FOOD AND DRUG ADMINISTRATION

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CENTER FOR DRUG EVALUATION AND RESEARCH

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NONPRESCRIPTION DRUGS ADVISORY COMMITTEE

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MEETING ON
LABELING AND REMARKETING ISSUES -
THE TODAY SPONGE
(NDA 18-683)

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WEDNESDAY
JULY 12, 2000

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The Committee met at 1:00 p.m. in the Versailles II Room of the Bethesda Holiday Inn, 8120 Wisconsin Avenue, Bethesda, Maryland, Dr. Louis Cantilena, Acting Chairman, presiding.

MEMBERS PRESENT:

LOUIS R. CANTILENA, JR. M.D., PH.D., Acting Chairman
GEORGE A. BLEWITT, M.D., Non-voting Industry Liaison
JAIME A. DAVIDSON, M.D., Consumer Representative
EDWIN E. GILLIAM, PH.D., Member
MICHAEL GREENE, M.D., Voting Consultant
JULE A. JOHNSON, Pharm. D., Member
EDWARD P. KRENZELOK, Pharm. D., Member
JODI LERNER, M.D., Voting Consultant
RICHARD A. NEILL, M.D., Member
DONALD L. UDEN, Pharm. D., Member
HENRY W. WILLIAMS, JR., M.D., Member
SANDRA TITUS, PH.D., Executive Secretary

ALLENDALE PHARMACEUTICALS REPRESENTATIVES:

GENE DETROYER
R.J. STAAB, PH.D.
ROBERTA GEIDNER ANTONIOTTI
ELIZABETH B. CONNELL, M.D.
MARY DELANEY, M.S.
FORREST GREENSLADE, PH.D.

PUBLIC SPEAKERS:

AMY ALLINA
ELIZABETH ARNDORFER
LIZZA GONZALES
ARMAND LIONE, PH.D.
DONNA RICHMOND
WILLIAM SMITH
R. WILLIAM SOLLER, PH.D.

I-N-D-E-X

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

(1:09 p.m.)

DR. CANTILENA: I would like to ask the committee members to return to their seats and we'd like to get started. I would like to welcome you to the July 12th, 2000 meeting of the Nonprescription Drugs Advisory Committee.

And before we get going, we'll start with the usual introductions. My name is Lou Cantilena, I'm head of clinical pharmacology at the Uniform Services University right down the road here in Bethesda. I'll be acting chair for this afternoon's meeting. If I can ask all of the individuals here at the table to please introduce themselves and say who they are and their role today. And we'll just start over there with Dr. DeLap and go around the table.

DR. DELAP: I'm Robert DeLap, Office Director for the Office of Drug Evaluation V at the FDA.

DR. GANLEY: I'm Charley Ganley, Director of Over The Counter Drugs.

DR. KATZ: Linda Katz, Deputy Director for Over The Counter Drugs.

DR. CHIN: Ling Chin, Medical Officer of Over The Counter Drugs.

DR. KARWOSKI: Claudia Karwoski, Safety Evaluator with the Office of the Post-Marketing Drug Risk Assessment.

MS. CHANG: Gloria Chang, Pharmacist, the Division of OTC Drug Products.

DR. NEILL: Richard Neill, NDAC Member from the University of Pennsylvania.

DR. GREENE: I'm Dr. Michael Greene. I'm the Director of Maternal Fetal Medicine, Massachusetts General Hospital and I serve as the Chairman of the Advisory Committee on Reproductive Drugs.

DR. TITUS: I'm Sandy Titus. I'm the Executive Secretary for the Nonprescription Drugs Advisory Committee.

DR. GILLIAM: Edwin Gilliam, I'm a family nurse practitioner from Tucson, Arizona.

DR. LERNER: Hi, I'm Dr. Jodi Lerner. I'm an Associate Professor of OB/GYN at Columbia Presbyterian in New York and on the Reproductive Drug Side Advisory Committee.

DR. WILLIAMS: Yes, I'm Henry Williams from Howard University from Committee Health and Family Practice and a member of the Advisory Committee on Over The Counter Drugs.

DR. UDEN: I'm Don Uden from the

University of Minnesota and a member of the Nonprescription Advisory Committee.

DR. JOHNSON: Julie Johnson from the University of Florida College of Pharmacy and a member of the Nonprescription Advisory Committee.

DR. BLEWITT: George Blewitt, Industry Representative to the Nonprescription Drugs Advisory Committee.

DR. KRENZELOK: Ed Krenzelok, Pittsburgh Poison Center and the University of Pittsburgh Schools of Pharmacy and Medicine and I'm on the NDAC.

DR. CANTILENA: Okay. Thank you everyone. What we'd now like to do is hear from Dr. Titus, who will go over the conflict of interest statement.

DR. TITUS: The following announcement addresses the issue of conflict of interest with regard to this meeting and as made a part of the record to preclude it in the appearance of such at this meeting.

Based on the submitted agenda for the meeting and all financial interests reported by the Committee participants, it is determined that all interests and firms regulated by the Center for Drug Evaluation and Research present no potential for an appearance of a conflict of interest at this meeting.

We would like to note for the record that Dr. George Blewitt is the non-voting industry representative and is on the committee to represent industry interests. As such, he has not been screened for any conflict of interests. In the event that the discussions involving any other products or firms not already on the agenda for which an FDA participant has a financial interest, the participants are aware of the need to exclude themselves from such involvement and their exclusion will be noted for the record.

With regard to all other participants we ask in the interest of fairness that they address any current or previous financial involvement with any firm whose products they may wish to comment upon.

DR. CANTILENA: Okay. Thank you Dr. Titus. What we'll now -- move to the open public hearing section of the meeting and at first I'd like to just announce there have been seven individuals who have registered as speakers. If there is anyone else who would like to make public comment, please at this time, if you can step outside and contact the staff and sign in. If not, if we don't hear from you in the next, say fifteen minutes or so, we'll just close it at seven speakers.

And as a reminder to the speakers, the

allocated time is five minutes. There's a light system here that we're using and with a timer, which is here. But when you see the yellow light, you have one minute left. And when you see the red light, you should be closing your comments at that time.

So, again, if there's anyone else who would like to speak, please sign up outside of the room with the staff from FDA and if not, we will move ahead to the first speaker in the open public section, which would be William Smith from SIECUS.

Mr. Smith.

MR. SMITH: Thank you. Good afternoon. My name is William Smith and I'm speaking on behalf of the Sexuality Information and Education Counsel of the United States or SEICUS, a 36-year-old national nonprofit that has been a leading voice for sexuality education and the right of all individuals to make informed responsible sexual choices.

I'm here today to urge you to approve the Today Sponge for reintroduction to the United States market. In advance, I want to thank you for the opportunity to offer my comments today.

The unmet need for increased contraceptive choices for women is glaringly obvious. There are more than three million unintended pregnancies every

year in the United States. Yet, at present, there remains a dirth of contraceptive choices often forcing women to prioritize and choose between safety, efficacy and accessibility. Different women have different needs and many of those needs are not fully recognized by the current selection of contraceptive options.

The contraceptive sponge offers women another choice that is in a word, unique. No other product on the market offers the same option for sexually active women. Further, the Today Sponge is a product we believe is important one and that allows women to exercise and maintain control over their own reproductive health.

In many instances, women cannot rely on their partners to make responsible decisions about contraception or more seriously are faced with negative or violent reactions when they either use or express a desire to use contraception.

The Today Sponge allows women to be discreet as it can remain the vagina for 24 hours. It can be used for multiple acts of intercourse and is generally undetectable by either partner during intercourse.

In addition, in terms of promoting women's

health, the Today Sponge offers women an alternative to hormonal contraception such as birth control pills. Many women cannot use or choose not to use methods such as birth control pills because they induce significant hormonal changes in the body, which can sometimes result in adverse side effects. As you know, the only active ingredient in the sponge is the spermicide Nonoxynol-9, which has been available for 40 years and has a proven safety record.

Finally, the Today Sponge is comfortable, convenient and accessible. For these reasons, the sponge was used by tens of thousands of women nationwide until it was removed from the market in 1995 and continues to be used in other countries including Canada at present.

An issue at this time seems to be product labeling and safety. These issues are certainly of great concern to SIECUS. In this case, however, as I mentioned, the safety of the product has already been established. The Today Sponge, if used as instructed, delivers a dose of Nonoxynol-9 that remains effective for multiple acts of intercourse without additional dosing. The studies that indicate harm in using N-9, including the one released this morning in Durban, seem to result from an over-dosage of N-9 by repeated

dosing over numerous acts of intercourse that in some cases, according to the actual study, reached nearly 40 times in a single day.

So the question then is to what is -- what extent does the proposed labeling of the Today Sponge help to assure proper and safe usage. It's unfortunate that at present, to my knowledge, there exists no uniform labeling requirements for products containing N-9. Our own informal review of over-the-counter contraceptives delivering N-9 including inserts, foams, gels and films indicate a vast disparity of guidelines for usage and safety warnings.

Given this to be the case, it's our judgment that the Today Sponge's labeling continues to instruct consumers in safe usage of the sponge. We're also to understand that the outer carton of the -- carton of the product will contain a directive to use condoms to prevent sexually transmitted disease. Well this directive eases some concerns over a consumer's possible mistaken belief that the contraceptive sponge also serves to prevent sexually transmitted disease, we suggest the inclusion of a clear, unambiguous statement to this effect.

For example, the contraceptive product and care which delivers N-9 via vaginal insert contains

the statement Athis product has not been shown to product against HIV Aids or other sexually transmitted diseases.@ This minor adjustment coupled with the FDA's previous approval of the sponge's labeling under the former manufacturer seems duly sufficient to assume that the proposed labeling is safe, accurate and ultimately geared toward helping insure proper use of the product.

Please consider the potential role of the Today Sponge in providing women with choices that will improve their health and their lives. We strongly urge you to support the production and distribution of this product.

And thank you very much for your time.

DR. CANTILENA: Okay. Thank you, Mr. Smith.

Are there any questions from the committee members for Mr. Smith? Okay. Thank you.

And if the speakers would actually like to come up and use the podium, that's okay, it's easier for you to see the warning lights. So, if you would do that, that would be great.

Our next speaker is, I believe, Amy Allina from the National Women's Health Network.

MS. ALLINA: Thank you. My name is Amy

Allina. I'm the program and policy director of the National Women's Health Network. The Network is a nonprofit science-based consumer advocacy organization that does not accept any financial support from pharmaceutical or medical device companies. We're supported by a national membership of 10,000 individuals and about 300 organizations.

Those of you who have heard the network speak before about contraception might expect that we would be here to advocate for the return of a woman controlled barrier method of contraception that offers an alternative to hormonal contraceptives and accessibility of over-the-counter distribution, all of which are characteristics of the sponge, the product under discussion today. And you're right, we are here to advocate for that.

As you heard from the previous speaker, and as I believe you'll hear from other advocacy groups today, the sponge was a popular product. It was used by thousands of women who were very satisfied with it and who were disappointed when it disappeared in 1995. It's return to the U.S. market will benefit women by expanding contraceptive choice in particular the range of non-hormonal options.

On the other hand, those of you who have

heard the network speak before might also be expecting that our skepticism and caution regarding drug and device side-effects would lead us to raise many questions about the safety of the sponge itself and also about the effects in the vagina of the Nonoxynol-9 that's part of the product. And in a sense you're right as well. The network has raised those questions and we've carefully considered the scientific data that goes toward answering them.

In 1983, when the Today Sponge first came on the U.S. market, we produced a position paper which called for more research on a number of safety questions, including the material used in the sponge and the possible risk of Toxic Shock Syndrome.

In the years following the approval of the sponge, the network carefully monitored both clinical studies and women's experience with the product and some important points emerged from the research and from the actual use experience. A small percentage of women reported allergic reactions while some women did experience vaginal irritation when they used the sponge, the vast majority of users were very satisfied with the method. There were a small number of toxic shock cases reported in women using the sponge. Although the increase in TSS risk associated with the

sponge did not appear to be greater than the risk associated with other vaginal barrier methods.

Today as the threat that that the HIV Aids epidemic poses has become increasingly clear, questions have been raised about the safety of the Nonoxynol-9 that is in the sponge. In particular, there's concern about one recent study mentioned by the previous speaker that was conducted by UNAIDS, which was a multi-center randomized double blind placebo controlled trial of N-9 gel used by female sex workers who were engaging in multiple acts of intercourse daily.

The preliminary analysis of this trial has found an association between the use of N-9 and an increased risk of becoming infected with HIV. While these results merit serious consideration, it is important to remember that no studies involving the sponge itself have produced any scientifically valid evidence that the sponge, used as recommended, poses a threat to women's health.

Additionally, it's worth noting that the sponge serves as a physical barrier as well as a chemical one covering the cervix which is a prime location for infection.

The important question for this committee

is whether the information about the possible infection risk associated with the use of Nonoxynol-9 in other forms and under specific conditions is relevant for users of the contraceptive sponge. The network is strongly committed to the principle that women can be trusted with complete information and that informed consumers can make responsible and good healthcare decisions for themselves.

We've carefully reviewed the data from the studies that have been conducted on Nonoxynol-9 and we believe that if the preliminary results of the recent trial are born out by further analysis, it would be appropriate to include some information for women about the possible risk in the label. That information could include something like the following: The sponge contains the spermicide Nonoxynol-9 which can cause vaginal irritation in some women. The sponge has not been demonstrated to offer protection against sexually transmitted infection and some studies have indicated that under extreme conditions with multiple daily acts of intercourse Nonoxynol-9 may slightly increase the risk of HIV infection.

Additionally, we believe the label should include information about the possible risk of toxic

shock and the symptoms associated with it so that women can -- will be aware of the need to seek medical attention should such symptoms develop.

In conclusion, the network wants to convey two important messages. First, that the return of the vaginal contraceptive sponge to the U.S. market will provide women with an important additional option for non-hormonal barrier contraception. And second, that with adequate labeling about the emerging research on Nonoxynol-9 and toxic shock, women can make informed decisions about the possible risk associated with this method and whether it's appropriate for them.

I'd be glad to answer any questions. Thank you.

DR. CANTILENA: Okay. Thank you very much for your comments.

Any questions? Go ahead then.

DR. GILLIAM: Do you feel that there should be information on the label about the efficacy of the product?

MS. ALLINA: Yes, I do.

DR. CANTILENA: Okay. Thank you. Further questions?

DR. UDEN: Are we going to be able to see the study that the past two speakers have referenced?

DR. CANTILENA: Charlie, any comment?

DR. GANLEY: No.

DR. UDEN: Okay. Thank you.

DR. CANTILENA: Are you curious as to why you're not going to be able to see it? Because I am. Is that -- is it, you know, not in file or, you know, has it not been filed yet or what -- what's the issue?

DR. GANLEY: It's -- we don't have access to the data, I guess is the best way to put it and so I think until we get access to data, I think we would be silent on that. And I think one of the speakers will bring up other issues and -- regarding the safety of N-9.

So, as I will address the committee later I think the issue that was brought up in the citizens' petitions that we had provided will be addressed by the agency and so I'm not sure that that's the appropriate discussion for this meeting and as the meeting progresses you will get an idea what the focus will be.

DR. CANTILENA: Okay. Thank you, Dr. Ganley and any further questions? Yes, Ed?

DR. KRENZELOK: Do you think the instructions, as they're now on the package or were on the package in 1995, are adequate for a whole cross

section of women to be able to use the product properly in terms of both insertion, removal and understand how to use it adequately?

MS. ALLINA: I am aware that there were some women who had problems with removal, but I believe that the instructions are -- are quite good and that women have been able to -- were able to get help when they needed it. So I -- I would have to say, yes, if people have ideas for improving them, I'd be interested to hear them but I -- my review was that they were quite good.

DR. CANTILENA: Okay. Well, thank you very much for your comments and the responses to the question. Our next speaker is Donna Richmond who is from the Association of the Reproductive Health Professionals.

Ms. Richmond.

MS. RICHMOND: Thank you and good afternoon. My name is Donna Richmond and I'm representing the Association of Reproductive Health Professionals or ARHP, which is an inter-disciplinary association composed of professionals who provide reproductive health services or education, conduct reproductive health research or influence reproductive health policy.

ARHP founded in 1963 has a mission to educate healthcare professionals, public policy makers and the public. The organization fosters research and advocacy to promote reproductive health. ARHP, as a non-profit educational organization, firmly abides by national accreditation guidelines for industry support by producing credible and independent enduring materials for clinicians and consumers. Our association in 1999 received 70 percent of our support from industry, 20 percent from private foundations and 10 percent from member dues and donations. And 2,000 Allendale Pharmaceuticals, Incorporated is one of 20 meeting supporters for our annual conference in September.

The statement is written to express our support for Allendale's application to re-introduce the Today Sponge to the consumer market. We recognize the important goal of improving reproductive health by reducing the unacceptably high rate of unintended pregnancy in the United States. We also recognize that every woman has a unique contraceptive needs or has unique contraceptive needs. To meet these needs, we strongly encourage all efforts to make as many safe and effective contraceptive methods available to American women as possible.

The Today Sponge, prior to the 1995 removal from store shelves, provided women with a valuable nonprescription option. It is a self-administered, non-hormonal method that appeals to many women and has been missed by both consumers and a reproductive health professional community. We strongly support the return of this product to the American market. We feel that the approval of Allendale's application by the FDA will be a positive step in expanding the number and variety of contraceptive options available in the United States. Thank you.

DR. CANTILENA: Okay. Thank you, Ms. Richmond.

Any questions from the committee members? Okay. Thank you very much.

Our next speaker is Dr. Armand Lione from the Associated Pharmacologists and Toxicologist.

DR. LIONE: Members of the Advisory Committee, it is a pleasure to be here today to comment briefly on some of the shortcomings of the labeling of the Today contraceptive sponge. Associated Pharmacologist and Toxicologist is the organization that I'm president of. It receives funding only from the production of educational

materials that we receive some royalties from. I'm also employed by the Reproductive Toxicology Center, which is here in Bethesda. I co-authored the database REPROTOX.

As you know, the Today Sponge contains one gram of the detergent Nonoxynol-9, N-9, that serves as a chemical spermicide in this and other OTC contraceptives. Whereas other OTC contraceptives involve acute exposures to N-9, that is comparable contraceptive products containing much smaller amounts of N-9, are introduced into the vagina and the N-9 is allowed to dissipate.

The Today Sponge exposes a woman to a chronic source of N-9 for the entire 24 to 30 hours it is in the vagina. Because the sponge is a source of chronic exposure to N-9, we believe it is more likely than any other OTC contraceptive to cause vaginal damage and to endanger a woman's health. Available research now shows that N-9 may alter the vaginal environment to favor the survival of pathogenic organisms and when used repeated N-9 may enhance the formation of lesions in the vagina.

As noted in the detailed references that accompany this presentation, researchers have found that women typically are unaware of the lesions

produced by high dose exposure to N-9. There is now general agreement among researchers that damage done by high dosages of N-9 may increase the risk of various infections including Toxic Shock Syndrome and infections with the Aids virus.

The details of the increased risk of TSS are quite clear being based on studies done by members of the FDA and the Centers for Disease Control. This should be stated clearly in the package label. The current label does not make clear the likelihood of vaginal damage caused by the repeated use of the Today Sponge.

For example, the instructions only recommend that the sponge not be used during menstruation. Indirectly, this suggest that the sponge may be used throughout this 21 days of each month when a woman is not menstruating. In the original data submitted for this product over 18 years ago, five of fifteen women developed vaginal irritation when they attempted to use the sponge for seven consecutive days.

In responding to the high level of irritation observed in this study, an FDA spokeswoman described the repeated use of the Today Sponge as a strong challenge and the irritation that occurred as

predictable.

The label for this product, therefore, should warn that repeated use of the Today Sponge is very likely to produce notable vaginal irritation and vaginal lesions. Currently, the label only states that a small number of men and woman may be sensitive to the spermicide in this product and previous versions of the packaging describe the spermicide as gentle.

To summarize, additions to the label for this product should warn the users that the sponge may cause vaginal lesions without her awareness and these lesions may increase the risk of various vaginal infections including infections with the AIDS virus. The package labeling should not suggest that irritation is a rare side-effect caused by the detergent N-9. Users must also be told the Today Sponge is very likely to produce vaginal irritation if worn for several consecutive days.

Thank you.

DR. CANTILENA: Okay. Thank you for your comments. Any questions for Dr. Lione? Okay.

Then I wish to thank you and we'll move on to our next public hearing speaker which is Lizza Gonzales from the Alan Guttmacher Institute.

Ms. Gonzales.

MS. GONZALES: My name is Lizza Gonzales. I'm reading this statement today on behalf of the Alan Guttmacher Institute and the National Black Women's Health Project about the importance of expanding contraceptive options for women in the United States and the role of the contraceptive sponge in pursuing that goal. We appreciate the opportunity to provide you with our comments on this topic.

Even a cursory examination of the reproductive health indicators reveals that there are unmet contraceptive needs in this country and women want more choices. There are more than three million unintended pregnancies every year in the United States. Ten percent of sexually active fertile women do not use any contraceptive method even though they do not intend to become pregnant.

In addition, the prevalence of sexually transmitting diseases, STD is increasing -- increasingly rapid in some groups of women. While lack of access to services and education contributes to unintended pregnancy in STD rates, dissatisfaction with currently available contraceptive options is also a significant factor in the equation.

Even women with access to family planning

services experience significant rates of unintended pregnancy and STDs. More than half of the unintended pregnancies in this country occur in women who are using contraception. Many of the women who are not using contraception have tried unsuccessfully to find a method that meets their needs. The Today Sponge offers women the opportunity to reclaim a previously popular contraceptive technology. Before its removal from the market in 1995, the sponge was used by tens of thousands of women nationwide. And today continues to be known and well liked.

When the sponge was taken off the market in 1995, many women were dismayed at the loss of the option. The sponge possesses specific characteristics which make it a desirable option for many at varying stages in their lives.

One very important characteristic of the contraceptive sponge is its availability over-the-counter. Other than the female condom the sponge is the only over-the-counter contraceptive option for women. Women appreciated the fact that it was available without a prescription and could be purchased at a corner drugstore without scheduling or waiting for an appointment with a healthcare provider. This convenience and accessibility are a great benefit

to women consumers.

Finally, the contraceptive sponge is a barrier contraceptive method which is important for those women who may be seeking an alternative to hormonal contraception. We urge the FDA to approve the return of this product to the U.S. And we thank you for your time.

DR. CANTILENA: Okay. Thank you for your comments. Are there questions for Ms. Gonzales? Okay. Thank you very much.

Our next speaker is Ms. Elizabeth Arndorfer from the National Abortion and Reproductive Rights Organization.

MS. ARNDORFER: Good afternoon. Thank you for holding this important meeting. My name's Elizabeth Arndorfer and I'm here representing NARAL, the National Abortion and Reproductive Rights Action League. NARAL is a grass roots advocacy organization with over 200,000 members and state affiliate network. NARAL is committed to insuring women's access to the full range of reproductive options including preventing unintended pregnancy, bearing healthy children and access to legal abortion.

We believe that expanding women's contraceptive options is crucial to preventing

unintended pregnancy and abortion and improving women's overall reproductive health. For this reason, we support the return of Today Sponge to the market.

Thirty-three million women in the United States are in need of contraceptive options. However, the options currently on the market do not fully address their needs. Nearly 50 percent of all pregnancies are unintended and 54 percent of those unintended pregnancies end in abortion. As a striking demonstration of the inadequacy of existing contraceptive options is the fact that over 50 percent of unintended pregnancies, and that includes 58 percent of women who have abortions were using some method of family planning in the month that they conceived.

Moreover, women are dissatisfied with the methods that they're using. The average woman will stop using a contraceptive method nearly ten times in her life. It is clear that women want and need a wider range of reproductive contraceptive options. The Today Sponge will provide that alternative. It has several very important advantages.

First, as you've heard from other speakers, it's over-the-counter. For women who don't have insurance this is particularly important. It

allows them to have access to a contraceptive without having to make and go to a healthcare provider. And even for women who are insured, it's important to have contraceptive options that are over-the-counter since many insurers don't cover contraceptive.

Second, as we've also heard, it's important because it's a non-hormonal method. And for many women the medical conditions preclude them from using hormonal methods or just the fact that they wish to avoid some of the side-effects associated with that. And finally, the contraceptive -- the Today Sponge was a very popular method when it was on the market and women used it. And we know that one of the most important is that women like their method so that they use it consistently.

While the sponge has important advantages, it is not the right option for all women. And for this reason, we fully support that women have adequate and full information that they need to weigh the risks and benefits of the option and also the information they need to use it properly. Labeling that is informative and easy to understand will allow women to make an informed choice about whether the sponge is appropriate for them.

In sum, returning the Today Sponge to the

U.S. market will be an important step towards expanding women's contraceptive options especially because of its over-the-counter availability, the sponge has the potential to increase women's access to contraception and help them avoid unintended pregnancy and abortion. We strongly encourage you to protect women's health by returning the sponge to the market.

Thank you very much.

DR. CANTILENA: Exquisite timing. Exquisite timing. Thank you, Ms. Arndorfer. Any questions from the committee? Okay. Thank you very much.

Our seventh and final speaker will be Dr. William Soller from CHPA.

DR. SOLLER: Thank you. Good afternoon. My name's Dr. Bill Soller. I'm Senior Vice President and Director of Science and Technology for the Consumer Healthcare Products Association which we appreciate CHPA. CHPA is the 119-year-old trade organization representing the producers of quality nonprescription medicines and dietary supplements including over 200 members across the manufacturing, distributing supply research testing and advertising sectors of the healthcare industry. And several of our members produce OTC spermicide products.

important to the safe and effective use of the product by the consumer. And this is a very important three part hurdle that there is directly on the consideration of comparative effectiveness labeling.

First, regarding the initial hurdle of scientific documentation, any decision on OTC labeling requires an evaluation by FDA that the suggested labeling, here related to comparative effectiveness labeling of vaginal spermicide products, is supported by high quality scientific evidence.

This means that before such labeling is recommended for all OTC spermicides which are currently covered under the public OTC review rule making process, FDA should ask for and be open to the public review and comment to evaluate the quality of the scientific documentation. It also means that if we're considering comparative effectiveness labeling, that is new valid evidence emerges, that there's a mechanism to expeditiously update that labeling in order to help insure competitive fairness in the market place.

Second, OTC labeling as a matter of regulatory policy contains only essential information necessary to the safe and effective use of the product by the consumers. The two hurdles in the policy

We're here today to address the issue of efficacy labeling and, therefore, the issue of comparative effectiveness labeling of OTC spermicide products and plan to submit comments to the relevant docket and records.

As background, about two million women use spermicide containing vaginal contraceptives. OTC spermicidal contraceptives serve an important role in meeting a women's choice of preferred contraception. Spermicides are chosen by women who wish a safe, simple readily available contraceptive method that offers many benefits including self choice and use without partner involvement, easy availability for immediate protection whenever needed irrespective of the interval between use, non-hormonal contraceptive control without affecting menses and a backup to the barrier method such as the condom, cervical cap or diaphragm.

Turning to FDA's on efficacy labeling and, therefore, comparative efficacy labeling on all -- all OTC contraceptive products, it is a matter of long standing FDA policy that decisions about drug availability or label statements including warnings or other information should be, and I quote, scientifically documented, clinically significant and

clinical significance and the importance to the consumer bear on this aspect of the essentiality of information and labeling. And the nature of the condition to be treated or preventive relates directly to these considerations.

In the case of prevention of pregnancy and the consequences of an unwanted pregnancy, the uniqueness of this condition and its consequences for the unborn, the mother, the father are unparalleled in any self care category. The life altering of an unwanted pregnancy are potentially profound. Providing comparative effectiveness information to a woman who is choosing a contraceptive method allows her the best opportunity for self determination of this unique situation. So on this background, questions to consider in developing efficacy labeling for OTC spermicide products are the following:

And that is, first, is the proposed labeling consistent with FDA's long-standing policy that label statements must be scientifically documented, a clinical significant and important to the safe and effective use of the product by the consumer.

Secondly, is there sufficiently a large database that is adequately, scientifically documented

to permit reasonable comparisons of product effectiveness for all products with the specific indications under review.

And, third, does the label statement communicate comparative effectiveness and a consumer friendly and easy to understand way and in a -- in a form that is consistent with FDA's final rule on OTC label content and format.

Hence, CHPA would support a public review and comment process on the issue of efficacy and specifically comparative effectiveness labeling on all OTC spermicides only because pregnancy is unique in the self-care category and requires special consideration.

In the past, CHPA has supported specialized labeling relating to pregnancy including, for example, the OTC drug pregnancy nursing statement on all OTC drug products and the recent voluntary program for label statements pertaining to pregnancy and nursing for dietary supplements which we recently adopted and submitted as a citizen's petition to FDA.

However, CHPA does not support comparative effectiveness labeling for other OTC indications in categories of drugs given that they do not rise to the level of uniqueness of the potentially life altering

consequences of failed pregnancy prevention. We believe public comment process would be important before extending comparative efficacy labeling to all spermicide products because this would provide the best opportunity for all stake holders to have adequate time to develop input on this important matter.

The fact that the question on efficacy and, therefore, comparative efficacy labeling for all OTC contraceptive products was not publically available with due notice before this meeting essentially makes this aspect of today's discussion in public, but essentially not by or of the public as it should be.

Thank you very much.

DR. CANTILENA: Thank you, Dr. Soller. Any questions from the committee for Dr. Soller?

Yes, Ed.

DR. KRENZELOK: You mentioned that the label should be consumer friendly presumably that it should be a readable label by a large segment of the population. Do you think this label for the Today Sponge is consumer friendly that -- that people can understand how to use it?

DR. SOLLER: I'm not here to comment

specifically on that aspect and haven't reviewed that labeling.

As I say, going into this meeting, we had anticipated that we would be monitoring this meeting, have not reviewed that label and then the specific question related to efficacy labeling came to our attention two days ago. And as for that reason that we offer these comments essentially on process.

DR. CANTILENA: Dr. Ganley, did you have a question?

DR. GANLEY: No.

DR. CANTILENA: Oh, sorry. Thought you were waiving at me. Yes, actually, Dr. Soller, I just have a quick question for you. So the -- so your comments are basically directed, if you will, at the second question regarding efficacy information on the carton.

DR. SOLLER: The sub-question A.

DR. CANTILENA: Sub-question A, right. Should it be required. Okay.

DR. SOLLER: As it relates to all. Now as you might relate that specifically to the sponge and come to a determination specifically to the sponge, that's one matter. As you then extend that to use the word all, then I think a very different matter comes

to play. And what also comes to play is that basic label statement because you're now thinking about plying this widespread. And that is scientifically documented, clinically significant important to the safe and effective use.

I would remind you if you're dealing just with efficacy for the sponge, that label statement should apply as well in a non-comparative sense, the scientific documentation, clinical significance importance to the consumer.

DR. CANTILENA: Right. But in terms of process, you know, correct me if I'm wrong, but because this -- this is a product that is under, you know, the NDA, anything that has to do with its specific label is really, you know, confined to this product. So your comments are, if I understand you correctly, addressed to the issue of, if the committee were to consider or recommend all.

DR. SOLLER: That's correct.

DR. CANTILENA: Okay. Thank you very much. Any other questions for Dr. Soller? If not, thank you very much.

DR. SOLLER: Thank you.

DR. CANTILENA: Okay. I think we're now at the point according to the agenda, this is where

Dr. Ganley welcomes us so I would like to please call on Dr. Ganley to speak to the Committee.

DR. GANLEY: Do I have a timer?

DR. CANTILENA: No.

DR. GANLEY: No. Okay. The floor drops down, is that it?

First, I just want to thank the members of the Advisory Committee for coming in for today's meeting on such short notice. I would also like to thank Dr. Cantilena for gracely acting as the rule of chair in Dr. Brass's absence. Dr. Cantilena is a past member of the Nonprescription Prescription Drug Advisory Committee and is starting another term with today's meeting. Dr. Brass will resume his role as chair at tomorrow's meeting.

And I will deviate somewhat from what I was going to talk about and I'm going to actually jump ahead a little bit to try to focus the meeting a little bit and see if this works here. And a lot of these slides were based on seeing the presentation of FDA, so I'm sort of jumping ahead here mainly to focus the discussion.

And the thing that I want to just discuss right now is the regulatory status of Today's Sponge. Today's Sponge is an approved drug product. It was

voluntarily withdrawn from the market in 1995. With Allendale Pharmaceuticals taking over the new drug application and changing the manufacturing facility for the drug product, they are required under our regulations to submit a chemistry supplement providing information on the manufacturing process.

So, I just want to point out there are outstanding chemistry issues, particularly manufacturing that need to be resolved by Allendale before they could market.

I just want to also point out that this is very important because good manufacturing practices are essential to the designation of safe and effective drugs. Okay.

The main focus of today's meeting is really to focus on the labeling of the product. And I think a lot of our interest is stemmed by a rare but serious adverse event that has been reported with the use of the product. And when Today's Sponge is re-marketed, Toxic Shock Syndrome will likely be reported with the use again.

So it becomes very important that the product is adequately labeled. And that's not only for consumers who have used this product in the past so they can assess their risk, determine signs and

symptoms or take measures to decrease risk. But also for consumers to understand whether they want to purchase the product. Okay. And there are a lot of consumers that will have access to the product that would not have been using it in 1995 because they were younger, particularly teenagers possibly.

And I think what you're going to hear today is some diverge in opinion on the part of the company and the FDA as the -- as what the appropriate label should read. And I just want to point out that since 1991, the FDA has made efforts to improve the OTC labeling so that it is more legible and readable. And this culminated in the OTC label ruling. Again, you will hear about this in the FDA presentation and I'm sort of jumping ahead here.

And we will also show that we are suggesting that there are substantial changes proposed in the labeling that justify us converting this to the Drug Facts format at this time before re-marketing.

So I'm going to end my comments here and allow Dr. Cantilena to resume the meeting and I'll be back later to provide some further comment.

DR. CANTILENA: Okay. Thank you, Dr. Ganley. We now have scheduled the sponsor presentation from Allendale Pharmaceuticals and we'll

start -- we've allocated 45 minutes. So, I'd like to ask the sponsor if you can please try to stay in that time frame.

And the sponsor will be starting off with Dr. Stabb, who will introduce the other speakers.

DR. STABB: Thank you very much. I want to thank the FDA and the Advisory Committee for their time in reviewing this product today.

I am Dr. Bob Staab. I'm from Allendale Pharmaceuticals and I am Chief Scientific Officer and Chairman of the company. We do welcome the opportunity to discuss the issues surrounding this label. We are very interested in getting the product back onto the market. We're getting pressured -- constantly getting questions constantly of what we need to do in order to get it back on.

There have been a lot of comments from the agency with respect to the labeling. And we think that there's time and our group today will take that time to point out some of the pros and cons of those comments. Because in the end, I do believe that the agency and Allendale Pharmaceuticals and probably just about everybody here is most interested in having a clear understanding and to make sure the consumer has a clear understanding of the pros and cons of the

product.

So we did bring some people here today, people who have been very, very experienced in the areas of contraception, OB/GYN, Toxic Shock Syndrome and so forth. You'll be hearing from them, and the first person we'll be hearing from will be Dr. Connell, Professor Meritus, the OB/GYN Emory University School of Medicine and she has had a lot experience with Nonoxynol-9 and with the sponge. She has actually sat on an advisory panel for the development of the OTC monograph for Nonoxynol-9. I look forward to hearing her comments.

Dr. Connell.

DR. CONNELL: Thank you very much. It's a pleasure to be back. This is deja vu all over again. I realized yesterday I've been coming here for 30 years. I don't know what that means but in any event I have always had a major interest in contraception and particularly this type of product. And this goes back to the days when women, many centuries ago, realized there's a relationship between the ejaculate and babies and at that point began to put wonderful things into their vaginas.

As you can see here, the Egyptians went to the oceans for sponges and cut them up. Cleopatra

became well recognized for developing pessaries against pregnancy and gonorrhea. Casanova made a gold ball. He reported using the same one for 15 years.

And then -- it's a wonderful, it's a very colorful history as you go through all the plant and animal pessaries that were developed over the years. It makes fascinating reading. This continued on -- next, into the more modern era. We had all kinds of liquids and chemicals and little pledgets of various types with strings on them. And we -- a number of years ago had the collagen sponge. It was kind of a dreadful, very rough unpleasant thing that never made it to the market. But it did culminate ultimately in the Today Sponge that we're talking about now.

Now we spent, as you heard, a number of us about, well most of the 1970s looking at over-the-counter products and our bottom line which is ultimately showed in the Federal Register we found Nonoxynol-9 to be safe and effective. A number of us came to the FDA in '82, at that point, the sponge was approved in March of '83. It was then, of course, sold as you know to Whitehall, American Home Products.

And I think the important thing, in addition to what's already been said, is that when it went off the market, there was a tremendous amount of

concern and I think a lot of that still persists that since it was taken off the market it was dangerous. And I think we still have this to be concerned about. People not realizing it was still FDA approved and it was not removed because it was dangerous.

And next, we move on through what actually went on in the development of the sponge. Seven years of trials, a lot of work that went on looking at very aspects of labeling and packaging, many, many hours looking at these things, looking at consumer data. During this time the 800 number was set up and it was extremely useful in terms of getting help as to what to do and when to do it and how to get through to consumers in an effective fashion.

Removal problems at that time were recognized to be a major difficulty. And the removal tab was changed to a different, from the braided polyester to a woven loop, simply because women were able to find it more easily and has helped a lot. And parenthetically, the VLI experience was that when women couldn't get them out, if they got to the 800 number, the vast majority of women, with the support of some wonderful people on the 800 number, were able to get their sponge out. This was a very, very useful thing that occurred during all those years.

Next, please.

During all of the studies, it was quite apparent that the sponge worked in three ways, a slow release of Nonoxynol-9 and a reasonably low but effective level, the blockage of the cervical os by the sponge and in the laboratory it was found that eight ejaculates in three days could be put in the milieu of the sponge and leave no viable sperm. So there is a lot of very good clinical and laboratory data.

Now you heard a lot about the advantages. There are many of them. I just pulled four I thought were probably the most important from a consumer point of view. We already know many people, many women are not happy to get into the healthcare system. Not only are they not happy, they're not able to and in today's situation very often. And so it was always wonderful to have a good option available over-the-counter. Many women like the fact that it is available.

Historically, it was going to be the two-day sponge. But the FDA said, no, thirty hour limit. And that's, of course, still in the labeling. But women didn't have to go back like they did with the diaphragm and keep adding spermicide each time they had sexual intercourse. Very easy to put in. Not

messy. And a lot of women and a lot of men find the other vaginal products very messy, unaesthetic and unattractive. And the nice thing about it is that unlike the condoms, unlike the female condom, the sponge can be put in in advance and this has certain cosmetic aesthetic advances.

Next.

Now, clearly there are disadvantages. One of the more important ones being the fact that it really is less effective than IUDs and all the hormonal methods. Quite clearly it does have to be used each time somebody has sexual intercourse which is a real turn-off to some women and some men. We recognize and we saw this with our extensive review of N-9 in the '70s.

There is local irritation, male and female in a small percentage of individuals. And then the issue of toxic shock which we looked at but Mary Delaney will talk about in much more detail so I want to skip over that. Removal problems, I think will continue to be an issue. Clearly the labeling is particularly important and as I already mentioned in the VLI days, the use of the 800 was extremely helpful.

I would like to just sort of look at what

I think are some of the more important general considerations without getting into the details of the chemistry. And I think the efficacy data that has just been talked about is very critical. I think those of us who spent a lot of time at the FDA looking at labeling and efficacy issue and trying to look at evidence-based medicine have always had problems because there are such variability in the various studies, in the various study populations over the years. It has produced a lot of problems in terms of how best to present efficacy data to the consumers so it's easily understood. We recognized years ago there were no comparative trials and I doubt will there ever be good comparative trials of the various barrier methods.

It's technically probably not an easy thing to do and it may never be done. Therefore, it's incumbent honest, I think, to develop language which will point out to women the importance of the efficacy data but give them a sense of the bottom line of the efficacy data, not overwhelm them with large numbers of numbers that are basically incomprehensible. So I think the issue that was raised a little earlier about efficacy is very, very relevant. And Forrest Greenslade will talk about that in greater detail.

Looking at the labeling, it's, as I said, something that a number of us have worked on over the years. I think the written and the particularly the graphics are extremely important particularly with a product like this. And another consideration always, is how would you pick up a problem if one developed that you perhaps are not aware of or perhaps you are not aware of the extent of the problem.

And if you review the current side-effect reporting, it seems to be that this is adequate for this particular reporting system would pick up anything of great significance. So I think that there's really not a major problem there in that area.

And finally, I think if you look at the issues of women, pregnancy, babies, all the things you've already heard about that when you look at the sponge in context, there is a decidedly favorable risk benefit ratio, clearly, and we saw this very markedly among the teens particularly. It was a method of choice for many of the reasons that you've already heard, personal reasons, for medical reasons. And I think all of us were disturbed when it went off the market. This was an extremely valuable contraceptive option that was missed. It is missed. It's still misunderstood. And I have no doubt that it would be

very profitable for women, particularly, if the sponge were to go back on the market. And, therefore, I would certainly encourage the re-institution of the use of the sponge.

Thank you.

I neglected my duty here. The next speaker is Mary Delaney from Brigham and Women's Hospital at Harvard and she will address TSS.

Sorry about that.

MS. DELANEY: Thank you and good afternoon. What I would like to address this afternoon is Toxic Shock Syndrome and the Today contraceptive sponge.

Toxic Shock Syndrome was first described in 1978 by Todd. And it received national attention in 1980 when unexplained febrile illness associated with shock, multi-organ dysfunction and high death rates were reported in healthy young women. TSS is a systemic disease characterized by the rapid onset of fever, vomiting, diarrhea, muscle pain, rash, hypotension, multiple organ system dysfunction and late desquamation. The incidents of TSS has declined dramatically. From six to twelve per 100,000 cases in 1980 to approximately less than one per 100,000 cases today.

TSS is characterized by the time of onset. There's menstrual TSS and non-menstrual TSS. Menstrual TSS occurs as a result of vaginal colonization with *Staphyloccocus aureus* during menstruation and is associated with tampon use.

While non-menstrual TSS results as a complication of Staphylococcal infections of the skin, soft tissue of the respiratory tract, following obstetric and gynecologic procedures, following influenza or without a known focus of infection.

The causative agent in TSS is toxin produced by the bacterium *Staphyloccocus aureus* called Toxic Shock Syndrome Toxin - 1, abbreviated TSST-1. *Staph aureus* is a normal member of the human micro flora and is commonly isolated from the mucosal services, skin and feces. To develop TSS, an individual must be colonized with the toxigenic strain of *Staph aureus*, conditions must ideal for toxins production by the bacterium and there must be an absence or insufficient level of neutralizing antibody to the toxin. These factors make TSS a rare disease. It has been reported that approximately ten to fifteen percent of women carry *Staph aureus* vaginally and that approximately one-third of these strains produce TSST-1.

In a recent study just conducted in our laboratory, we examined the colonization rates of over 3,000 healthy women to determine the colonization rates in the nares, vagina and anus. We found that overall 26 percent of all women were colonized with *Staph aureus*. Nine percent were vaginal carriers, eight were anal carriers and 18 percent were nasal carriers. We further analyze these isolates to determine if they could produce the toxin TSST-1. And as you can see from the graph, there's a substantial decrease in the number. There's only one percent of all *Staph aureus* strains capable of producing TSST-1.

In addition, we looked at serum antibody levels in these women and we found that 98 percent of all women had protective antibody levels to the toxin. There was only one subject that had vaginal -- that had a vaginal micro flora with producing TSST-1 that did not have the protected antibody levels.

In 1989, Schwartz published a case controlled study using TSS surveillance records from five states from January, 1986 to June, 1987 to determine the rate of a non-menstrual TSS associated with all barrier contraceptives. It's important to note that 49 percent of all TSS cases were non-menstrual. And most of these cases were associated

with surgical or cutaneous wounds or occurred within three days post-partum. Those made up 53 percent of the cases. Of the remaining cases, only 13 percent were associated with barrier contraceptives including the sponge. At five percent, the diaphragm, seven percent and the cervical cap, one percent.

Schwartz went on to report that the relative risk of non-menstrual TSS attributed to all barrier contraceptives was 2.4 cases per 100,000 users per year. And the death rate was 01.8 deaths per 100,000 women per year. Although this risk may be elevated, the number of cases assists still small and that can be seen in the next overhead.

In a recent publication by Hajjeh at the Centers for Disease Control on the surveillance update of TSS from 1979 to 1996, the years were divided into three based on the epidemic years, the active surveillance years and the present time. And as you can see from the overhead, the cases of menstrual TSS decrease over the time period and that there's an increase in the non-menstrual cases. But what's important to see is that the non-menstrual cases related to barrier contraceptives have not changed over the years.

More specifically, when the Today Sponge

was introduced in 1983, the cases still remained low. And again when it was removed from the market in 1995, there is not a significant difference among the rates.

Data obtained from the Today Sponge sponsors and the FDA adverse event reporting system describing the incidence of TSS cases reported to the sponge so that the incidents remains low and that there are no reported deaths from TSS attributable to sponge use. And this data is found in Ling Chin's OTC medical officer's review and Claudia Karwoski memorandum.

Furthermore, some of the reported cases of TSS had predisposing and extenuating circumstances, including the wearing of the sponge for longer than the recommended 30 hours, using the sponge while postpartum or while menstruating.

In addition to the epidemia logic reports, there are various in vitro studies that report on the sponge and Nonoxynol-9 on the growth and production of TSST-1. All three of these reports indicate that *Staph aureus* is inhibited by the sponge and Nonoxynol-9.

In summary, TSS is a rare disease cased by a toxin, TSST-1, produced by the bacterium *Staph aureus*. *Staphyloccocus aureus* is not introduced into

the vagina by the sponge but rather it is a normal component of the vagina micro flora. For disease to occur, the woman must be colonized with a strain of toxin producing *staph aureus* and she must lack protected antibody. These are two facts which make the disease rare. Tampons and barrier contraceptives have been shown to have an association with the occurrence of TSS, although they are not the causative agents in the disease. The sponge does not pose a risk any greater than that associated with tampons.

In fact, the cases of non-menstrual TSS associated with barrier contraceptives are far fewer than menstrual tampon related TSS, two percent versus 50 percent. And several of the reported cases of TSS while using barrier contraceptives have resulted from misuse of the product.

However small the risk of developing TSS while using the sponge, it is essential to provide the necessary information to the consumer regarding the possibility of developing TSS, consequences associated with TSS, as well as ways to decrease the small but present risk while using the sponge.

The information contained on the carton itself, as well as in the user instruction booklet, adequately informs and advises the consumer of the

risks of developing TSS, the severity of TSS, symptoms associated with the disease process, safeguards to reduce the risk of developing TSS and guidelines to follow if TSS-like symptoms occur. This information is clearly marked as a warning on the carton and in the enclosed booklet.

What I have up here is the currently improved -- approved 1991 label as well as a proposed revised 2000 label. And the arrows point to where these pertinent statements are found regarding TSS. The information contained on the product label adequately informs the consumer for safe and effective use of this product.

I'd like to introduce the next speaker. It's Roberta Geidner Antoniotti. She's -- she will present the relative public health need for the Today Sponge.

MS. ANTONIOTTI: Good afternoon. Thank you very much for this opportunity to come and really talk about the public health need for improved contraception with the vaginal sponge being one additional option that we could look at for that.

I represent Planned Parenthood of Maryland, which serves 16,000 patients a year in 22 counties in the State of Maryland. We are one of 132

affiliates for Planned Parenthood Federation of America and our seven health centers are part of a network of over 850 health centers serving over 4 million men and women a year with different forms of reproductive health services.

One of the things I do want to make clear is that my presentation here and my participation in this as a representative of Planned Parenthood Federation is not an endorsement of Allendale Pharmaceuticals or of this particular product that they may be able to bring to the market. But we do strongly commend them for looking for ways to bring additional options to women and our effort to reduce the high rate of unintended pregnancy.

As one of the oldest and largest reproductive health providers in the country, Planned Parenthood Federation of America has a strong interest in insuring women have easy access to safe, effective and affordable contraception.

One of the key problems that we face in assisting men and women prevent unintended pregnancy is the lack of innovation and approved technology in contraceptive research and methods. And one of the documents that has come out in 1995, that's documented very well, is the Institute of Medicine research on

unintended pregnancy and its affect on the well being of families and children in our United States.

I think you can see here, as many of the speakers previously documented, we have an epidemic rate of unintended pregnancy in the United States where close to half of all pregnancies are unintended and close to 10 percent of that half are totally unwanted children. We have the highest rate of any unintended pregnancy of any industrialized country in the world. In fact, the rate of unintended pregnancy in this country in 1983 was even higher than our planned pregnancies. And if you look at our rates compared to Canada or Great Britain, we are at least double and in some cases close to six times higher than other industrialized countries.

Unintended pregnancy remains a serious problem in the United States. Although the birth control has been available for 40 years and other innovations and contraception have been introduced in the past several decades, most pregnancies, as I've stated, are still unintended.

The last major introduction of a new contraceptive was Depo-Provera in the early 1990s. American women need safe and accessible birth control and they need more options that are affordable for

those without health insurance or for those with health insurance that do not provide coverage for contraceptives that still plages women across the country.

In terms of Planned Parenthood, we serve almost two million women every year for contraception. And that is one of the relationships that we may have with Allendale in the future if this product is approved. It is possible because we do serve two million women, as we do with many other pharmaceutical companies, we will have a conversation with them about how to increase access to the products that they can provide to reduce unintended pregnancy.

Of the women that -- of that two million, 12.6 percent of them preferred non-prescriptive barrier methods. There are important benefits to contraception that can be obtained without a prescription. While birth control methods such as the pill and Norplant or Depo-Provera involve one or more visits to a healthcare provider. The vaginal sponge appealed to women with busy schedules and accessibility issues because it could be bought over-the-counter at a local pharmacy sometimes 24 hours a day, seven days a week, where that's the only source of care that they have.

In a recent study published in Family Planning Perspectives, 19 percent of Missouri women surveyed reported that it was hard to get time off of work or out of school to go to a clinic. While 25 percent said that they would more likely to use birth control pills if they were available without a prescription. With easy access to contraception, the key to preventing unintended pregnancy, over-the-counter products makes sense.

In Maryland, where Planned Parenthood of Maryland serves women and men with reproductive healthcare, there's over 1,273,000 women of child bearing age between the ages of 13 and 44. We serve this population through the seven health centers that we have available.

According to a 1995 assessment of contraceptive needs and services, that was part of the Allen Guttmacher Institute study of contraceptive needs and services across the country, of the 664,000 women who need contraceptive supplies and services because they're at risk of an unintended pregnancy, more than a third of them are at or below 200 percent of poverty, close to a quarter of a million -- a little over a quarter of a million women.

And these women, whether they're black,

white, Hispanic, Korean, whatever race, culture, ethnicity, they need publically funded and support health services. This is the group who could benefit most by the reintroduction of the vaginal sponge product, a safe, affordable birth control method which should be permitted from our perspective over-the-counter.

Many of the women in this demographic will not use contraception if they do not have access to a viable over-the-counter method because of the difficulty in accessing the public health system as Dr. Connell so adequately described.

In Maryland alone, it is estimated that only 46 percent of the women in need of publically funded services are being served through the private and public healthcare system and that leaves a little over a 150,000 women at risk of an unintended pregnancy. And you can see by county and by our major city in Maryland how this impacts women across the state, whether they're rural women, urban women, suburban women, it affects them everywhere across our state and across the country.

Another valuable benefit of the non-prescriptive products like the vaginal sponge is its affordability. As I said, may low income women cannot

afford to pay for prescription contraceptives such as the pill or a diaphragm, yet they can remain protected from unintended pregnancy by purchasing the vaginal sponge, a more affordable alternative.

For millions of uninsured Americans, over-the-counter medicine is the only means of healthcare that's available to them and this includes contraception. Our hope would be that we would get contraceptive coverage passed at a federal level. I'm going to give my one little political statement here, so that all insurance companies have to provide this as an option as they provide Viagra to men, we should be providing contraception to women.

And, in fact, even women with health insurance aren't always guaranteed access to contraceptive care. Maryland, I'm proud to say, was the first state in the country that did pass a law requiring equity and prescriptive coverage.

The issue of privacy as well is another issue that needs to be considered when it comes to purchasing contraception. While obtaining a prescription for birth control pills or getting fitting for a diaphragm involves visiting a healthcare provider and getting the necessary tests, many women need the privacy and anonymity of purchasing a product

like the vaginal sponge if it is made available over-the-counter. It's easier to use and longer lasting in providing protection against pregnancy than other over-the-counter methods available such as spermicides and condoms.

We would also promote the use of condom with the vaginal sponge in order to provide full protection against sexually transmitted infections and HIV.

Although the goal of Planned Parenthood Federation of America and other reproductive healthcare providers that we've heard from earlier is to increase access to all types of contraception, we understand that the unique properties of the vaginal sponge fills a void that has remained empty since it was taken off the market five years ago.

When it was discontinued in 1995, it was one of the most popular contraceptive choices that did not require a doctor's visit with one quarter of a billion sold over 12 years nationwide. In addition to its ease and affordability, women who do not engage in regular intercourse found the vaginal sponge to be an ideal method of contraception.

A survey conducted by the CDC, National Center for Health Statistics, shows that births from

unintended pregnancy are increasing among never married women. We saw that they're increasing among married women as well, it's increasing among never married women. A lot of the myths that unintended pregnancy only affects certain categories of women is totally inaccurate and I think Best Intentions has very well done -- done a very good job to dispel some of those myths.

Many of the women, though, who fall in a never married category who has occasional sex could use this particular method where they don't want to use a method like the pill and a Norplant, Depo-Provera or IUD which are more expensive and not necessary when you have an occasional act of intercourse.

According to research by James Trussell, the vaginal sponge has been proven to as effective as a diaphragm and the cervical cap for women who have no previous births. The effectiveness of any method, of course, often is more determined by the human factor in appropriately and consistently using the method.

From the anecdotal information that I was able to obtain from our medical director and associate medical director, the problems that they saw in the early 90s -- late 80s and early 90s with the sponge

with removal, more often than not, was the practice of the woman and not the labeling, the instructions to the woman, it was a matter of her own awareness and her own ability to follow the directions that were provided to her.

And as far as we're concerned, the use of any contraceptive method is always much more effective than no method at all at preventing unintended pregnancy. We feel that the vaginal sponge in the 12 years that it was on the market was -- has proven itself to be a valuable and popular method of over-the-counter contraception. When it was taken off the market, it meant the removal of another opportunity for women to choose for themselves how best to prevent an unwanted pregnancy.

If we are to diminish the epidemic of unintended pregnancy in the United States, we must provide women and men with more options, not less. At Planned Parenthood we feel strongly that women should be able to benefit from its ease of use, accessibility and affordability. And we ask you to reinstate the vaginal sponge as an over-the-counter product.

I'd like to introduce Dr. Forrest Greenslade, who will be our next presenter.

DR. GREENSLADE: Good afternoon. I'm

really pleased to have the opportunity to speak with you today. My name is Forrest Greenslade and for well over forty years, I've worked on the development and introduction of reproductive health technologies.

While working at Ortho Pharmaceuticals, I served on the OTC panel for vaginal contraceptives that Dr. Connell chaired. When working with the Population Council, I guided the introduction globally of Norplant and the Copper T380 IUD. And for the last almost decade I've served as President of Ipas, an international not for profit women organization that confronts the issue of maternal mortality.

The reintroduction of the Today Sponge is really important. Unwanted pregnancy, as you've heard, is a really serious issue for many women. No contraceptive is ideal for all women and as a matter of fact, no contraceptive is ideal for any one woman throughout her reproductive life. Women need choices. And the Today Sponge fills that niche for many, many women. Women also need information by which to make those choices and I'm sure that Allendale Pharmaceuticals and the FDA want exactly what I want, labeling, that is accurate and both consumer friendly.

Let me put the first overhead up. This is

blow up of the 1991 approved labeling. And there's lots and lots of information here. And people who like lots and lots of information will enjoy this labeling. You can see that there was a large study, it was done in the U.S., done internationally, a large database of 1,800 patients. You can see that there's method effectiveness and use effectiveness and they're defined and you also can see that somewhere between 9.2 and 11 percent method effectiveness and 13 to 15.5 percent use effectiveness was obtained. Lots and lots of data, not very consumer friendly.

I like actually what the FDA is proposing in the proposed labeling -- the 2000 labeling. It's very straightforward. It says in clinical studies with the Today Sponge, about one in ten women, that 11 to -- 9 to 11 percent became pregnant using this product correctly all the time. It also says the possibility of getting pregnant increased to about one in seven women, that 13 to 16 percent, when the product was not used correctly.

Not yet, not yet.

Now, there's one problem with this. And that's time frame. Was that one out of ten chance of getting pregnant with the first intercourse? No. It was a one out of ten chance during an entire year of

the first use of it. Was that one in seven with that first intercourse? No. It was during the first year.

And to put this in perspective, think about it, 2.5 acts of intercourse per week is the average times 52 weeks times those hundred women, it took about 13,000 acts of intercourse to produce those ten pregnancies. This needs to have that kind of perspective. And what I suggest is simply adding language like, during the first year or within a year or something like that. This would make this very accurate, give good perspective and be very, very consumer friendly.

Now, on a subsequent paragraph in the proposed labeling, it says, no birth control product can prevent pregnancy all the time and refers to a table. And it's the table that's in the package, it's the table that comes from contraceptive technology. And to be quite honest, this is not very consumer friendly at all. And as a matter of fact, there's some very troubling aspects to it.

Now, remember, the FDA's proposed labeling says, one out of ten women can be expected to be pregnant within a year. But look at this labeling. Therefore, the vaginal sponge for previous births, it says up to 40 percent. What is a woman to believe.

Is it one out of ten or is it 40 percent. I needed to take a pencil and a calculator to figure in what does that come out to be, like one out of 22 women. What is the woman to interpret from this? What else is she to interpret?

Is she to interpret, for instance, that withdrawal or natural family planning is more effective than the Today Sponge, or is she to believe that a spermicide, a gel, foam, suppository or film is more effective than the Today Sponge? It's very hard for someone just to take a look at that, especially someone who's not really attuned to looking at tables and really figure out what is it that she's to interpret among all of those.

I'm actually concerned with the way in which these data were collected. I'm going to just read from you a sentence, the description of how these data came about. One would look at these data and say, oh, these were observed in a clinical trial. I guess that would be my first interpretation. But this is not the case. Let me just read this one sentence.

In the sponge/diaphragm trial, the proportion becoming pregnant in the first year of typical use for parous users of the diaphragm, 12.4 percent was marginally lower than for nulliparous

users. In the cap diaphragm trial, proportion becoming pregnant among parous users, 29.0 percent is almost double that among nulliparous users, 14.8 percent. Faced with this estimation, we set the estimates for nulliparous users of the cervical cap and sponge equal to the estimate for all users of the diaphragm based on the NFSG survey, 20 percent.

Now, listen to this, we doubled the estimates for nulliparous users for the cervical cap and sponge to obtain the estimates for parous use. That 40 percent is not an observed data -- piece of data in a clinical trial. It is an estimate based on a bunch of assumptions. Now, the writer's of this book did a very good job. And we all try to do this to try to interpret the data. But when compared to clinical trials conducted under FDA mandated good clinical practices, this 40 percent should not have the weight of the one in ten that you propose in the 2000 labeling.

Now, we've wrestled with this idea for years and years and years -- the other way, that's okay, that's a good way too. That's fine.

For years we've all tried to figure how does one compare studies done in various countries under different conditions with totally different

kinds of contraception. And here's a table that was -- a graphic that was generated by Parker Mauldin at the Population Council several years ago. And it's -- it's pretty straightforward, isn't it? If you look at, on the bottom periodic abstinence, spermicides, diaphragm, et cetera, you can see that there's wide range of effectiveness information that comes from studies under use conditions. A wide range ranging from somewhere between 10 and 30 percent. In the next range, condoms, orals, et cetera and then in the final lowest range things like injectables, surgical sterilization, Norplant.

What is very clear from this is that with those kinds of ranges to present to a potential consumer, the finite difference between 40 percent and 20 percent as being real, as being something that they should really make a judgment about their -- controlling their own fertility is -- is really not a rational thing to do. Let me suggest something that is much more in line with the user friendly approach that the FDA has proposed in the previous labeling.

Over the years when people have asked me, well, Forrest, what are the relative effectiveness of different ones. I've come up with a relatively simple straightforward approach. I say, if women don't use

any contraceptive method, more than eight out of ten of them will become pregnant within a year. With natural family planning or periodic abstinence, it's about one to three out of ten will become pregnant. It works.

Female barrier methods, probably one to two out of ten will become pregnant. And this includes things like the sponge, diaphragm, cervical cap, female condom, foams, jellies, creams and films. The male condom about three to fifteen out of a hundred will become pregnant. The pill, either combined or many, about one to five out of a hundred. Provider-base methods such as the copper IUD, Norplant, injectables, tubal ligation or vasectomy, about one to five out of a thousand.

Now, these are basic relative odds that I think anyone can understand. These are consistent with our understanding over years and years of clinical research, both on method and user effectiveness.

And I suggest to you that these are totally consistent with a rationale interpretation of the table that comes from contraceptive technology. And I think that these are consumer friendly and say in simple straightforward terms what a woman can

anticipate when she picks up a product and says, will this serve my needs for effectiveness or will it not. She can say, well, all of these are going to give me some level of protection. Obviously, the provider-based methods will give me a higher level of protection. The ones that I have to take, such as an oral, are a little bit less than that. And all of the barrier methods are a little less than that. But all contraction gives me a better chance to control my own fertility.

Now, obviously comparing effectiveness is only one of the things that a woman has to decide when she's trying to make a rationale choice because every contraceptive technology has its own set of advantages. But issues like reversibility, side-effects, frequency of administration and those special considerations for use are all important. There's no time for dealing with that today but in the handout that I left for you, I've given you my insight as to what those relative things are.

For me, the bottom line is this, the more choices that a woman has, the higher probability that she will find the one that meets her needs at her particular time in her reproductive life. I'm delighted that she soon will have again the Today

contraceptive sponge. And what's most important is for us to find a way to communicate to her whether or not this is the best choice that meets her needs at that time.

I'd like to pass the baton on to Dr. Staab, who will summarize.

Thanks for your attention.

DR. STAAB: Yes, we can go right -- okay. Just as an introduction, some people don't know Allendale, so I think it's worthwhile mentioning who Allendale is. We're a small start-up company. We have some -- a small number of people work in marketing, manufacturing and finance. And I happen to be a toxicologist, I'm a board certified toxicologist. We currently have no products on the market. No income. However, we're accumulating debt is what we're doing as our activity.

Just to give a small amount of evidence, as to how small we are, the gentlemen who's flipping the slides is the President and CEO of Allendale Pharmaceuticals, Gene Detroyer. Next slide, please.

We come here, even though we're small, with some relevant experiences though. I had worked for Tambrands, the maker of Tampax tampons in the mid 80s during the Toxic Shock Syndrome heyday, if you

will, when there was big issues. Working on TSS and consumer labeling. I've also worked for Schmid Laboratories, London International with condoms, Nonoxynol-9 and the labeling of those products. I don't come to the Today Sponge for the fist time. As a matter of fact, even when I was at Tambrands, I ran into Forrest who helped us to do an assessment as to whether or not Tambrands should acquire the Today Sponge when it was being sold by VLI. We did an extensive review at that time. So this is not a new product for me or for the people that I am associated with.

Next slide, please, Gene.

And the people that we came to speak here today are not seeing contraception and the issues related to consumer products labeling for the first time. Besides the people who have already spoken, we had Dr. Onderdonk from Harvard write some background information made available to the FDA and to the panel. And also Dr. Mike Burnhill, V.P. of Medical Affairs for Planned Parenthood Federation of America, got it right.

Unfortunately, those two gentlemen had previous commitments out of country, they are both not here, although both had express an interest in being

and both are very supportive of the return of the product and an interest in keeping a label which communicates properly, simply and clearly. Again, a common goal.

What I did, and I'm going to try and go through this quickly because I think you're getting an idea from where we're coming from, we're trying not to clutter up a label. We trying to communicate. We trying to do it simply and we're trying to get the key information in the right place. The medical officer who wrote the recommendations for what's needed in a label put these things down as something which would be needed on the outside of the label, something like Toxic Shock Syndrome to address it, allergy to Nonoxynol-9, post-partum advice, TSS and menstrual use should be contra indicated, miscarriage and abortion, see a doctor if a vaginal infection exists or occurs in use.

Indeed, those things are in the label now, maybe not the exact same words but its pretty good and that's the kind of advice that the FDA and American Home Products had in the 1991 label that was on the market in 1995.

Gene, next one.

Also, they asked on the insert, which is

the insert which comes inside the box with this particular OTC product, if you had TSS, avoid the use of the product. That's there. Dropping down to the bottom of this slide, see the doctor if infection exists or if signs of infection exists. That information is there. And do not use if pregnant or if there are signs of pregnancy. Those things were there.

The two dots, number one and two on this particular slide are not on the label. One suggestion was explain the post-partum uterus to the consumer in the labeling so that they could understand whether or not the sponge would adequately fit and be used and so forth. Quite frankly, we think -- I think that that information is probably best being B- being a discussion between the health care provider, physician and the potential user of the sponge, nurse practitioners and physicians and so forth. These are people in this case particular who have given birth. More than likely they have someone that they're talking to with respect to their health care.

And the next one is use a condom to avoid STDs as something that was not on the label, we would not take exception to putting that onto the label. It's a -- it's probably a good recommendation today

considering the mortality and morbidity associated with sexual transmitted disease acquisition.

Going again, wash hands, 30 hour maximum retention time, don't use -- don't douche following use, difficulty removal. If you have difficulty removal, read the instructions. We have the 800 and also call your doctor. Those are things that were on the current label. We say let's retain them. I think that there's good information. With respect to that 800 we've heard over and over again from Dr. Connell and from people that I've spoken to American Home Products in the Consumer Affairs Department where they took these -- they're very capable of communicating removal issues with the consumers when they have these difficulties. It's a very effective way of getting in touch with your consumer if they're having a problem. So we are supporting them as well.

Again, under insert information, we're asked to talk about the local effects of irritation and so forth which is in the current label. And we're ask to, if they're signs of infection, fever and so forth, see your doctor. That's in the current label.

The one issue where, quite frankly, I'm struggling a little is how do handle -- should we be putting questions about or information about and

education about sexually transmitted diseases, what do you do if you're using multiple partners as sexual and if you have a new partner and so forth. I guess I personally feel that if you tell the people that if they want protection from sexually transmitted diseases, to use a condom, you've addressed that issue.

Now, I don't know how much public health we could -- public health expounding that we can do in a label that would be effective. I think there are very effective communications that are available today through clinics and through the public to get that information across. This is an NDA product and since it's NDA product we do send in annual reports. And that 800 number that I spoke about before that was so very effective in communicating with the consumers is also effective to getting adverse events and reports. The consumer is never afraid to pick up the phone and to call 800 -- a 1-800 number. We believe that we do get good information about the use of this product. We don't believe there were any major increases in TSS, for example. And I think Mary was very clear in saying that there was not an increase in TSS.

Go ahead.

So, our post-market surveillance, we feel

pretty comfortable in staying with the 800 number. And lastly, efficacy I'm going to stand by what Forrest had said. I'm running out of time and I'm getting bad glares here. But if somehow we can communicate the hybrid between what the FDA is asking for the one in ten failure or one in seven failure rate for imperfect use along with the time frame so that people know that we're talking about 1500 acts of intercourse that wind up getting a failure rate instead of ten people have intercourse once and you wind up with a pregnancy. I think that we've come together where we should be.

The major issue that we have is if we wind up trying to put all of the usable information onto the outside of this package, it is going to be unreadable and it is not going to be tool for the consumer to learn about the use of the product. We've got minimize the amount of information that is on the outside of that package.

For example, we don't need full directions for use on the outside of the package. I think you should state this is a product that has to be moistened and inserted vaginally, see instructions on the inside. But if we can come together to find the right key information, mention TSS and so forth, I

think we have a way to move forward.

I do thank you very much. I know that I -- I'd be willing take any questions that you folks might have and I know the panel will as well.

Thank you.

DR. CANTILENA: Okay. Thank you very much, Dr. Staab. And, if you wouldn't mind actually staying at the podium and perhaps you could triage the questions as they come up --

DR. STAAB: Sure.

DR. CANTILENA: -- to members of your team. I'd actually like to open up this to questions from the entire panel for the sponsor at this time.

Dr. Greene, would you like to start?

DR. GREENE: I just -- just point of clarification, when Ms. Delaney presented her data on Toxic Shock Syndrome toxin, she said at one point, I believe, that one percent of strains of *Staph aureus* produced TSST-1, except it looked like you graph was more like one percent of the people carrying *Stap aureus*.

DR. DELANEY: That was one percent of the total nine percent of women that were carrying *Staph aureus*. Of those nine percent, one percent carried the TSST-1 producing *Staph aureus*.

DR. GREENE: Okay.

DR. DELANEY: That's going at the rarity of the disease essentially is what the point I was trying to get across.

DR. GREENE: Okay. So of the nine women in a hundred, one of those nine?

DR. DELANEY: Correct.

DR. GREENE: Got it. Okay. And the other --

DR. DELANEY: One of those nine percent. I mean there was not just nine, there were, I believe, a percentage.

DR. GREENE: Right. Okay. And the other question I had was you mentioned a figure of the incidents of anti-TSST-1 antibody, and it wasn't clear to me whether the percentage that you mentioned, I think you said 98 percent.

DR. DELANEY: 98 percent. Yes.

DR. GREENE: It wasn't clear to me whether that was of all women studied or of the women who carried *Staph aureus* or of the women who carried *Staph aureus* with the toxin?

DR. DELANEY: That was of all women studied.

DR. GREENE: Thank you.

DR. CANTILENA: Other questions? Dr. Gilliam, did you have a question?

DR. GILLIAM: Just a comment, I guess, to Dr. Stabb. I appreciate the comments that you've made, the only, I guess, problem I have with them is you're saying, you know, you're wanting this product to be over-the-counter and yet you're saying there are issues that they should talk with their healthcare provider about. And recognizing that a lot of women who possibly might use this aren't going to get healthcare from a healthcare provider.

And so that's my concern regarding some of the comments that you've made.

DR. STAAB: Actually, I didn't quite understand your question. You were going back and forth from the microphone.

DR. GILLIAM: You were just, in your comments you were saying that, I forget the exact references you were saying, but you were saying that there were certain items that the user should talk with their healthcare provider about. And yet this is a product that you're recommending for over-the-counter use and that many of the many might not go to their healthcare provider to discuss these issues. And that's the point I'm trying to make.

DR. STAAB: Currently, the FDA approved label does call for getting back to your healthcare provider with a whole series of questions. That's not unusual. The specific ones, I believe, where I was focusing, was a woman who had just a birth, just had abortion, she was -- she has been speaking to a healthcare provider who she can go back to. And that was point that I was making there. Rather than -- rather than having a large amount of additional text in an insert, which I think we have to realistically recognize, there's just so much that consumers are going to read.

I'd say, or the contraction of the uterus and so forth following birth, she's just had a birth, she can talk to her physician about it. I think those issues are more appropriate to go back to the physician rather than trying to do an all encompassing explanation of the female physiology hoping that we're going to cover that particular person.

DR. GILLIAM: Okay. Thank you.

DR. CANTILENA: Yes, Dr. Lerner?

DR. LERNER: Everybody keeps referring to the problems with removal. Do you have any data over the course of the 12 years that it was on the market, what percent of women had trouble removing, what

percent were then sort of fixed by the telephone call, and then how many of those really needed to go see their physician? Because I think that's -- has very important clinical implications if ten percent of the women called but, you know, 197 percent of those couldn't be talked through it by your 800 number and then had to go to their physicians. Do you have any data on that?

DR. STAAB: Well, you're talking about several, and I don't have the numbers in front of me, you're talking about several thousand complaints with a quarter billion units sold. So the percentages are extremely low and of those that went to see a physician, it is having -- it is relatively low as a complaint but having said that, it is the number one consumer complaint with the Today Sponge, first time users, a lot like a diaphragm, someone who's inserting a diaphragm do have a certain amount of difficulty with this but the 800 number has been able to minimize the number of people. Once you get to the 800 number it's already a complaint. So even if you help them with it, they're recorded as a consumer who made a complaint on the issue.

DR. LERNER: Just as a follow-up, I think it would be interesting, I don't know that I saw it in

any of the background material, just the registry of the complaints and, you know, I think that would just be interesting information to have available.

DR. STAAB: That information -- that information is available, is recorded. And we do report on that by the way on an annual basis. That's what I was saying. When we have the -- the reason that we know that it is the number one complaint because we do record that through our 800 numbers or if people happen to write and we put that information in a tabulated format for review by the agency each year.

DR. LERNER: I suppose in some ways I have a vested interest in that as a very clinically oriented OB/GYN, I want to make sure that if I have, you know, a thousands patients using, I'm not going to have 500 walk-ins per week. And I think that we as the, you know, healthcare providers are going to be very interested in finding out that your numbers that occur.

DR. STAAB: I thought maybe Dr. Connell, who's got a lot of OB/GYN experience as opposed to this poor lonely toxicologist might have a comment about this. Thank you.

DR. CONNELL: I think it was difficult as

you might imagine to come up with an absolute figure. What we have is basically what has just been stated, that of all the complaints, and, you know, this is not evidence-based medicine really. Of all the ones, and I used to keep track of what the calls were to the 800 number back in the VLI days, and certainly this was the number one problem, as you reasonably knew you could talk most women through the removal process.

But I don't recall that anybody has ever been to deal with the two million women and come up with a figure of the various complications, then a subset of removal problems. It's one of those things you'd like to be able to quantify, but I don't think it's true. I think you have to be a little bit global in terms of the side-effects and the percentage of those that are removal related.

So I -- it's a good question but I'm not sure the data are out that that you can do anything other than say, side-effects are not common but of the ones that have been problems in the past, removal problems rank right up front. That's the reason that the loop was changed because in the very beginning this polyester thing, women couldn't feel it. And if you can't feel it, you know, this was a real problem. But once it was changed to a braided loop, then again

the problems got less because they could find it and it was much easier to take it out.

So numbers would be lovely but I don't think you're going find an accurate number with the scientific credibility that you might like. I think we still have to go sort of globally.

DR. CANTILENA: Okay. Dr. Uden?

DR. UDEN: Dr. Staab, if you could clarify some confusion for me. Dr. Greenslade presented quite of bit of good information in terms of labeling, suggest that wording changes in terms of time per year. He didn't finish his presentation and he also had quite a few additional charts back there that were, I think are very interesting and can be a lot of information. In your comments, you wanted to be brief. The labeling to be as brief as it can be. What is your stand on Dr. Greenslade's suggestions in terms of those additional tables that are there? What do you want included? What didn't you want included with that?

DR. STAAB: I think Forrest will address that.

You're referring to the tables in his handout as opposed to the contraceptives. Okay.

DR. GREENSLADE: I was not suggesting that

the last set of tables that I handed out should be in labeling. What I handed them out for was to simply to provide background that in addition to making a decision upon comparative effectiveness, women have a lot of other things to think about. And it is virtually impossible to provide all of the different pieces of information about all of the different methods in one place. But I thought for you on the panel, it would be useful just to have that insight as perspective to look at the comparative effectiveness numbers. And they are basically my interpretation of a lot of reading over a lot of years about a lot of technologies.

DR. CANTILENA: Dr. Johnson?

DR. JOHNSON: I have two questions. One is for Ms. Delaney, so she can move to the podium while I'm asking my first question. And my first question may be really belongs with the FDA. In our packet, we have this, I think, proposed label and it has to do with the efficacy. And it just says, no birth control product can prevent pregnancy all the time. See table of pregnancy rate. So, I'm a little confused because that doesn't tell you anything about the efficacy except that it's not a hundred percent.

And, again, maybe this question really

goes to the FDA, this issue of one out of ten over a period of a year, are you proposing that goes in the package insert inside or on the outside box?

DR. STAAB: All right. Historically, the efficacy data has been in the insert with the product. We take no great exception to putting a single statement about the efficacy for the Today Sponge as part of Drug Facts labeling as long as some of the other information is compressed so that, I mean as it is now, we'd have to go one and three quarters way around the box with Drug Facts Labeling.

We're just saying there's a certain amount of critical information that we should have on the outside of the box. The reference that you're referring to refers to the table that Forrest had spoken about that was developed for technical people in contraceptive technology which was fraught with difficulties -- with some technical difficulties and certainly readability. If you talk about sixth grade reading level or something, that table -- a consumer will not walk away from that table and understand what they need to know about relative rates of contraception.

For my perspective, if there was a simplistic statement, verbal or numerical similar to

what, what I'll call the combined Forrest Greenslade and FDA comment, where the various methods are compared and that was scientifically accurate backed up. And we would take no exception to putting that into the insert.

DR. JOHNSON: Okay. My question for Ms. Delaney is just about toxic shock in general. In the materials that we received, I think, from your laboratory are some data, I believe from the CDC, with definite and probable cases of toxic shock with a peak in 1980 of 892, down to 4 in 11 in '96 and '97.

My first question, is this the number of cases total in the U.S. or is this per --

MS. DELANEY: I'm not -- which -- I'm confused as what to your --

DR. JOHNSON: This was, I believe, part of Dr. Onderdonk's materials.

MS. DELANEY: Oh, okay.

DR. JOHNSON: Right. And -- so one of my questions is are these absolute numbers?

DR. STAAB: I can tell you the source of that. I'm sorry.

MS. DELANEY: Okay.

DR. STAAB: I made that available to Andy Onderdonk, that is from the Center of Disease Control,

an '87 summary of the total number of reported cases of Toxic Shock Syndrome.

DR. JOHNSON: Okay.

DR. STAAB: A total number reported in the U.S. to the Center for Disease Control.

DR. JOHNSON: So there were four reported to the CDC in 1996, for example?

DR. STAAB: I don't have the table.

DR. JOHNSON: Well, that's what, I mean that's what the table says. So, my question, which hopefully you can answer, is what is the explanation for this very, very dramatic drop in the incidents of TSS over 15 years or so.

MS. DELANEY: Are you referring to the menstrual. The drop in the menstrual TSS.

DR. JOHNSON: Well, either one. If you look at menstrual or total, they've both dropped from, you know, near the 1,000 mark to down to like ten.

MS. DELANEY: The menstrual TSS cases have dropped because of the removing of the Rely Tampon from the market, consumer has been advised to alternate between pads and tampons, to use the tampons that are most, the less absorbent that conforms to their needs.

The cases of non-menstrual TSS cases, the

increase they believe because a majority are due to cutaneous wounds, surgical wounds, they think it's because of the new healthcare rules where people are not hospitalized as long. A lot of the outpatient surgeries, they think that that's why those cases are increasing.

DR. JOHNSON: Yes, I guess from this table I don't see an increase. I mean, it looks like -- it looks like everything is decreasing whether you look at total.

MS. DELANEY: I think the total cases are decreasing but the percentage of menstrual -- what my data was showing that the menstrual and non-menstrual are now becoming close to 50 percent each as opposed to before where it was 80 percent and 20 percent.

DR. JOHNSON: Okay. So, I guess your answer is that they main reason that it's -- the TSS has dropped nationwide is because of more appropriate use of tampons.

MS. DELANEY: Exactly.

DR. CANTILENA: Okay. Dr. Davidson?

DR. DAVIDSON: You know, most of us here have lived, you know, in the U.S., there's a percentage that are not, you know, full literate, 47 percent or so may not understand clearly what the

label is. Did you do any field testing on your label to see the comprehension from the general public?

DR. STAAB: Since we had acquired the label, we were going to retain the label that had been approved by the FDA. We did not do any additional comprehension or readability on that label. Okay.

DR. CANTILENA: Other questions? Yes, Dr. Krenzelok?

DR. KRENZELOK: If you'll bear with me, I have a few questions and a couple of comments. I'll address the last one in just a moment.

You're going to have an 800 number or there was an 800. And it would appear that removal problems can be a 24 hour a day, seven day a week problem. It's not a nine to five problem. Will you have this 800 line available for women, 24 hours a day, seven days a week so that you can attend to those needs no matter what time zone they're in or what their particular predicament might be?

DR. STAAB: We are setting up an 800 -- we have the 800 number is place right now. We are setting up with a beeper system. It is not set up right now, but yes, it is our intention to answer questions, urgent questions, to have a triage system within the phone system so that if they're worried

because they bought three sponges and there's only two in the box, we don't want to handle that at three o'clock in the morning. But urgent questions we would have an opportunity to beep the healthcare professional.

DR. KRENZELOK: Now, you also mentioned that you didn't want to make the package basically a compendium of every piece of information.

DR. STAAB: Right.

DR. KRENZELOK: And, as I recall, the product, it comes in a small box.

DR. STAAB: Gene, do you have one you can hold up? Just, it's outside, sorry.

DR. KRENZELOK: But it is, I recall -- there's one, I see. Okay. So, there's a box.

DR. STAAB: There's a three pack.

DR. KRENZELOK: Now, we're you intending to have one package insert in there or would you have a package insert with each sponge? Because the package inserts would certainly have an opportunity to get lost as people put these in their purse, in a briefcase, in a suitcase. Would that be an intention of yours?

DR. STAAB: It would not be out intention to put an insert with each unit, rather one per

carton. That's been historically the way that's been handled.

DR. KRENZELOK: Well, given the use pattern of this particular type of product, it seems to me that might be a reasonable thing to do. Now, Dr. Greenslade talked about a variety of ways to present the data in terms of pregnancy and I agree this should be very consumer friendly. Peoples should look at that and say, these are my odds of getting pregnant.

One of the things you might want to consider changing would be in each of those things you had a different denominator, so it was --

DR. STAAB: One out of ten.

DR. KRENZELOK:Yes. One out of ten, one out of a hundred, five out of a thousand, and it might be good to bring those all to common denominator so that people can really understand them.

DR. STAAB: Forrest will comment on that but that's a good comment.

DR. GREENSLADE: Yes, I wrestled back and forth with that for many years. If you make it a common denominator, say a hundred, then you're talking about a tenth of a woman sometimes. And that's kind of confusing when you talk to people and say, well,

what does this mean. If you set it up to a thousand women or 10,000 women, then the -- then the numbers are looking kind of large. And one of the things I wouldn't want to do is frighten people from considering a very effective safe option that she could choose.

And so I agree, this is a way that you kind of flip a coin and say, what communicates the best for most women. And whether you set it all at one denominator and wrestle with the numerators or the reverse is probably something that we have to talk, you know, in focus group with real potential consumers and get a sense what communicates best to them.

This was the compromise that I came up with talking to a few people over the years. But I'm not an expert in focus group interviewing. It's a very good point.

DR. KRENZELOK: Thank you. As it relates to probably the issue of literacy, I think was Ms. Antoniotti, discussed unintended pregnancies. And I was wondering if there's any kind of data that have been collected showing a relationship between unintended pregnancies and low literacy women, for example? To see if -- what I'm getting to here in just a moment is something to do with the label in

terms of literacy but I'm looking the population that uses these is literacy an issue?

DR. STAAB: There -- there may very well be some information. Do you have something you could add on that, Roberta?

MS. ANTONIOTTI: Part of the -- part of the information that the Institute of Medicine looked at in terms of the Best Intentions research was literacy levels, cultural norms, just experience with reproductive health issues in terms of background.

So, part of the things that we look at in our clinical practice in dealing with a lot of low income men and women who are disadvantaged in terms of educational opportunities as well as a number of immigrants. I agree with Dr. Davidson that some of the issues in terms of language barriers and literacy levels, that's why we liked in the label the whole graphic display because at least from that perspective any woman can have an understanding or she has a minimal knowledge of her body, how to use the product.

But I think Best Intentions is probably one of the best resources to take a look at how literacy impacts a woman's ability to get access to healthcare.

DR. KRENZELOK: Thank you.

DR. STAAB: I was just going to say, I think you're see with tampons, the industry that I've worked and with the sponges, a liberal use of those graphics for that very reason.

DR. GREENSLADE: Dr. Trussell and his colleagues published a relatively recent paper where they used survey data and stratified it according to a whole bunch of different strata and one that they did was socioeconomic level. And across all methods, the lowest the socioeconomic level, the higher was the pregnancy rate or the higher was the failure rate. So I suspect there's some sequelae point that you're making that people of lower socioeconomic status have a lessor access to the information and to the way of assimilating the information. So finding ways of getting it to a simple communicative level is very, very important.

DR. KRENZELOK: Thank you. Along those lines of communication, I don't purport to be a readability or label expert by any means. But I took the liberty yesterday of just typing in parts of the label to Microsoft Word 2000 and running a Flesch Readability Score on it. And for those of you who are unfamiliar with Flesch, as I was until yesterday --

DR. GREENSLADE: So you are a world

expert.

DR. KRENZELOK: Exactly. I'll acknowledge that immediately. But they have two different scores. So all you have to do is you do basically spelling and grammar and then look at the options and it gives you this readability score. So they have a readability score basically and it's based on a 100 point scale. And the higher the number, the more easily comprehendible the label is or the paragraph or whatever it is you're looking at is. And it said that most standard documents aim for a score of approximately 60 to 70.

Then they have something called the Flesh Kincaid Grade Level Score, where they have a very complex formula, basically it says that a score of eight means that and eighth grader can read this. And it says again that most standard documents aim for a score of approximately seven to eight. So, if you bear with me for just a minute, I took two parts of the label, of the prosed 2000 label.

DR. STAAB: Of the current label?

DR. KRENZELOK: Of the 2000 proposed label in our package. Yes, the 2000 one. And there was one where it descried toxic shock which I thought was important for people to understand. And it said,

Toxic Shock Syndrome, some cases of Toxic Shock Syndrome, TSS, have been reported in women using barrier contraceptives including the sponge. TSS is a rare but serious disease that may cause death. Warning signs of TSS include fever, nausea, vomiting, diarrhea, muscle pain, dizziness, faintness or a sunburn-like rash on the face or body.

If you have any of these signs, remove the sponge and get medical help right away. Now the reading ease score on that was 58.1 percent. So it was a little bit less than what the ideal document should be. The grade level was 9.4. Now that's in contrast to the very first part of the instructions were -- it illustrates how to insert the sponge but also describes how to insert the sponge.

And it says, Today vaginal contraceptive sponge is inserted through the vaginal opening and placed in the deepest part of the vagina just below the cervix. The cervix is the bottom end of the uterus. It has a small opening through which sperm must travel to reach and fertilize the egg. The reading ease on that was 52 percent but the grade level was 11.9. So we're talking about a high school senior being able to comprehend that.

So, again, those are two very isolated