the body and that's our energy output. That's the output, the expenditure side of the equation, and that really comes off in two forms, two main forms. That is, at rest, it's called our resting metabolic rate. That's about two-thirds of the energy we expend and the remainder is physical activity. There's a few other small things, but physical activity is the rest. So, that's the output

side of the equation.

On the input side of the equation, we eat food that has energy in it and that energy is in the form of protein, fat and carbohydrate. So, all of that energy we expend in our tissues to commute life, then, is replaced by the energy in the food that we eat.

Now, there's a little bit in between and that is we don't absorb all of the energy we eat. We absorb normally about 95 percent of the energy we eat. The rest comes out in our stool and urine. That 5 percent we lose is normal. It's the non-absorbed components of our diet. So, if you eat 2,000 calories a day, you lose about 1,000 in terms of undigestible and unmetabolizable components.

Then once we absorb that energy, it's used by the tissues and it really distributes into three different forms of energy in the body; carbohydrate, protein and fat. Fat is the main storage depo in the body. It's very high energy density, as you know. It's nine calories per gram. It's very high energy density. That's most of the calories in our body.

Then we also store energy as protein. It's not really a storage energy depo, it's what really creates function. It's the protein in our muscles that give us strength and so on. So, we have protein in the body as a form of energy.

And then, finally, we have a small amount of carbohydrate and that's in the form of glycogen and glycogen's in cells and it's only a small amount, about 1 percent of the total energy in our bodies in the form of glycogen. But what's interesting about glycogen and protein both, they require a fair amount of water to keep them in solution, and so their energy density is actually very low. It's about one calorie per gram whereas fat's nine calories per gram. So, it's very low energy density and glycogen is only a small amount, about 1,000 to 2,000 calories in the body.

Now, when we change energy balance -- let's say we're all eating normally here and we change our energy intake, and we go down, say, 500 calories a day or something like that. We immediately go into negative energy balance and that will cause us to lose weight because we have to replace that missing energy with energy from our tissues. The first place it's drawn from is from these glycogen stores, this small amount of glycogen. And that glycogen has a lot of water. So, for the first five to ten days that you're on a hypo-caloric diet, you will lose a fair amount of weight because that glycogen has a very low energy density.

Then after that you begin to consume some of the fat in your body at an accelerated rate and your

weight loss will slow down at that point and you'll be consuming most of the energy deficit from your fat stores. But also, you do burn a small amount of protein, and we know that on the average person who goes on a diet, about three-quarters of the weight loss comes from fat and about one-quarter comes from protein, after the first week or two, when the glycogen stores are exhausted. So, that gives you a little bit of a picture.

Now, we have certain rules we follow, these are very rough rules in the weight control field. We know that roughly one pound of weight loss requires a deficit of about 3,500 calories, roughly 3,500 calories per pound, and that means if you drop your intake 500 calories per day, that after one week, you lose about one pound. Those are rough estimates. And we know that most adults have somewhere -- depending on how heavy you are, 200,000 calorie stores in your body. This is a normal weight adult, 200,000 calories. So, people can survive without eating somewhere around 70 or 80 days depending on how overweight you are, just without eating at all, creating deficits of, say, 100,000 calories or something like that.

So, that gives you some sense of this overall energy intake and energy output and energy balance situation.

Now, I just want to sum up by saying, how can we lose weight in terms of therapeutics. Physicians and scientists have identified four different ways you can lose weight in this energy balance equation.

The first is to reduce your food intake; that is, protein, fat and carbohydrate in your diet, that energy in your diet. If you reduce that, you will go into negative energy balance.

The second way is if you block the absorption or limit the absorption of one of those nutrients. So, for example, if we give you an agent that blocks the absorption of fat, that will have the same net effect as reducing your intake. And there are agents that will do that. So, absorption is the second mechanism.

The third mechanism, overall, is to increase energy expenditure, and that is the output side of the equation, and that can be accomplished really through a voluntary effort as physical activity, or involuntarily through augmentation of the amount of heat your tissues produce, increasing the resting metabolic rate. There are very few agents at present that do that. Really none that are very potent in increasing your energy expenditure separate from physical activity.

And, finally, the fourth way, which is, again, not very widely available, is to re-partition the energy

in your body. This is done widely in the cattle industry where you can change the proportion of body as fat, muscle and bone, using various hormones. If you repartition the body and all of your weight becomes muscle instead of fat, that's yet another way to change sort of this balance, this energy balance equation, and people have done that -- say, for example, when you go on a diet and you also add some type of physical activity, it can have some influence on the partitioning of energy in the tissues.

So, then just to sum it up, most of us are in energy balance. If we change energy balance, we can do that by any one of four ways: reduce intake, absorption, repartitioning and energy expenditure. Thank you.

MR. CLELAND: Thank you, Dr. Heymsfield. We're actually a little bit ahead of schedule and that's good because we have -- like I said, we have the eight claims that we're going to go through and we have a limited amount of time. All of these are claims that we could probably spend hours discussing and debating, but we're going to try to distill it down into the matters of mere minutes.

I'd like to take this opportunity to introduce Dr. Bruner.

DR. BRUNER: Thank you.

MR. CLELAND: It's good to see you.

DR. BRUNER: The D.C. traffic, I live here, you should know, but it doesn't help.

MR. CLELAND: Doctor, everybody took about 30 to 60 seconds to kind of introduce themselves and give some background and identify any conflicts that they might have. You want to take that opportunity?

DR. BRUNER: Okay. Sure. I'm Dr. Denise Bruner, immediate past president of the American Society of Bariatric Physicians, a group that's been about 51 years old, who we are dedicated to the treatment and modification of risk factors and problems related to obesity and weight management. So, I'm here representing a scientific group. I really have no particular interest in any company, but I certainly have a great and vested interest in the health of the American public.

MR. CLELAND: Thank you, Dr. Bruner.

Dr. Heymsfield, there was one question that I had about your presentation. I wanted to make sure that this just wasn't a misstatement. In a 2,000 calorie diet, did you say 1,000 calories are lost or 100?

DR. HEYMSFIELD: A hundred.

MR. CLELAND: A hundred, okay.

DR. HEYMSFIELD: Absorption.

MR. CLELAND: Right. All right, let's move on

to a discussion of the specific claims. At the end of the time that we have allotted for the discussion of the claim, I will poll the panel here individually as to each claim, whether in their opinion it's scientifically feasible, not feasible or uncertain. If the discussion does not last the allotted time, whenever the discussion is complete, we'll go ahead and take a quick poll.

We're going to start with the claim that, 'The advertised product will cause substantial weight loss for all users.' I've asked Dr. Greene to take the first shot at this particular claim.

Before we start, I'd like to give you an example from some ads that we've seen of this type of claim. 'No will power required.' 'Works for everyone no matter how many times you've tried and failed before.'

Dr. Greene, is there any product out there that we know of, other than surgery, that works for everyone?

DR. GREENE: I don't think so. I guess I can answer that with an affirmed no.

MR. CLELAND: Okay. So, in the terms of the framework that we're talking about here, you would say it's not theoretically feasible?

DR. GREENE: No.

MR. CLELAND: Well, I told you some of these would probably be easy. Anybody else want to add

something?

DR. HEYMSFIELD: If I can --

MR. CLELAND: Yes.

DR. HEYMSFIELD: Well, I could probably try and put some numbers on that. If you take the commonly used prescription drugs, Phentermine, Meridia, Xenical, the types of drugs we work with, I think that about a third to a half of people, just as a ballpark, respond to these drugs, and a very good drug response might be a little more than that. But we're very accustomed to non-responders. And one of the outcomes of that is when you report these pharmacologic trials, you report responder analysis, the number of people who lose no weight, the number of people who lose 5 percent, 10 percent and so on, categorical weight loss. And you do see in these trials that many people either gain weight or don't lose weight even with a pharmacologic agent. So, it's never -- or very, very rarely 100 percent response.

DR. GREENE: I could expand a little bit on that on what Steve has already said and that has to do with energy balance. Several years ago when we were developing our live-in calorimeter at Vanderbilt, it became clear that everybody had a different level of energy expenditure at the resting metabolic rate, and for that reason, even if you have the exact same caloric

intake, the amount of weight loss is going to be different based on the individual metabolic rates.

So, taking that into account, one wouldn't expect everyone to lose at the same amount of rate even if they had good compliance to exactly what they were supposed to be taking in.

MR. CLELAND: Dr. Blackburn?

DR. BLACKBURN: Well, as a surgeon, I would like to add a footnote. I wish that we could guarantee you 100 percent success with surgery, but we cannot. This happens because if a person doesn't modify their caloric intake, they won't be in compliance with the principles that Dr. Heymsfield has told you and they can not lose weight and regain weight and weigh more. Also, there are people who are intolerant to the surgery, that need to have the surgery reversed. That would be another criteria.

And, finally, surgery is reserved for a selective group of population, so not every person who has a problem with severe or morbid obesity, anything more than 100 pounds overweight, is a candidate for surgery.

MR. CLELAND: Tony or Anthony?

MR. ALMADA: Harkening back to what Dr. Hubbard said in his introductory comments, with the revelation of

the human genome and given the intensive quest for a suite of obesity genes, which apparently is not one gene but a multiple cluster of genes, perhaps it may be very distant or unrelated. I think it is feasible that there will be, at some time, an ability to detect an agent or a delivery system that would enable anyone to lose weight. The question is, how long will it be, and that will also change the landscape of marketing to individuals, not in the drug realm, but in the over-the-counter or the on-the-shelf realm, self-care realm.

How can we find an agent that would fit you as an individual that would be efficacious and safe and minimize the chance of it becoming a non-responder? So, I think it is definitely feasible.

MR. CLELAND: Would you say at the current time it's feasible?

MR. ALMADA: I would say it is not.

MR. CLELAND: Dr. Stern?

DR. STERN: Yeah, I would add probably not feasible within the next five years or the next ten years because it's such a complicated area.

MR. CLELAND: Dr. Hubbard?

DR. HUBBARD: Just to further comment, even if there are developments relating to increased genomic information that becomes available, I still do not think

it's feasible that any one product will work for all people.

MR. CLELAND: Dr. Stifler?

DR. STIFLER: It might be helpful, Richard, if you could read that list again of products that we are talking about because, clearly, if people go on a restricted calorie diet, using Dr. Greene's product, for example, you will lose weight and everybody would lose weight. So, can you narrow down again exactly what we're talking about?

MR. CLELAND: Right. We're talking about, to the extent there is an OTC drug category, OTC drugs, dietary supplements, creams, wraps, patch devices, patches, those types of products.

DR. BRUNER: I'd just like to add, you know, looking at the medical model when we treat hypertension, there are a multiplicity of agents because there are multiple modalities that play a role in the effective treatment of hypertension. So, again, to say, using a beta blocker as the one treatment, I think that's the same analogy. Using a beta blocker will treat all hypertension, using one thing can treat all obesity.

MR. CLELAND: Dr. Yanovski?

DR. YANOVSKI: Yes. I think it's also important -- in the example you gave it says, no

willpower required, works for everyone no matter how many times you've tried and failed before, that, well yes, people can lose weight if they take in fewer calories. This assumes that everyone is going to use a certain product that may require taking in fewer calories. So, I don't think one can make the assumption that everyone is going to adhere to a certain regimen and lose weight with any of these products.

MR. CLELAND: Although I did -- my assumption here is not that it's a question of adherence, but it's a question of just being -- the agent, itself, being capable of producing weight loss in everyone who uses that particular agent.

DR. YANOVSKI: Well, I'm making the assumption here -- let's say there was a dietary supplement and it tells you to use that dietary supplement and a certain way to use it. I guess you're excluding meal replacements. But if it says to use it with a certain dietary regimen and that dietary regimen caused you to eat fewer calories, everyone, if they adhered to that, might lose some weight. That's the only caveat.

MR. CLELAND: Yes? Dr. Wadden?

DR. WADDEN: Just going back to what Dr. Heymsfield said, that whenever you have a product of any kind, you're going to find a distribution of responses in

people. Say if the average weight loss for people is 10 pounds with a product, you will have a distribution such that 15 percent of individuals who receive the product are going to lose less than three or four pounds. This is just a bell-shaped curve normal distribution.

So, just about any product you give, you'll have a tail-end that does very poorly and another tail of the distribution that does very well. So, no product is going to produce substantial weight loss for all individuals regardless of what product it is.

DR. GREENE: I guess the caveat is -- the way this reads is substantial weight loss and all users, and in biological systems, it's never all, right?

MR. CLELAND: Okay. More discussion? Dr. Heymsfield?

DR. HEYMSFIELD: Well, maybe I'm preempting later questions, but is there a number we should put to substantial?

MR. CLELAND: Well, to sort of -- yeah. I would say that for the purpose of this question, unless it's necessary and unless there's a sentiment that it needs to be done for this question. I agree that with regard to some of the later questions we will, based on our previous discussions, need to define some of these terms. The question is whether we need to define that

for this particular claim.

DR. HEYMSFIELD: I guess I don't think you do because by having the word "all" users in there, I think it pretty much implies that this question is valid as it stands; in other words, that all people won't lose substantial weight from most, if any, products.

MR. CLELAND: Dr. Stern?

DR. STERN: Rich, I would even feel comfortable modifying this question. The advertised product will cause weight loss for all users, and I would say all users will not lose weight. So, I don't even think it has to be substantial. It could be Tom's two or three pounds in, what, six, 12, 14 weeks or even six months.

MR. CLELAND: Any of the panelists have an objection to that modification?

DR. STIFLER: I think substantial makes it more conservative, and if somebody makes a claim that there's substantial weight loss, whether they say 10, 20 or 30 pounds, that makes it even less feasible. So, if you want a conservative approach, you use substantial and all users. I think it sounds pretty unanimous that that's simply not feasible.

MR. ALMADA: Rich, I would add, if I may, that given the objective of marketing and namely advertising in the context of this discussion, an operative modifier

needs to be placed that would convey to the prospective buyer of the product a magnitude of change that goes beyond just one pound or half a pound. So, I think it would be wise to retain substantial.

MR. CLELAND: Well, unless there's an objection, let's retain substantial then and I think we'll poll on this question. Actually, on the polling, we will start off at one end and move down, and then on the next time, we'll go on the other end, so, Anthony, you don't always have to be the first person to indicate.

So, the question is, is this claim scientifically feasible? Yes, no or uncertain on this.

MR. ALMADA: Uncertain.

DR. BLACKBURN: No.

DR. BRUNER: No.

DR. GREENE: No.

DR. HEYMSFIELD: No.

DR. HUBBARD: No.

DR. STERN: No.

DR. STIFLER: No.

DR. WADDEN: No.

DR. YANOVSKI: No.

DR. WADDEN: I do think it's important -- Rich, down here, it's Tom.

MR. CLELAND: Yes.

DR. WADDEN: Just to add, given the current state of the knowledge.

MR. CLELAND: Well, that is the assumption for all of these claims, that we're working as the knowledge that we have today.

MR. ALMADA: If I may change then, in that comment, change my vote to no.

MR. CLELAND: Okay.

DR. BRUNER: So, it's unanimous.

MR. CLELAND: Okay. Moving on to the next claim: 'The advertised product will cause permanent weight loss.' As an example of this claim, 'Get it off and keep it off.' 'You won't gain the weight back afterwards because your weight will have reached an equilibrium.'

Dr. Yanovski, you want to take that one first?

DR. YANOVSKI: I'd be happy to. And don't we all wish? I think that anyone who's ever struggled with their weight realizes that the most difficult part of weight management isn't really the initial weight loss, but rather trying to keep that weight off long-term. And so, it's not surprising that consumers would be really taken by a claim that you could use a product or service over the short term and never have to worry about your weight again.

And in specific, I was asked to address the fact that you could use a product or service and stop it, and your metabolism, in some way, would be reset and you would not have to worry about your weight. Unfortunately, as we all know, weight regain after weight loss is the rule rather than the exception, and those individuals who do manage to maintain weight losses over the long term do so by changing their diet and changing their physical activity.

And, in fact, there is a weight maintainers' registry run by Doctors Jim Hill and Rena Wing, in which they are following thousands of individuals now who have lost substantial amounts of weight, at least 30 pounds, and maintained a weight loss for at least one year. And many of these people have kept their weight off for many more years. And the vast majority of them report carefully monitoring their diet, and they report high levels of physical activity.

Just as we talked earlier about the analogy with the hypertensive drug, if you've been taking a medication to control your blood pressure and you stop the blood pressure medication, we can expect that blood pressure will go back up. Similarly, when you remove an intervention, whether it's eating fewer calories, increasing your energy expenditure, if a supplement did,

in some way, work to increase metabolism, stopping that, you would expect that any benefit from that product or supplement would also be stopped.

There are no known supplements, devices, programs that give you a permanent alteration in your body's metabolism, and there is no way that lost weight will be maintained, that we know of, in the absence of taking in fewer calories and increasing your energy expenditures, such as Dr. Heymsfield talked about, to keep yourself in energy balance at that new and lower weight.

We also don't know of any products or supplements that will permanently reduce appetite once the supplement's been discontinued. Even in the case of weight loss surgery, which I know we're not discussing today, but that was brought up as an example in which patients lose a large amount of weight and keep much of that weight off for years, there's an ongoing intervention. If you have weight loss surgery, you've reduced your stomach capacity. If you've had a bypass component, you're also reducing the number of calories that are coming in.

So, if we're looking now to say, can we advertise a permanent cure for obesity in which a time-limited treatment is going to lead to permanent changes

in body weight, my conclusion is that, at this point, that doesn't exist and it's not likely to exist in the foreseeable future.

MR. CLELAND: Dr. Greene?

DR. GREENE: Based on the question and based on the response, I just had a question. You're assuming that this permanent weight loss will continue in the absence of continued treatment if I understood the argument from Dr. Yanovski. Is that correct?

MR. CLELAND: That's the assumption of the question, yes.

DR. GREENE: So, do we need to modify that to make certain it says that this product will be ceased, will be no longer used, and therefore, the weight loss will continue? Does that imply then if you do continue the use of the product that the weight loss could be permanent?

DR. YANOVSKI: At this point -- I was asked by Rich to look at the question of even when it's discontinued. But I have no trouble right now with saying that I'm not aware of any products or supplements that will give you permanent ongoing weight loss even if they're continued, even in the case of weight loss medications, which may help -- and we're not discussing prescription medications -- but which may help you

maintain a lower weight over an extended period of time. There is still some degree of weight regain even if you continue on the medication.

MR. CLELAND: Dr. Greene?

DR. GREENE: But in the Weight Loss Registry, you said that these people had maintained the weight loss.

DR. YANOVSKI: Yes, that's correct. And they --

DR. GREENE: So, that would have to be qualified with the caveat then that if you continue on that dietary regimen, the weight loss would be able to be maintained.

DR. YANOVSKI: Well, it depends on what we're talking about here. The people on the Weight Maintainers' Registry are generally -- they're eating fewer calories and they're exercising and I think that the idea here is that people are talking not about dietary regimens. We're specifically excluding low calorie diets and physical activity programs. But rather that there is some weight loss device, supplement that will produce permanent weight loss, in which you cannot modify your diet and physical activity and yet in some way your metabolism is reset so that you no longer have to worry about it. Is that correct?

MR. CLELAND: I think that that is correct. I mean, you know, going back and we'll probably have to keep reminding ourselves of the class of products that we're talking about here, you know, the dietary supplements, creams, wrap, OTC drugs, and those types of products, and, you know, just in terms of -- I'll throw this out as a question.

The assumption here -- well, let me first say, the assumption here is this is an unqualified claim, so that I guess the way that I'm interpreting this question and the way we meant this question to be interpreted, unless you tell somebody that, yeah, this will work as long as you keep using the product, the implication is, if you tell them it's permanent weight loss, that I can use up the bottle, I'll lose the weight and it will stay off. Unless you tell me otherwise, that's what I'm going to assume. So, that is the assumption of the question.

Now, the one question I have is that there are some products out there that claim to affect the ratio of body fat to lean muscle mass, and whether or not -- if that is true, would that result in permanent weight loss and part of that may be the question of, is there enough of this conversion, do we see evidence of enough of this conversation that it's going to be significant in the long run?

DR. GREENE: No.

MR. CLELAND: Dr. Stifler?

DR. STIFLER: I don't know if I'm missing something here, but going back to the previous question, isn't it kind of irrelevant, permanent weight loss? Since you're not going to get the weight off with these products in the first place, then the issue of permanent weight loss becomes somewhat meaningless. So, clearly, from the previous question, the answer has to be it's not feasible because you're not going to get the weight off anyway. Aren't they implying that when they say that?

MR. CLELAND: Anthony?

MR. ALMADA: I think, in part, we're exercising an argument of ignorance because no one has done a long-term perspective trial evaluating an agent, an over-the-counter agent that's ingested in a solid dosage form or applied to the skin. We can't answer that from a basis of logic and evidence. We're simply speculating.

Now, the question is, is there a group like Jim Hill's group, actually their group also engages in a low-fat diet and, also, they eat breakfast, a typical finding among their long-term, non-recidivistic weight losers, is there a group that has been doing that or following along prospectively people that are actually taking these types of products? And I would say the answer is no. So, we

have to answer this from a question of not knowing rather than knowing.

MR. CLELAND: Well, let me follow that up with a question of, okay, what kind of mechanism would have to exist in order for there to be a permanent weight loss from the use of an OTC product or a dietary supplement? What would you have to do to the body permanently for that to have an effect?

MR. ALMADA: Well, like Dr. Heymsfield related, I think there are two or three things that could be done. They, perhaps, would be toxic outcomes. One would be affecting the gut, what's absorbed or actually an increased amount of excretion or affecting one of the appetite centers in the brain so you just don't eat as much, forever. Forever.

MR. CLELAND: Is that --

MR. ALMADA: Basically, an oral surgery, so you ingest something and it does a surgical deletion to a part of the body that effects a change wherein they don't store or process calories in the way they used to, or they burn much more than they had in the past.

My comment was related to chronic use versus cessation of use, and you're claiming -- you used the word or the descriptor "afterward" implying either after cessation of an agent or after the weight loss is

achieved, which is important.

MR. CLELAND: Dr. Stern?

DR. STERN: Well, I do -- if you look at the ads and you, perhaps, look at the interpretation that consumers put on the ads, I really believe that what we're talking about is permanent weight loss even after you stop using the product. We certainly do have some evidence in the drug area with mechanisms, something like Xenical, which prevents the absorption of about a third of the fat that you eat. There are long-term trials that show that you can take weight off and keep weight off for over a two-year period. But certainly, when you stop using the medication, weight is regained. There isn't anything permanent about that weight loss.

And so, I think that here we have to be very conservative and say, when we stop using the product, is there any evidence or anything, in fact, that the weight loss is permanent?

MR. CLELAND: Um-hum.

DR. STERN: I would have to answer no.

DR. YANOVSKI: And I would go even further than Judy because I would say, even with the prescription medications, you don't maintain --

DR. STERN: Right.

DR. YANOVSKI: Most people don't maintain all

of that weight loss. Even on medication there is still some regain. So, I think it's an unrealistic claim regardless.

MR. CLELAND: Okay. Well, I'm going to poll the question starting with the other end this time, Dr. Yanovski.

DR. YANOVSKI: I would say it is not scientifically feasible.

DR. WADDEN: Not scientifically feasible.

DR. STIFLER: Not scientifically feasible.

DR. STERN: Not.

DR. HUBBARD: Not.

DR. HEYMSFIELD: Not.

DR. GREENE: Not.

DR. BRUNER: Not.

DR. BLACKBURN: Not.

MR. ALMADA: An emphatic not.

MR. CLELAND: Moving on to the next question. Consumers who use the advertised product can lose substantial weight while still enjoying unlimited amounts of high calorie foods. An example of this kind of a claim, eat as much as you want, the more you eat, the more you lose, and we'll show you how.

Dr. Stifler?

DR. STIFLER: I think this is related to later

question seven, also, on calorie management. Probably just a little quick background. I think there are hundreds of studies indicating that this epidemic of obesity is related to calorie management. As people consume more calories and exercise less, individuals and whole nations gain weight.

An interesting article by the USDA that showed that calorie availability to individuals since 1970 has actually gone up 15 percent. So, unlike what most people, I think, believe, we probably are eating more food and we're certainly, everybody agrees, exercising less. So, that probably takes care of the epidemic. The CDC staff said in a JAMA article last year that with more than 60 percent increase in the number of obese Americans, just in the last nine years, this can't possibly be related to biology or physics. So, this is a cultural problem related to calorie management.

In terms of the treatment, again, I think there are hundreds of studies showing that there is actually a dose response relationship which makes it even more convincing between the amount of calories you cut out of your diet and the amount of weight you lose and the amount of physical activity that you do and the amount of weight that you lose. So, I think the data is pretty clear on this.

The bottom line is you have to manage calories in order to lose weight. So, a claim that you can eat as much as you want or lose substantial weight while enjoying unlimited amounts of high calorie foods just has no support for it whatsoever. And as obvious as that may sound, if we look around, we can see that most people who pick a diet don't necessarily agree or, as you said earlier, they want to believe to the contrary.

An interesting study that's been repeated now with 184,000 people, I think, in JAMA, published last year, essentially saying that more than 80,000 of the people who pick a diet pick one that's almost guaranteed to fail because it doesn't relate to managing either incoming or outgoing calories. So, it may be obvious that this claim from the scientific end is groundless and can't happen, but I'm not sure that the public is ready to accept that yet. So, that's probably another reason these ads attract so much attention and people continue to buy these products.

MR. CLELAND: Well, we saw examples in both of the clips that we watched this morning. This is an almost universal type of claim in weight loss advertising. Additional comments? Van?

DR. HUBBARD: Well, I think that people -- it's human nature to be more receptive to interventions or

claims that people want to believe in rather than that may be actually realistic. So, when people hear about these claims, if it's something that they want to believe in, they tend to want to try it, even though if they really thought about it from a rational standpoint, they might have other expectations. But in my mind, again, it is a law of physics and you cannot lose weight unless you change your energy balance.

MR. CLELAND: Dr. Heymsfield?

DR. HEYMSFIELD: I was trying to look at the sentence and see it. Even if we took out the words 'high calorie' it just says unlimited amount of food. It would still not hold scientific validity in any case. It could be low-calorie foods. It wouldn't matter. The fact is that if you ate an unlimited amount of food, you're not going to lose a substantial amount of weight.

DR. WADDEN: Just a comment. Steve, I was thinking the same thing. I think the only caveat you could make is that you ate unlimited quantities of fruits and vegetables or low-calorie foods, eat as much as you want, there's some evidence you can eat a low-fat, high-carb diet and potentially lose weight on that. But even so, I think you're right, if you have unlimited amounts, you're not going to lose weight.

DR. HEYMSFIELD: Yeah, it would be close.

MR. ALMADA: There's an implicit interpretation here that I can easily discern. If unlimited means more than what you were eating prior to using this agent, that's one scenario. If unlimited means eating to satiety, that's a different scenario. So, if you have a person who's weight stable and they're eating X number of calories per day, they begin using the agent or remedy X, they still are eating as much as they want to, but they could lose weight.

MR. CLELAND: Doctor, did you --

DR. STIFLER: Well, back to Tom's point again. That's correct, but I've never seen an ad that suggests if you take these pills, you can eat all the broccoli you want. I think these ads always suggest it's the food you really like and the ads clearly show -- are talking about high calorie foods generally.

MR. CLELAND: I see the point that you're making here. In one sense, we don't want to get wrapped up in this discussion, in an ad interpretation issue. I think that if looking at the specific example that I gave you, while there might be some people in the world that would discern that, well, I may not want to eat as much as I ate before, therefore, this claim might be true, that's not the way this claim is going to be interpreted. There is a significant number of -- in fact, probably

most consumers that look at this type of claim would take away that I can eat everything I want, especially if I see people eating all these cheeseburgers and french fries and all of this kind of food. That's the message it's intended to convey.

DR. STERN: And I just had one comment because I'm a nutritionist and I think about food. Let's talk about two Krispy Kreme doughnuts, chocolate covered, creme-filled and --

MR. CLELAND: My breakfast this morning.

DR. STERN: Right. So, that isn't unlimited. One could potentially eat that a day. And if you put that on top of your diet, that's 680 calories and basically you would gain weight. It would take only about four days for you to gain a pound.

And I guess the other way I think of looking at it, for the average person, if there is an average person on the nutrition label who consumes 2,000 calories a day, that would be 34 percent of their daily intake if they didn't overeat. So, I think it makes it very difficult for people to eat unlimited quantities, especially of things like Krispy Kreme doughnuts because they taste good.

MR. CLELAND: Are we ready for a poll on this one?

Okay, we're going to start on my right this time. Anthony?

MR. ALMADA: No.

DR. BLACKBURN: No.

DR. BRUNER: No.

DR. GREENE: No.

DR. HUBBARD: No.

DR. STERN: No.

DR. STIFLER: Unfortunately, no.

DR. WADDEN: No.

DR. YANOVSKI: No.

MR. CLELAND: Unfortunately, you're right, this is like the reality check this morning, folks, and our next workshop is going to be on Santa Claus.

Our next claim is: 'Consumers who use the advertised product can lose weight only from those parts of the body where they wish to lose weight.' Example of such a claim is, 'And it has taken quite some inches off my butt, five inches, and thighs, four inches, my hips now measure 35 inches, I still wear the same bra size, though, the fat has disappeared from exactly the right places.'

Dr. Wadden?

DR. WADDEN: Well, if I can echo my colleague, Dr. Stifler, unfortunately, no, once again. This speaks

to the issue of desiring to spot reduce very clearly, and I think there are lots of claims from creams and wraps that if you use this product, you can reduce your thighs, your tush, whatever that unsightly part of your body is that you wish to reduce.

It also speaks to the issue of body fat distribution, that we store fat throughout the body. When you think about it, you carry fat in your chest, in the gut, in the legs, the arms, the extremities, and there are differences in body fat distribution. Women tend to store body fat in their lower body to a greater degree than men who store weight in the upper body. I think you've all heard about the differences between the apple-shaped figure, which is the upper body fat patterning, and the pear-shaped figure, which is the lower body fat patterning.

Now, unfortunately, when you go on a diet or use most of our conventional weight loss means, you do, in fact, lose weight from all over the body. You lose fat from all of your fat stores. You cannot preferentially reduce from a single fat store. So, that is the difficulty, that you can't, in fact, just turn on those fat stores in the thighs or in the buttocks. In fact, you're going to lose weight from the top as well as the bottom. And the way I heard this said to me most

eloquently was by a patient of mine I saw about 10 years ago, and as she was completing a program and had lost about 40 pounds she said, Dr. Wadden, when I started your program, I had a large pear-shaped figure; now, when I'm finishing your program, I have a small pear-shaped figure. And that speaks to the reality that you can't change your body type for the most part.

Now, if you have an apple-shaped figure -- if a man comes into your practice and he's got primarily a gut, when he loses weight, you will see a reduction in his gut. You will, however, see that his legs probably get somewhat thinner and that his chest gets somewhat thinner, also. So, even men, with this upper body fat distribution, still are going to lose fat from the extremities and from the lower body as well. It's most pronounced looking when a male loses weight because the gut does remit, does disappear. For the female, she is still going to have prominent hips and thighs. She will actually, in many cases, have a smaller top. So, she will lose her chest and be disappointed and, in fact, the hips will flare almost as much as they did previously. So, you don't see much of a change in it.

So, in terms of, is this scientifically feasible, currently, this is not scientifically feasible.

MR. ALMADA: Here's where it starts to get

interesting. This is the first comment or claim that actually has a scientific evidence base that actually could be used to -- some would use it to refute this claim -- or actually to lend support. There are two scientists of significant distinction, George Bray and Frank Greenway that a couple of panelists here have collaborated with, and they actually have a patent and they developed an agent, or a mixture of a cream that was used to spot reduce. It was a thigh cream. It was introduced in the early ‘90s. It underwent a resurrection in the past three or four years. It’s a very aggressively marketed product by one company based in Utah and they claim spot reduction with a topical application of a regional area of choice.

Now, these two scientists of eminent distinction have chosen to take a very low profile, off-the-radar stance. However, going back to their patent, and I believe there have been two clinical trials that have been published, which one of them they were collaborators on, they have evidence, although it may be very specious -- I shouldn’t say specious, but rather thin evidence, indicating that this preparation with this composition works. I’m not validating that, but there is some evidence to support this claim.

DR. WADDEN: Well, I was aware of that abstract

that was published by Dr. Bray and Dr. Greenway and they are very esteemed colleagues, they're good friends, but I have not seen anything published in a reputable journal that has corroborated that initial abstract that was published. And furthermore, I don't think there was good evidence of actual showing fat loss in the thigh. I think that they showed a 'reduction' perhaps in the circumference of the thigh, but there was never an analysis to show that there was a loss of fat. So, I think, perhaps, the word 'specious' is an appropriate word.

MR. ALMADA: Well, actually, there was a full-length publication that emanated from their research.

DR. WADDEN: Where was that published?

MR. ALMADA: Current Therapeutic Research.

DR. WADDEN: Thank you. I will go look that up. I wasn't aware of that.

DR. STERN: Rich?

MR. CLELAND: Dr. Heymsfield?

DR. HEYMSFIELD: I think that just expanded on the abstract. I don't think that was anymore definitive than the original abstract, but --

MR. ALMADA: But it was a full-length publication.

DR. HEYMSFIELD: It was a full-length

publication, yeah.

DR. STERN: Just to comment, we also did a study just about -- I think just before George did that work -- with a comparable cream, rubbing it on the thigh. The placebo was rubbing a placebo on the opposite thigh and we didn't find any effects.

We, also, as I recall, took fat from the area and looked at lipolysis with the cream, without the cream and didn't find effects. So, I can't confirm it and really think that clinically or practically, it doesn't result in significant effects.

MR. ALMADA: My comment was not to validate the claim, but rather just to give a perspective. I would actually agree that the techniques that are available right now to assess regional fat loss have not been applied to that actual type of remedy or product.

DR. STERN: But, I guess -- I would agree that potentially it might be scientifically feasible, it might be. If you could have a delivery system that could really penetrate, but practically, right now, there's nothing to my knowledge that's out there.

DR. WADDEN: I think that's an important point. That's why I kept asking. Are we talking about the current state of knowledge or what is theoretically feasible?

DR. STERN: Theoretically.

DR. WADDEN: I think theoretically it could be feasible as we learn more about fat cell morphology and function, but right now it is not scientifically feasible.

DR. BLACKBURN: Rich, can I just ask Dr. Heymsfield, in weight loss, now that you have a regional MRI and DEXA, does the fat reduction come off proportionally or are there certain phenotypes that selectively reduce the weight in some spots versus others?

DR. HEYMSFIELD: Well, the limited information we have is that there are tremendous variations in how people lose weight, but that's not under their control or any pharmacologic control. But when people lose weight, they lose it very differently. It depends on age, race, a high variety of factors.

DR. WADDEN: And just a follow-up, in the limited number of studies that I've seen that we've done, also, is that we've looked at people when they've lost weight and found that they looked like they've lost the same proportion of weight from the upper body and the lower body, that you don't even -- with people with visceral obesity, they do lose weight clearly from that depot, but they're still going to lose some weight from

the lower body as well, and often, the same proportion of weight is lost.

DR. HEYMSFIELD: I don't know if this helps us, but just for discussion, the absence of studies on this topic, not just negative studies, but the absence of studies, speaks volumes, I think. Often, scientists, you know, don't indulge in publishing negative results, and I think that could be a big part of what you're seeing here is that if this really did work, say these spot creams, the technology is out there to really investigate this thoroughly, I honestly think it would have been reported.

DR. BRUNER: Dr. Heymsfield, just a question. I was wondering if you were aware of any particular studies looking at the effective recombinant human growth hormone just as it is a catabolic agent in terms of just overall general fat loss.

DR. HEYMSFIELD: I think, in fact, there's an article in JAMA this week, right, showing growth hormone does reduce total body fat, yes.

MR. CLELAND: Are we ready for a poll? Dr. Yanovski?

DR. YANOVSKI: Under theoretically plausible, I would say that that would be yes, and under scientifically feasible, at this point, I would say no.

DR. WADDEN: No, given the current knowledge.

DR. STIFLER: Agreed, no.

DR. STERN: So, theoretically plausible, yes; scientifically feasible, no.

DR. HUBBARD: Currently, no. It's theoretical that there may be opportunities in the future, but it would require further investigation.

DR. HEYMSFIELD: Yes and no.

MR. CLELAND: I understand that.

DR. BRUNER: Okay, yes and no.

DR. BLACKBURN: Yes and no.

MR. ALMADA: Yes and uncertain.

MR. CLELAND: Okay, all right. Well, now we're going to move on. The next claim is: 'The advertised product will cause substantial weight loss through the blockage or absorption of fat or calories.' An example of such a claim is, 'Lose up to two pounds daily. The named ingredient can ingest up to 900 times its own weight in fat, that's why it's a fantastic fat blocker.'

This is one of the -- the question, I think, at this point where we may get into a definitional issue on substantial weight loss given particularly the data on Xenical and, perhaps, some others. So, Dr. Stern, do you want to address this first?

DR. STERN: And I guess I should give this disclaimer now. We got funding from a Napa County DA's

Office to study Fat Trapper Plus from Enforma, and the results of that study were published in the January issue of the International Journal of Obesity.

MR. CLELAND: Thank you.

DR. STERN: So, the way I began to address this question was to ask the question, what would it take in terms of malabsorption of fat to lose one pound a week, two pounds a week, two pounds daily. And in terms of calories, to lose one pound a week, it would take mal-absorption of about 500 calories a day or about 55 grams of fat. To lose two pounds a week, it would take mal-absorption of about 1,000 calories or about 110 grams of fat. And to lose two pounds daily, it would take mal-absorption of more than 7,000 calories and that would be about 750 grams of fat daily.

And I guess in my clinical experience, I have never had a patient, even a patient that I studied when I was at the Rockefeller University, who weighed 500 pounds, that took greater than 7,000 calories to maintain his weight, and we're not talking about marathon runners, triathletes, whatever they do in a day to run a triathlon. But that's the limit of that.

Now, the question would also be, with Xenical, the observations, Xenical, taken as directed, if you have a relatively high fat diet, meaning not a low-fat diet,

you mal-absorb about a third of your fat calories, and the problem is greater than that, you get great GI disturbances. One of the problems with Xenical is if you mal-absorb too much fat, you have very loose stools. We would call it, as lay people, diarrhea. It can be explosive. There can be great gastric upset, a lot of pain. And so, that's the other problem that one would have to look at.

So, now, when we look at actually, perhaps, the study that we did with Fat Trapper Plus, which certainly has made a number of these claims. What actually happened? We studied a limited number of people, the seven young men, they normally ate about 110 grams of fat a day. They were active, so we didn't have to increase their cardiovascular risk. And what we did was we put them on a prescribed amount of food that maintained their weight. It was frozen food, it was Haagen-Dazs ice cream, you name it. They liked it, they ate it. And at some point, we gave them charcoal markers to see what feces were associated with what diet.

At another point, they had a four-day supplement of this chitosan supplement, taken in excess than directed. They were getting about four or so grams of this supplement. And there wasn't any significant mal-absorption of fat. The actual number was about

seven-tenths of a gram of fat a day. It wasn't significant from the prior period, and we estimated that it would take over a year if this were significant, which it wasn't, for them to lose a pound of fat based on mal-absorption of fat using this fat blocker.

So, even if the seven-tenths of a gram were true, or even if the seven-tenths of a gram became two grams, I mean, it still wouldn't meet my definition of substantial weight loss because -- Tom, I'm sure you can comment on this -- a pound in a year or even two pounds in a year really wouldn't meet the claim of substantial.

If we then go on to talk about a pound a week, perhaps meaning substantial, but I don't think a pound a week would be substantial to the consumer. Again, that's mal-absorption of 55 grams of fat a day. I would anticipate, based on the Xenical studies, that that would create great GI disturbances and people wouldn't be on it.

And some of the side effects that are claimed for these products are loose stools and/or constipation. Obviously, they're completely opposite.

Two pounds a week, which comes closer to my definition of substantial weight loss, would result, again, in mal-absorption of about 110 grams of fat a day, and two pounds daily is just out of the realm.

So, I don't think -- theoretically, is this feasible, perhaps. I don't think it's even feasible, theoretically. Scientifically, is it feasible? I don't think so. But I'd be interested in my colleagues' comments on this.

MR. CLELAND: For the next -- just based on what Judy said there, let's assume for the rest of this discussion -- and we may notch it up or down, but for our discussion now, let's assume that we're talking in terms of substantial weight loss as something that exceeds more than a pound a week. Again, we can adjust that up and down, but let's discuss that as part of our discussion of the claim.

Anyone else?

DR. HEYMSFIELD: Do you mean that we should use this term "substantial" for --

MR. CLELAND: For this question.

DR. HEYMSFIELD: For this question only?

MR. CLELAND: For this question only, we're looking at -- and this is the first time where we've sort of had to, I think, think in terms of what do we mean in this context by substantial weight loss.

DR. BLACKBURN: Rich, I wonder if it shouldn't be a half a percent of body weight per week. I mean, we could have a huge range from a little over 100 pounds to

300 or 400. But if you make it a half a percent of body weight per week so the median would be a pound per week, to fit other definitions that have been used by other government agencies in talking about safe, effective changes in body weight.

MR. CLELAND: Generally, what would a half a -- I mean, in terms of a generalization across populations, what would a half a percent of body weight per week -- what does that look like in terms I would understand?

DR. BLACKBURN: For a 200-pound person, it would be a pound a week.

MR. CLELAND: For a 200-pound person?

DR. STERN: But if we say that it has to be more than a pound a week sort of in baseline, George, we almost would be talking about two pounds a week, so it would almost be a percent -- 1 percent a week if you were 200 pounds. But it would be four pounds if you were 400 pounds.

DR. BLACKBURN: I'm just talking back to the U.S. Dietary Guidelines. I think when they're advising changes of weight of a half to 1 percent, you know, thought to be one to two pounds per week by the scientific and health guidelines for the rate of safe, effective change in body weight.

DR. GREENE: So, you're suggesting use both?

DR. BLACKBURN: Well, my concern is if you just use pounds and don't translate it into percent, we already have on the table 400-pound people for the most rapidly-growing population in America in the area, and the average body weight, and if we tie it to a percent, we're just like the BMI, we will probably avoid having exceptions that someone would debate us about.

DR. STIFLER: Richard --

MR. CLELAND: Well, let me -- yes?

DR. STIFLER: We're going to probably visit this issue on the last question, which deals more with safety in terms of weight loss. This deals more with the mechanism. I would agree with George that it's still probably individual. But certainly, in the issue of safety, it needs to be highly individualized. So, you couldn't just say one or two pounds. You have to look at it as a function of the weight of the individual. We could do this here, too, although I don't think it's quite as critical when we're dealing with the mechanism as opposed to the safety and the effect on the individual.

DR. WADDEN: Rich, Tom, a couple of comments down here.

MR. CLELAND: Yes.

DR. WADDEN: Just going back to some of the

things that Judy said. If you look at the product that has been best studied to date, which is Xenical or Orlistat, Orlistat blocks the absorption of about one-third of the fat that you consume a day, and the manufacturers of the drug say, well, you can't eat more than about 60 grams of fat a day or you're going to have terrible GI side effects, which you, in fact, do. So, 60 grams of fat a day you'll block one-third of that, that means you've blocked the absorption of 20 grams of fat. That's just 180 calories a day that you've blocked. And based on fat blockage alone, if you just go with that, you're only going to lose about a third of a pound a week. So, it's very, very modest before you're going to start to run into some very serious GI side effects.

Now, people sometimes lose more than a third of a pound a week on Orlistat, but they do so by decreasing their calorie intake overall. So, they reduce their calorie intake and they may, in fact, reduce their fat intake even below this 60 grams a day. So, I don't think that we have anything currently that's going to approach a two-pound weight loss from blocking fat absorption without running into sort of horrendous GI side effects. I don't think there's any empirical evidence we have anything that works, though, beyond what I've seen with Orlistat.

MR. CLELAND: Van?

DR. HUBBARD: I think on this particular question, I don't think we need to get into the issue of whether we use pound or percent. I think this is relatively straightforward and I think go with the simplest answer in regard to causing blockage of absorption of calories. I think where we get into the issues of how we should express the amount of weight loss, that's really on the safety issue.

DR. HEYMSFIELD: I think mal-absorption has been very well studied as a means of weight loss. For example, the oleo bypass surgery produced significant mal-absorption. Olestra, compounds like that, you could replace out all the fat in the diet with olestra and you get very substantial mal-absorption. I think what would worry me and what is known is the incredible side effects that we've heard everybody talk about, and also, the fat soluble vitamin deficiencies and kidney stones and all kinds of medical side effects that are rife with mal-absorptive therapy.

So, it seems to be really implausible that you could produce this with anything that we now know about that's in the categories of agents you talked about and that would actually be safe.

MR. CLELAND: Well, am I getting the sense here

that the panel may feel that we don't necessarily need to define substantial weight loss for this question, that they're comfortable with ‘substantial’ weight loss is not achievable through this mechanism --

DR. STERN: I guess I'd go back to what Tom is saying is that to lose that pound a week, you'd have to mal-absorb 55 grams of fat a day.

MR. CLELAND: Okay.

DR. STERN: And even with Orlistat, we're talking about only 20 grams mal-absorbed a day. It's prescription. It's been well-tested. You go much higher, you get really significant side effects. So, it isn't scientifically feasible now, I don't think.

DR. YANOVSKI: I think it's just important that this is not to say that medications, you know, such as Orlistat don't work in terms of decreasing fat absorption. They clearly do. But the amount of calories lost is really modest, and that if people lose substantial amounts of weight, it's because, perhaps, to avoid symptoms or because of following a doctor's advice, they're also consuming fewer calories. That if someone makes a weight loss claim that through fat absorption or fat blockage alone, any product is going to lead to large amounts of weight loss, that this is not right now plausible.

MR. ALMADA: Rich, one comment.

MR. CLELAND: Yes.

MR. ALMADA: I think we have a discussion here -- a dichotomy. One is pharmacology, the other is clinical outcome. And independent of the mechanism, there are some data that suggest that blockage of absorption and calories or presumed blockage of absorption of calories yields weight loss that could be four, five, six or seven pounds. The data or the studies that are designed are less than rigorous. The methods used to measure body composition are anemic at best. There's a new category of agents that goes beyond that in fat, actually goes on the absorption of carbohydrates. There's a drug called Acarbose, the generic name marketed by Bayer. And in their studies, they have not shown robust weight loss among people that are taking it primarily for Type 2 diabetes.

There is a bean extract that has undergone a resurrection in a study done in alliance with UCLA presented earlier this year at a trade show. It showed some substantial weight loss associated with an agent that would achieve weight loss through a mechanism by absorption -- inhibition of absorption of carbohydrate calories. If that is a method of action, to the consumer, ultimately, it's irrelevant. Do I lose weight?

That's what counts.

DR. YANOVSKI: I'm not aware of a study showing significant weight loss with Acarbose, and also, are the studies you talked about, have they been published in peer review journals -- of the bean extract?

MR. ALMADA: My comment was there are no -- that's not typically found in weight loss with Acarbose use. The studies on chitosan, there are a number published primarily by one gentleman in Italy. Again, those studies are less than rigorous. The study that actually was presented earlier this year will be submitted for publication. But, again, it's just a preliminary indication of a new direction from a marketing and advertising perspective.

DR. STERN: I'd go even further. Those studies in Italy were fatally flawed and I've examined those studies in detail.

MR. CLELAND: Additional comments?

AUDIENCE MEMBER: How were they flawed?

DR. STERN: Inappropriate controls, among other things, and --

MR. CLELAND: Whoa, whoa. I'm going to poll the question, Judy. I'm going to poll the panel.

DR. STERN: Oh, okay, sorry.

MR. CLELAND: Okay. I forget which direction

we're starting from this time.

DR. STERN: Start from the middle.

MR. CLELAND: Well, I could. I could start from the middle. Dr. Heymsfield, do you want to begin here?

DR. HEYMSFIELD: I don't think this is scientifically feasible. It's not scientifically feasible. It is theoretically possible.

DR. GREENE: No.

DR. BLACKBURN: No.

DR. BRUNER: No.

MR. ALMADA: No.

DR. HUBBARD: No.

DR. STERN: No.

DR. STIFLER: No.

DR. WADDEN: No.

DR. YANOVSKI: No.

MR. CLELAND: We are still slightly ahead of schedule, but I think we're scheduled for a break this morning. We were going to do it at 11:00, but I think we will take a 10-minute break at this point and we will start again at five minutes to 11:00.

(Whereupon, a brief recess was taken.)

MR. CLELAND: Everyone take your seat, please, so we can get started.

Thank you. Welcome back, and we are, I think, on our fifth claim now. That claim is, 'Consumers can lose substantial weight through the use of the advertised product that is worn on the body and rubbed into the skin,' and essentially the types of products that would be included in this type of claim are creams, wraps, patches, earrings, shoe inserts, rings. An example of a claim; 'Lose weight safely with the original herbal patch, now available in the U.S.A.'

Dr. Blackburn, you were going to start with this one.

DR. BLACKBURN: Right. I think the first thing we have to harken back to is just how challenging it is to change your behavior to change your body weight, which we've already heard requires that you have some other influence for making decisions about food intake, particularly portion sizes, and exercise. I don't need to repeat that. We also know by virtue of the epidemic, even with the most highly invasive techniques that are possible, including injecting medications, as you do insulin, into the body. As you know, if you inject insulin, it's highly effective in controlling diabetes and blood sugar. We have injectable medicines that have failed to have substantial influence in this regard.

Now, if we get to the transdermal patch

technology, as you know, that is currently being used effectively for a variety of things, in the intensive care unit, nitroprase or nitroglycerin on patches of different sizes. The higher the dose, the bigger that patch. That you can, in fact, successfully get the effect of that medication. They're currently working in the area of asthma to see if asthma medications might not be able to be worked through in that regard, and perhaps, the best known, of course, as a component of smoking cessation is to use nicotine patches. Now, these all require a unique compound that, in fact, can be effectively absorbed through the skin in a fashion to achieve these narrow goals.

So, theoretically, it would be possible to administer a compound or a treatment. The problem in the weight control area is that there is no scientific evidence that -- and controlled trials that have been used in other techniques, as I've already talked about it, injectables or transdermal patches. It is even a less of a rationale of how an instrument in your shoe or wrapped in your body would be able to effect something that would, as we've already heard from previous claims, have to be with you every day to be effective. I think it's generally agreed we have no treatment that if a treatment is stopped, that you will sustain the change in

weight loss.

So, it would be my opinion, though the technology has been applied other places and, perhaps, there could be a compound that would work, as of the day of this meeting, no such instrument, wrap, patch has any scientific basis.

So, it would be my recommendation to say that as of this day, is it scientifically feasible to apply this technology to the weight control area? The answer would be no.

MR. CLELAND: Anthony?

MR. ALMADA: I think the other underlying discussion element here that is tacit is, is it legally allowable. When you're dealing with something that's transdermal, by definition becomes a drug, and the question is for these patch devices or patch products, do they deliver the agents into the system in circulation. If they do, they are, by definition, a drug. So, now you're entering the purview of the FDA because the dietary supplement has to be ingested through the oral cavity and enter the stomach.

The feasibility of delivering, for example, ephedrine and caffeine into -- or incorporated into a patch and rendering an individual responsive to that by delivering to the circulation is very much existent. But

I think it's much more an issue of the law rather than science.

MR. CLELAND: Anthony, are you aware of anyone who has actually tried to deliver ephedrine or caffeine transdermally?

MR. ALMADA: No.

MR. CLELAND: Anyone else on this question?

DR. HEYMSFIELD: Are there any other types of products that you're considering here, like acupuncture, acupressure, things that are actually worn or placed onto the skin?

MR. CLELAND: Well, there have been some products that, at least purportedly, rely on principles of acupressure, not acupuncture, but acupressure as the mechanism for weight loss. These usually, at least, the argument is that they somehow stimulate the vagus nerve, therefore resulting in a reduction of appetite. Now, does that sound theoretically plausible?

DR. STERN: I mean, I'm aware of a study, certainly, that George Bray published with an acupressure earring where they were looking at the pressure points for weight, and he found no difference -- and it was published in a peer review Journal -- he found no difference when the earring was tweaked at the pressure point for weight versus a low side that were not

associated with weight.

MR. CLELAND: I'm also aware of some unpublished research by Dr. Allison on a similar type device that indicated there was no difference over a placebo.

DR. YANOVSKI: We actually had a lay activist come to our obesity task force meeting with something she had purchased called the Fat Be Gone Ring that you were supposed to put on various fingers depending on which part of the body you wanted to lose fat from.

MR. GROSS: Did it work?

UNIDENTIFIED MALE: How many rings do you have on, right?

MR. CLELAND: Yeah. I think that in terms of at least the -- probably the most serious types of products that we're talking about in this category would be the patches with the transdermal applications, and perhaps, also, we had talked earlier and I think dismissed, to some extent -- maybe that's not the right word, but we had talked about the cream, the thigh creams earlier would be the other product that might fall within this category as well. And I think, you know, Anthony is absolutely right in terms of the legal issue here, that either of those products, to the extent that they claim to actually cause weight loss, would be, I think,

classified as drug products and not -- these couldn't be classified -- let me say it. They couldn't be classified as dietary supplements.

That issue aside, though, in terms of the advertising claims for these products is sort of what I want to get at here in terms of whether or not it is scientifically feasible for either of those classes of products to cause substantial weight loss.

DR. BRUNER: Rich, would that include the shoe insert slippers, because those are worn?

MR. CLELAND: Well, those are included. Again, I didn't get any responses to my question about whether or not it's theoretically plausible that the stimulation of the vagus nerve, through inserting something in your shoe, is even theoretically plausible. So, I'm assuming the answer is probably no.

DR. STERN: Actually, Rich, could we ask, again, the question because I'm having trouble with this. Let's say if you could deliver ephedra/caffeine by a patch -- I mean, forget about the law just for a minute.

MR. CLELAND: Um-hum.

DR. STERN: Could that -- do we have evidence that it could cause substantial weight loss via patch? Could we deliver a significant amount systemically?

MR. CLELAND: Well, I am -- I guess every study

-- and please help me out here if I have missed something -- that I have seen on those -- either of those ingredients were ingestibles.

DR. STERN: Right.

MR. ALMADA: It's an issue of basically doing pharmaco and bio-equivalent studies. If you can incorporate the dose and deliver it, theoretically and scientifically, it's plausible that you would be able to achieve a change in body composition.

DR. STERN: But legally, now, certainly they couldn't make claims for it as a dietary supplement because it would be a drug?

MR. ALMADA: You said to avoid the issue of the law.

DR. STERN: I'm adding that now. But then -- so, I'm not sure how we answered this question, because it's a drug then.

DR. BLACKBURN: Well, I think --

MR. CLELAND: I guess the question is -- and we're going to have to address this issue in the later questions in terms of the weight loss effects of ephedra and caffeine and whether or not that is substantial weight loss or as we're going to talk about it. But I guess what I would ask if that -- I mean, does anyone have a question on whether it's scientifically feasible

to deliver a dose of caffeine transdermally or a dose of ephedrine alkaloid transdermally?

DR. BLACKBURN: Well, I mean, we know the doses of caffeine and the doses of ephedra that are required. Certainly, the bioavailability, I think, is complete of those in the digestive tract. It would only be that you would bypass the liver if you delivered this transdermally. But you'd be talking about several milligrams of ephedra.

I mean, I think that the effective doses talk about 25 milligrams four times a day, 75 or -- that would vastly exceed the type of transdermal absorption that we could achieve for the current transdermal activities, such as nicotine, which is -- so, this would be orders of magnitude. I think there's no scientific evidence to think that that would be feasible to achieve the use of ephedra by a transdermal delivery system.

MR. CLELAND: And just as an aside, I think that the other point I would make is that in the products in this category it is, I would guess, extremely, extremely unlikely that anyone would attempt to market -- that any of the products on the market would be -- the transdermal products would contain ephedrine. I can't think of a good reason, and if someone else can, why one would go to that method of delivery on ephedrine

unless -- well, does anybody -- Susan?

DR. YANOVSKI: Yeah. I mean, why would you go to any herbal supplement and put it in a patch? I have a little trouble with this particular question because I'm not an expert in pharmacology or drug development. I think that if people are making any kind of a weight loss claim that a patch or any other substance works, they ought to be able to back it up with some science.

I think just as there are transdermal nicotine delivery systems or transdermal estrogen delivery systems, theoretically, maybe there could be a transdermal system that delivered ephedra and caffeine. Whether this was safe, whether this was a drug is another question. But I would have to say that I, personally, would be uncertain. I don't know if anybody's working on this, but I certainly wouldn't think that it should be advertised unless there's something to back it up.

MR. CLELAND: Are we ready to poll this question? Anthony?

MR. ALMADA: Uncertain.

DR. BLACKBURN: No.

DR. BRUNER: No.

DR. GREENE: No.

DR. HEYMSFIELD: No.

DR. HUBBARD: No scientific evidence.

DR. STERN: No.

DR. STIFLER: No.

DR. WADDEN: No scientific evidence.

DR. YANOVSKI: I'll say no for scientific evidence. But if the question is feasibility, I'd have to say uncertain.

MR. CLELAND: Well, let me poll the question again since this is the first one we have polled. The question is whether or not given this claim, consumers can lose substantial weight through the use of an advertised product that is worn on the body or rubbed into the skin. Is this scientifically feasible given the current state of knowledge?

DR. YANOVSKI: I'll say no for that.

MR. CLELAND: Tom?

DR. WADDEN: No.

DR. STIFLER: No.

DR. STERN: No.

DR. HUBBARD: No.

DR. HEYMSFIELD: No.

DR. GREENE: No.

DR. BRUNER: No.

DR. BLACKBURN: No.

MR. ALMADA: No.

MR. CLELAND: The next claim, ‘Consumers who

use the advertised product can lose substantial weight without reducing caloric intake and/or increasing their physical activity.' An example of such a claim, 'U.S. patent reveals weight loss of as much as 28 pounds in four weeks and 48 pounds in eight weeks. Eat all your favorite foods and still lose weight. The pill does all the work.'

Anthony, would you start us off on this one, please?

MR. ALMADA: One underlying theme that has been alluded to is the mind set of the consumer. Why would they opt to choose or seek a product such as a transdermal or a product that claims to offer magnificent reductions in body weight or fat?

There's a culture that I've long called nutritional evangelism where my church and my product offers the way to spiritual enlightenment in terms of how your body looks, and that's a very, very infectious element that's often overlooked.

These so-called weapons of mass reduction that exist -- timely -- happen to play upon the emotions and the vanity elements of an individual. And one seeks, as a Holy Grail element, a product that works without changing one's lifestyle habits or features or selections.

And when we delve into the evidence, which is the only place that we should be delving into, and that's scientific human studies, well-controlled, using the right techniques to measure changes, we find a number of studies going back at least almost 20 years showing that agents that are available over the counter, that are naturally occurring, can achieve significant reductions in body weight within a period of two to three or four weeks ranging from a certain fiber extract that was shown in '84 in the International Journal of Obesity that produced weight loss of about four and a half, five pounds in four weeks without any changes in eating and no change in physical activity to the advent of ephedrine and caffeine, a synthetic variety, to the advent of the herbal variety of ephedra or another plant source that contains ephedrine and related chemicals, and any botanical or herbal caffeine source, to now some evidence, although albeit preliminary, indicating that green tea or an extract thereof, not the brewed beverage, can produce changes in body weight without changing eating patterns or activity.

That was published earlier this year. It was not placebo-controlled, but nonetheless, it did show some evidence. There are studies showing that other agents derived from other parts of the world, when ingested in

perhaps economically unfeasible amounts, that most consumers could not afford -- for example, an extract of Garcinia cambogia consumed in large amounts can change body weight. Dr. Heymsfield did probably the best study to date that's been published, at least, on that actual ingredient. He found no effect in a well-controlled study published in JAMA a few years ago. But I would say that there are several ingredients that have been shown in different populations over short periods of time to effect changes in body weight and body composition.

The question is going back to previous questions: Do these changes persist after one ceases or does one continue to lose weight incrementally over time if they continue to use the product?

MR. CLELAND: Can we, in terms of the issue of scientific feasibility and going back to, for example, the example that I read about 28 pounds in four weeks, Anthony, is that something that these studies would suggest was scientifically feasible?

MR. ALMADA: Absolutely not.

MR. CLELAND: Is there a rate of weight loss that we can articulate at which we could conclude that weight loss beyond that amount was not scientifically feasible given our current knowledge?

MR. ALMADA: The sweet spot appears to be about

one pound plus or minus a quarter to a half a pound a week over a limited duration of time.

MR. CLELAND: Can you say that again, please?

MR. ALMADA: One pound plus or minus a half a pound per week for up to, perhaps, eight, maybe 12 weeks.

MR. CLELAND: Dr. Stern?

DR. STERN: I would like to go back and ask the question, what constitutes evidence. And, you know, NHLBI and NIDDK published their guidelines and they reviewed level of evidence that's necessary to say that a treatment is effective. And the highest level of evidence you have to have, a randomly controlled trial, do you have to have a control that gets everything except the active ingredient? And, Susan, if I'm stretching this too much, please break in.

But, you know, if you don't have an appropriate control group, if the control group isn't getting a placebo, you know, that doesn't constitute the highest evidence, because there is a placebo effect, as Dr. Wadden said, and that can effect, in the short term, 15 percent, 20 percent of the people.

MR. CLELAND: Yeah, I think that -- I don't think the suggestion is that the studies that were referred to are scientifically conclusive, but that they may be sufficient, that at least in an abstract sense of

raising the question of scientific feasibility, even though there may not be conclusive evidence today as to the effect.

Now, assuming that that is the case, if we change the question slightly and define substantial weight loss as exceeding a pound a week, does that change our response in terms of scientific feasibility?

DR. STERN: But also we have to say, over what period of time, because things that cause fluid shifts can cause substantial weight loss in a week, even five or six pounds of weight loss in a week.

MR. CLELAND: Um-hum.

DR. STERN: But I think that we also have to look over what period of time and I would look over, let's say, a four to six or an eight-week period of time to sort of sift out those fluid shifts.

MR. CLELAND: Dr. Stifler?

DR. STIFLER: Just a couple of quick points. I think, given the response to some of the other questions, it would be hard to say yes to this one. It would be illogical. Second, I think most of these ads, the ones I'm familiar with, go back to the very first question and that is, they imply that this is true of all consumers and unless they have disclaimers or qualifiers, they are implying. So, even if there were minimal evidence on a

few people, that's really not how the ads are being presented, I think.

So, I would say just in terms of what we've already looked at, there isn't a great deal of evidence here, in any event. And I think under what we currently know, it would be virtually impossible to say yes to this and no to the previous questions.

MR. CLELAND: Dr. Heymsfield?

DR. HEYMSFIELD: The way I read this is that you could lose a substantial amount of weight without reducing your intake and/or increasing your physical activity. Just scientifically, how much you do that you would have to block absorption, change partitioning or increase your resting metabolic rate. Those are the three ways that are left after you eliminate food intake and physical activity. We've already heard that you can't block absorption to the extent that would be safe or effective even. Partitioning, there are no agents that we really know of, and resting metabolic rate, I'm unaware of any compound that will increase your resting metabolic rate safely or to the point that it would cause substantial weight loss. So, I would agree. But theoretically, it's possible.

MR. CLELAND: Does it make a difference what we define substantial weight loss as meaning in that

context? If there's a -- for example, let's assume -- and if I'm wrong on this, somebody give me the right number. Let's assume that a person who sustained a half a pound a week of weight loss for periods of time, four weeks, six weeks, whatever, that clinically that might be significant even though -- I mean, the question is, at that level, the answer to this is not scientifically feasible or do we have to notch that up somewhat over the half a pound a week?

DR. HEYMSFIELD: You mean the definition of substantial basically?

MR. CLELAND: Yes, yeah.

DR. HEYMSFIELD: Well, I would think substantial is more than half a pound a week, but I'll look to others to define that.

MR. CLELAND: Dr. Wadden?

DR. WADDEN: Just a couple of comments, in terms of what is substantial, I would come back to probably George Blackburn's and Judy Stern's and others' definition that substantial is probably going to be that you achieve a loss of about 5 percent of your initial body weight, because at that point, you do have potential health benefit, you do have potential cosmetic benefit. So, if you lost half a pound a week for 26 weeks and you lost 13 pounds and that was 5 percent, you know, that

might be "substantial." So, I would define it medically as well as potentially cosmetically.

In terms of what is it on a weekly basis --

MR. CLELAND: Yeah. I mean, what is it not just necessarily on a weekly basis, but what is it from a -- I mean, this is sort of where we have to translate the science to the advertising or to the marketing claims. And in a sense, I guess, to be the most direct, that this question reads or our understanding is that substantial here means at least a half a pound a week, do we come out with a different answer than if we say that substantial here means more than, something greater than a pound a week over a period of at least four weeks?

DR. WADDEN: Well, going back to the question, I don't think we do come out with a different answer. If you go back to what Steve has just said, that it's going to be impossible, based on what we currently know, to lose even a half a pound a week unless you are reducing your calorie intake or you are, in fact, increasing your physical activity or you are increasing thermogenesis, and I think, as Steve has indicated, we're not aware of any of these products now that are going to result in an increase in thermogenesis producing even a half pound a week.

MR. CLELAND: And, certainly, that would

include without diet and exercise components.

DR. WADDEN: Correct, yeah. Originally, Steve, I wanted to ask, in your study -- I think you've got the best study to date on caffeine/ephedra. Do you see reductions in food intake in those individuals?

DR. HEYMSFIELD: You do. I'm not sure how well that was quantified. The food records are not always easy to get accurately, as you probably know. But our impression is that you do see a reduction in food intake.

DR. WADDEN: And, so, it does look like weight loss is occurring through reduced food intake rather than by increases in resting metabolic rate.

DR. HEYMSFIELD: Primarily. There are some studies reporting increases in resting metabolic rate with caffeine and ephedra, but the effect is a very small effect.

MR. ALMADA: I would add that back in the early '90s, the group that's done the most work, based in Europe, has actually ascribed over half the weight loss to at least synthetic ephedrine and caffeine to appetite reduction.

DR. STIFLER: Richard, since people may be of different base weights when they take these products, I'd be a little skittish about defining in terms of a percent. If people weigh 400 pounds, you're going to

have a different effect. I like substantial because most of the advertising claims define that themselves, you know, lose all the weight you want, et cetera. If they want to say that a quarter of a pound a week is what they mean, then presumably, they'll have to substantiate that.

I also want to reiterate my point. If we've said no to the previous six questions, I don't see how we could possibly say yes to this one.

DR. STERN: Again, just to amplify, I think that we have to distinguish clinically significant from substantial. They're not always the same thing. So, this half a pound or a pound or a pound of weight loss a week, over time, certainly can be clinically significant as, you know, we've said, if it reaches about 5 percent of initial body weight. But I don't feel that half a pound or a pound a week, or, George, let's talk about a half a percent of body weight, that we can then translate for the consumer into that half a pound or pound a week, that isn't substantial.

Substantial, to me, means more as interpreted by the consumer. And I don't even think one pound of weight loss a week, as interpreted by the consumer, is substantial.

DR. BLACKBURN: Susan, can I ask you to comment about what's in the U.S. dietary guidelines? I think it

makes mention -- it uses the language of a half to 1 percent as the safe, effective guidance for weight loss.

DR. YANOVSKI: I'm going to defer to Van on the dietary guidelines.

DR. BLACKBURN: Van?

DR. HUBBARD: Well, as I said, the dietary guidelines basically refers to a general recommendation that you shouldn't lose more than one to two pounds and if you want to -- because of the caveat that some people can be extremely overweight, there is a reference to using it as a percentage. I don't think that's, again, pertinent to this question.

From the statements that Steve and others have made, if you don't change your caloric intake and change your level of activity, I don't think there's -- I don't care what level of weight loss you're talking about, it's not feasible to see a reduction in weight that would have any significance.

MR. ALMADA: Rich, if I may address a perspective that perhaps my fellow panelists haven't delved into perhaps because of their academic or government focus, and that's the consumer relevance. For the consumer, and Judy was speaking about it, would a pound a week be substantial to the consumer? I would argue that many consumers would find a pound a week to be

very substantial and desirable.

Given my experience directly and indirectly with marketing science-backed products for weight changes or body composition changes, there are many consumers that seek, as their -- seek the weight scale rather than body composition as their index of performance, and if they see a shift of two or three clicks on a weight scale in two or three weeks, they are enchanted if they have had to do nothing else than just take a supplement or rub a cream on, assuming that the cream works.

So, I would argue on behalf of the consumer that substantial to them would be a weight loss that would be desirable and that they could measure easily and freely and that would be using a scale or a dress size or a pants size, in the context of how a consumer would interpret this.

We have a tendency, being scientists, to take a reductionist approach and address mechanisms, address clinical significance and impact, which are of utmost importance, but because we're talking in the context of advertising, the consumer relevance, I think, is paramount.

DR. WADDEN: Just -- go ahead, Van.

DR. HUBBARD: I'd like to hear Tom's comment, but just as a follow-up for education and to also give

you an opportunity to provide another guestimate, you're talking about a level of weight loss that the consumer would find useful or significant. How would you interpret the consumer's estimation of how long that weight loss should be there to be substantial or significant?

MR. ALMADA: Are you asking me the question? I'm sorry.

DR. HUBBARD: Yes.

MR. ALMADA: Are you addressing the issue of persistence of weight loss?

DR. HUBBARD: Right. You said maybe a change in two to three pounds the consumer would think is significant. If it's two pounds for two weeks and then they're back up to where they were, would that consumer have felt that that was a significant change?

MR. ALMADA: Well, let me give you -- again, going back to my sweet spot of one pound a week. I used just a framework of two to three weeks. Here's a classical example that's often used. A woman or a man is going to their 25th high school reunion. I need to lose five pounds in four weeks, and they find a product that fits that description or their objective, to them, if they lose those five pounds or four and a half pounds in four weeks, they are captivated by that product and they

will tell their friends and their relatives and their coworkers, this product works, it worked for me. Wow, I lost an inch in my waist. That's all they need.

DR. WADDEN: Just a quick comment. First, I don't know a lot about consumers since I'm an academic, but I do think if consumers were happy with one pound a week, we wouldn't be here today because we wouldn't have advertisements about lose a pound a week. I mean, we would have -- the advertisements we're concerned about is lose 28 pounds in four weeks, lose 30 pounds in 30 days. If consumers were happy with a pound a week, we wouldn't be meeting today. It's the fact that they're not very excited about a pound a week is that you have all this advertising that promises so much more.

And to reiterate, I'm not an expert on consumers, but in our patients that come to our clinics who are all obese individuals -- these are not individuals just wanting to lose five or ten pounds or whatever. You know, they're folks who want to lose 25 to 35 percent of their starting body weight. So, it's a female who's 200 pounds who wants to lose 50 to 70 pounds, and a pound a week does not cut it for most people. If it did, you would find that prescription medications were probably selling better. They produce about a pound a week. But that does not keep people's

attention. So, I don't think a pound a week for most consumers is very exciting.

MR. CLELAND: I'm going to take one more comment and then I have to poll this question so we can move on to our final one.

DR. STIFLER: Again, I haven't seen any ads that say lose up to a pound a week. I don't think people would buy that product. But I want to go back to the other issue. Given the class of products that we're talking about, not pharmacological agents approved by the FDA, no product is going to lose weight without reducing caloric intake or increasing physical activity. So, I'm not stuck on substantial weight loss, I'm stuck on weight loss. So, the answer is no, there's no weight loss, substantial or not, if you don't modify those, given the class of products that you've defined for this discussion.

MR. CLELAND: Okay. I am going to poll this question, and actually, this one I may poll -- I'm going to poll in a couple of different forms given the comments. First, I am going to poll the question as, 'Consumers who use the advertised products can lose weight without reducing calorie intake and/or increasing their physical activity.' Susan, would you start on that one?

DR. YANOVSKI: Yeah. Can you go ahead? I'm sorry.

MR. CLELAND: I read it without the word "substantial" in the question.

DR. YANOVSKI: I'd still say no.

MR. CLELAND: Dr. Wadden?

DR. WADDEN: I'd say no as well.

DR. STIFLER: No.

DR. STERN: No.

DR. HUBBARD: No.

DR. HEYMSFIELD: No.

DR. GREENE: No.

DR. BRUNER: No.

DR. BLACKBURN: No.

MR. ALMADA: Based upon the literature, absolutely yes.

MR. CLELAND: The other formulation that I'm going to use based on Anthony's suggestion here is -- or in part on his suggestion would be substantial with the understanding that substantial is a mean weight loss of at least a -- greater than a pound a week.

Anthony, would you start there?

MR. ALMADA: Uncertain.

DR. BLACKBURN: No.

DR. BRUNER: No.

DR. GREENE: No.

DR. HEYMSFIELD: No.

DR. HUBBARD: No.

DR. STERN: No.

DR. STIFLER: No.

DR. WADDEN: No.

DR. YANOVSKI: No.

MR. CLELAND: Okay, all right. Let's move on then to the last question or the last claim, and actually, this is very related. 'Consumers who use the advertised product can safely lose more than three pounds per week for a period of more than four weeks.' It's like deja vu all over again.

Dr. Heymsfield is going to address this question first and I'm wondering, Doctor, whether you think it's maybe worthwhile to address the question without reference to the word "safe" first and then consider the word "safe" or whether we should take it as a whole.

DR. HEYMSFIELD: I think taking it as a whole is probably more desirable this first pass.

MR. CLELAND: Okay, let's do that.

DR. HEYMSFIELD: Okay. Well, if I'm not mistaken, this is the only one that has numbers in it and, certainly, for me, it makes it the most difficult.

I'll just give you my views and then I hope others will contribute. The question comes up first about a rate of weight loss which we're giving here at three pounds per week. I'd like to frame that in a context. We have a little bit of -- actually, we have quite a bit of information about rates of weight loss.

If we take the Irish fasters a number of years ago who literally starved and drank nothing but water, they survived about 70 days and lost about 70 pounds or something in that range, about a pound a day. One pound a day or seven pounds per week would be an extraordinary fast rate of weight loss; in fact, a lethal rate of weight loss eventually. These were normal weight individuals, so people who are obese might lose more weight and live a little longer. But that gives you a frame of reference. Seven pounds a week is a very fast rate.

Very low calorie diets, Larry is here and he probably can maybe embellish this a little bit, but most very low calorie diets, my impression, produce weight losses in the range of two to four pounds a week over a period of time. These are diets taken under medical supervision. They're usually less than 800 calories a day and there are risks associated with them, and that's why they're usually done or always done under medical

supervision. But a rate of two to four pounds a week would be a very high rate of weight loss and nothing that anyone would recommend without medical supervision.

We know that from randomized double-blind trials of the two agents we have now, Meridia and Xenical, that at six-month time points, we produced rates of weight loss in a range -- most of these studies had subjects who were 100 kilograms to begin with and lost about 10 kilograms at six months. That would be fairly effective treatment. Fine, that rate of weight loss is about a pound a week, one pound a week. So, that gives you a little bit of a framework.

Now, the problem we have interpreting this a bit is that early weight loss by almost any treatment method is fast for the reasons I mentioned earlier; that is you get glycogen and water loss. So, for the first two weeks of almost any diet, you can lose a substantial amount of weight loss, not unusual to lose three to four pounds a week or even more depending if you have fluid overload and other conditions like that. So, it's very fuzzy in that first week or two.

But my projection would be -- and this is just a number I'll throw out, that if you lost three pounds a week for the first two weeks, that's six pounds and then come down to a rate which is acceptable to most people

for reasons of safety, not under medical supervision, two pounds a week would be the maximum we would recommend. That would come to a weight loss in the ballpark of about 10 pounds a month for that first month or two and a half pounds a week.

So, the proviso then is, yes, you can lose one pound a day if you'd like, seven pounds a week, but it's not safe and it would only be something done totally under medical supervision. And then at the other end, when we recommend safe rates of weight loss, we're down to something like maximum rates, even for the first month, of about two and a half pounds a week. So, that's sort of my numerical analysis.

DR. GREENE: Rich?

MR. CLELAND: Yes, Dr. Greene?

DR. GREENE: If I'm not mistaken, the data you are pointing to are average numbers, they're not the bell-shaped curve, for example. So, does that change -- if you use the upper limit, would that change your approach at all?

MR. CLELAND: Steve?

DR. HEYMSFIELD: I mean, that was what did get me concerned when answering this is that -- I mean, I've seen patients lose 50 pounds in two weeks who were extraordinarily fluid overload and people like that. So,

that's what you mean, you can lose extraordinary amounts of weight at the extreme.

DR. GREENE: No, I'm referring to the data from say Xenical or some of the other weight loss programs where you're quoted average data and this is worded as if you can use something other than average.

UNIDENTIFIED MALE: Um-hum, that's a very good point.

MR. CLELAND: Let me follow up on that point. I think that that is sort of -- that issue is relevant if you're talking about the absolute limits of what the possible weight loss is as opposed to what would be safe weight loss.

DR. HEYMSFIELD: Is that part of a definition of feasible or am I wrong?

MR. CLELAND: I guess I wouldn't see it necessarily as part of the definition of feasible, more, I guess, of the definition of safe, of how do you determine what safe is in this context and associated risks. But, Larry, you want to help me out here?

DR. STIFLER: Sure. I think it's important that we do discriminate between diets under medical supervision, as Steve said, and not. So, off the table, I assume is the amount of weight loss acceptable and considered safe under medical supervision. We needn't

argue that here.

It still bothers me a little bit with respect to the issue not under medical supervision because back to George's point earlier, I think you have to define that in terms of the base weight that someone has. If you come in at 350 pounds, I'm not sure I would agree that more than two pounds a week is necessarily unsafe, with or without co-morbidities.

Second, I don't usually hear this in the discussions, but I'm also concerned about if people are dieting on their own, the nutritional quality of diets. I'd rather see someone lose three pounds on a nutritionally sound diet who weighed 250 pounds than some of these really weird diets or even a high fat diet, whether you define that as weird or not, and lose two pounds a week. So, I think the nutritional quality of what people's intake is is important, even independent of whether they're doing activity.

Also, I think there's the issue of efficacy. There's this view that the public has, not supported by any science at all, and correct me if I'm wrong, that slow weight loss is the way to go. Well, I know three review studies encompassing maybe 50 or 60 studies in total and there's not a single study that I know of that indicates that slow weight loss is effective long term,

that people even get weight loss. As a matter of fact, two of the articles are essentially entitled -- if I can paraphrase -- the more rapidly you lose weight, the more weight you lose and the more weight you keep off. So, even there, Steve, I'd rather see someone lose two and a half pounds on their own on a reasonably nutritional diet, and keep losing weight and not get discouraged and not drop off the diet. There's nothing safe about losing a pound a week if you quit the diet in three weeks. You're still 250 pounds and you still have five medical risk factors.

So, I think you have to balance the reality of what a consumer can really do, their expectations and whether they will comply with a diet against the safety. So, I'm not sure where I'd put that number with people that aren't under medical supervision. I may go back to George's suggestion that you define it in terms of a percent of existing body weight. But even there, there's so many other issues, again, like nutritional quality and whether people will stick to the diet that I think this is a difficult question to come up with a precise answer that meets the science and meets the requirements of the average dieter.

MR. CLELAND: A couple of reactions to that, Larry. One is that, yes, we are talking about safety in

the context of medically unsupervised self-medication essentially, and two, the word "safe" here is -- I got a sense from what you were saying is that you were thinking of safety in a context of not -- well, that there's a comparative offset. By losing this weight, by losing three pounds a week or four pounds a week, you may be reducing these other risk factors and, therefore, the sum total of the risks for the individual may be ultimately less, which isn't necessarily the same as saying that what you're doing is safe.

DR. STIFLER: But that's my problem. It may be safe, but you really do have to look at the alternative, which means that if you're not losing weight or you're not complying in the diet or you're on a nutritionally inadequate diet, is that safe? So, it's hard for me to define safe independent of what the alternatives are. If you don't lose weight and you have co-morbidities, you're not in a very good place. That's not safe either.

DR. HEYMSFIELD: Maybe Van and Sue can speak to this, but I think our current culture about the safe rate of weight loss comes largely from the study of gallstones where people collected, literally, hundreds of cases of gallstones and looked at the relationship between the risk of gallstone development during dieting and the rate of weight loss, and pretty much the cut seems to be

somewhere around that several pounds a week as being the upper limit that still is associated with the relatively low risk of gallstones. But, Sue or Van, do you want to comment on that at all? Am I right about that?

DR. HUBBARD: To some degree. I mean, the onset of gallstones, and also symptomatic gallstones, to a large extent, are those -- in a few studies they have done prospective analysis. The onset of gallstones is also somewhat dependent upon the diet itself. And so, many of the studies in which they saw a rapid onset of gallstones had a low-fat component. So, you weren't physiologically stimulating the gall bladder. So, there is a physiological relationship as well.

I think as we are making statements about relative rate of weight loss and the safety thereof, there are always individuals who can lose larger amounts of weight safely compared to others, and what we're trying to do is establish some level that is reasonable to be safe for the general population that is not seeking any type of medical advice. And I think when we do that, we do assert some level of increased caution.

MR. CLELAND: Let me go back to one point, Dr. Heymsfield, a statement that you had made that you had seen an individual lose as much as 50 pounds in a couple of weeks, I think you said. Can you elaborate on the

circumstances where that might occur?

DR. HEYMSFIELD: Sure. If you have a patient who's morbidly obese and they come in for obesity surgery and you put them in the hospital ward, it turns out that many of them will have latent congestive heart failure and other fluid retention states and when they're put into bed, a low-salt diet, calorie-restricted, they often dieresis, it's called, and lose a tremendous amount of water weight. It's very common.

MR. CLELAND: Any additional comments on this question? Dr. Wadden?

DR. WADDEN: Just a quick one. Just to reiterate, I think, what Larry has said that I think you have to distinguish between medically supervised weight loss and unmedically supervised weight loss, and the last thing we want to see is people being encouraged to lose more than three pounds a week for longer than four weeks.

Dr. Blackburn can recall better than I can, 1977, liquid protein diets. People went on these diets. Fifty-nine people died nationwide. They were losing weight at the rate of three pounds a week or more --

DR. HEYMSFIELD: Right, that's the other example is the liquid protein diets.

DR. WADDEN: So, I think, to echo what Van has said, you want to impose a measure of safety, to set a

safe standard for the public. Certainly, you can lose three pounds a week on some of these radical diets, but I don't think you can do it safely. You have to be medically supervised to lose that much weight safely for that period of time.

DR. STIFLER: George, I keep mentioning you. Can we go back to the suggestion maybe of a percentage -- I mean, I'm not opposed to setting a weight. You know, we do our diets under medical supervision, but I'm not sure where you want to make that cut-off and I'm not sure at 300 pounds, if somebody is dieting, that I want it to be at the same place as somebody at 160 pounds if we're trying to define safety.

DR. BLACKBURN: Still, if we're talking about fat loss and now we're leaving the 200-pound person to 300 pounds, you know, then there's another 1,000 calories on the table and I still think that you can -- if you're talking about fat loss, get rid of this front-end dieresis and I think in this example, we're picking it up after -- are we including the first week or not? Let's see --

UNIDENTIFIED MALE: Well, the way it's written, it does.

DR. BLACKBURN: In the first two weeks, right. So, it includes that. I'm a little bit surprised. I

don't have an elephant-like memory, but I remember as we walked through -- we're now at about the fourth set of the U.S. Dietary Guidelines. It used to be 1 to 2 percent, that was thought not to be safe, and we reduced it to a half to 1 percent. And why we're having science silenced from the agencies who developed this is a little bit surprising to me. But I'd be willing to bet that it now says a half percent to 1 percent is a safe, unsupervised public guideline for changing of weight, reduced from earlier editions that were 1 to 2 percent.

DR. HEYMSFIELD: So, 1 percent would be three pounds for someone 300 pounds?

DR. BLACKBURN: That's right.

DR. HEYMSFIELD: That's pretty heavy. So, the three pounds here would cover most people.

DR. BLACKBURN: I certainly think it's safe. I think it was with scientific evidence that the velocity of weight loss, in part due to the liquid protein fiasco, was reduced from 1 to 2 percent to a half to 1 percent for unsupervised, public health change in body weight.

MR. CLELAND: Let's go ahead and poll this question with the assumption again that safety here is without medical -- we're talking about safety without medical supervision.

Dr. Yanovski, yes, no, uncertain, at the three-

pounds-for-more-than-four-weeks level?

DR. YANOVSKI: Again, if we're not going to do it as a percent, I would say no, but really changing it to something like 1 percent would probably make more sense, more than 1 percent.

DR. WADDEN: I'd say no as it's written.

DR. STIFLER: At three pounds, I'd still say no, yes. No, period.

DR. STERN: I'd say no. But is there also a way, Rich, that we could add in Dr. Yanovski's caveat about greater than 1 percent a week?

MR. CLELAND: Well --

DR. STERN: In the sense that then that could be applied to all people.

MR. CLELAND: Yeah. I mean, the 1 percent can't be applied to all people in a context of a -- if you're looking to develop -- I mean, what we're looking for is something that we can say is or isn't scientifically feasible. In the context of this claim, if it is -- I think it does -- in an instructive context, it does matter whether it's weight or percentage. It's just not generalizable as a percentage when you're looking at it from a marketing point of view.

DR. STERN: I'll vote no.

MR. CLELAND: If it's three pounds, if it's

four pounds. But based on what George said down here, I think three pounds, if that's 1 percent, 300 pounds --

DR. STERN: Right.

MR. CLELAND: Okay.

DR. WADDEN: Well, given the nation's math skills, it's hard to take even 1 percent of your starting weight.

MR. CLELAND: Yeah, I know that's what you're thinking. Van?

DR. HUBBARD: I would say no as currently described.

DR. HEYMSFIELD: I think what Van said is very important, that there's a margin of safety that we should consider for the public. So, I would say no, too.

DR. GREENE: No.

DR. BRUNER: No.

DR. BLACKBURN: No.

MR. ALMADA: No.

MR. CLELAND: That concludes all the claims that we were going to look at this morning and consider. I certainly want to -- don't get up from your seats yet, please. I certainly want to thank all of the panelists this morning. It was tremendous from my perspective just to be able to sit here and have this discussion. So, again, I want to thank you very much.

I would also like to invite any members of the panel, and as the Chairman said this morning, we will continue to take additional comments, so if the panelists have any additional comments or any references that they would like to provide to us, authority that they think we ought to take a look at on any of these points, we would certainly encourage you to do so and commit that we would review that material. So, thank you very much.

(Whereupon, at 12:00 p.m., a luncheon recess was taken.)