Between March and August 2003, the Endometriosis Research Center (ERC) asked its members and visitors to its web site (www.endocenter.org) to complete a questionnaire regarding their medical history and their use of menstrual cups (1). Among the stated goals for this questionnaire was an attempt to uncover some specific cases in which users of these products had developed endometriosis. It was clearly stated in the introductory information for the questionnaire that any reports that were collected could not be used to demonstrate a relationship between the product and the development of endometriosis. Rather, the intent was to publicly ask a question that had not been previously discussed among users of the menstrual cups, since information on endometriosis was not included in the packaging of these menstrual products.

The questionnaire only solicited 9 responses. Three of the women who responded had endometriosis, which developed after they began using menstrual cups. One of these women had used a menstrual cup for less than 1 year and the 2 others had used menstrual cups for more than 2 years. The six additional responses seemed to be from women who were supporters of the use of the menstrual cups. Five of them had used the products for less than a year and one for more than 2 years, and none reported any problem with symptoms of endometriosis.

The small number of responses seems to reflect the very limited use of menstrual cups among the women who had access to the questionnaire. In subsequent efforts to have information on endometriosis made available to women who use menstrual cups, we have petitioned the Food & Drug Administration (2, attached). This petition spelled out in detail the physiological basis for concern that the use of menstrual cup might increase the frequency or severity of endometriosis.

Endometriosis is the growth of endometrial tissue in the peritoneum or other inappropriate parts of the body. The reflux of endometrial cells during menstruation is a readily identified route for these cells to reach the peritoneum. It is commonly acknowledged that menstrual reflux occurs in most women from time to time. In the sciences of pharmacology and toxicology there is an awareness that the dose of an agent is a critical component in determining the likelihood that a physiological reaction will occur. The menstrual cups are devices that are likely to increase the volume of menstrual reflux, and it appears important to study how an increase in menstrual reflux affects the appearance of endometriosis. In a baboon model for studying endometriosis, it has been shown that an increase in retrograde menstruation did increase the incidence of endometriosis (see discussion in the Cup Petition, ref 2).

When research attempts to identify a toxic effect, an agent that causes a unique adverse effect is easiest to pinpoint. The most difficult toxic relationship to uncover involves a product or drug that increases the incidence of a condition that has a slow onset and is only found sporadically. Endometriosis is a condition that sporadically affects millions of women, in the US and throughout the world. The causes of endometriosis are not clearly defined, and it appears to be the result of many factors, ranging from a woman’s anatomy to possible elements of her immune response. The use of menstrual cups prolongs and seems likely to increase the retention of menstrual fluids. We are concerned that the use of menstrual cups alters the normal process of menstruation and increases the burden of endometrial tissue that enters the peritoneum, thereby causing an increase in a woman’s risk of developing endometriosis.
In their subsequent response to the Petition (3, attached), the FDA noted that our concern about Cup use and an increased risk of endometriosis was "physiologically plausible." However, the FDA reply specifically cites the absence of data from a "well-designed clinical study" as a limitation on their ability to take action on withdrawing the menstrual cups as unsafe. They did not explain why no action was taken to label the products regarding this "physiologically plausible" risk.

Clearly what is needed to assure the safety of the menstrual cups is clinical data. The one available report that associates a menstrual cup and endometriosis was published in 2003 (4). That report describes a woman with ligated fallopian tubes who used one type of menstrual cup ("The Keeper") over a period of four years and subsequently required a complete hysterectomy because of her development of severe uterine endometriosis. The FDA reviewed this citation in their reply and commented that it was not a sufficient basis for regulatory action.

It should be kept in mind that the menstrual cups were brought on the market by "grandfathering" their approval status, not though the use of clinical studies to support their safety and effectiveness (see detailed discussion in ref 5, Cup Petition, Addendum A). In contrast with the untested menstrual cups, there are many examples of drugs and newer medical products that have been subjected to premarketing studies, and appeared safe, but were subsequently proven to be too dangerous for public use. The history of such products includes the Dalkon shield, the Rely tampon and, most recently, the drug, Vioxx.

Our questionnaire demonstrated one of the many problems involved in studying the safety of the menstrual cups, that is, identifying a large enough population of users to produce meaningful data. Among the additional factors that will be important to control in future research will be the criteria used to diagnose endometriosis and the suitable matching of menstrual cup users with controls regarding key risk factors for endometriosis. Although the FDA groups all menstrual cups in one category, data on users of menstrual cups should be divided into at least two categories. The product, "Instead" is designed to sit tightly over the cervix, and data from users of this product should be analyzed separately from that of users of "The Keeper", "The Mooncup," "Lunette" and "The Diva Cup," which sit lower in the vagina, to determine if there are practical differences in the amount of endometrial reflux the products produce.

At this time, we have the worst of all possible risk situations - Menstrual cups are not being studied for their possible effect on the incidence of endometriosis, and users of the products are not being warned about the "plausible" risk of endometriosis associated with the menstrual cups. We will continue to explore all possible means to improve the information available to women on the menstrual cups and promote clinical research to determine if they can be used safely.

References (attached)
1. Menstrual Cup Health Questionnaire. ERC 2003.
2. Citizen Petition to the FDA on Menstrual Cups and Endometriosis (03P0166), 4/17/03
3. FDA Reply to Petition 03P0166, 11/18/03
5. Citizen Petition to the FDA on Menstrual Cups and Endometriosis (03P0166) Addendum A, 4/17/03
"MENSTRUAL CUPS"
BACKGROUND INFORMATION & VOLUNTARY SURVEY

On February 4, 2003, the NY Times featured an article on alternative menstrual products, specifically, menstrual cups. "Menstrual Cups: At Age 46, Begin to Make Up for Lost Time," by renowned journalist Donald McNeil, Jr., briefly mentioned Endometriosis in the following context:

"Dr. Arnaud P. Lione, an independent toxicologist in Washington, recently warned about the use of menstrual cups. He thought they might increase the risk of toxic shock syndrome because they hold blood in a bag. The syndrome is caused by toxins from staph or strep bacteria; an outbreak in the early 1980's that killed about 59 women was linked to superabsorbent tampons, prompting tampon makers to change the materials they used. Dr. Lione argued that cups might also raise the risk of endometriosis, a condition in which cells of the uterine lining slough off at menopause flow back into the abdomen and attach there."

The entire article is available at this writing online at: http://www.nytimes.com/2003/02/04/health/women/health/04KEEP.html

Dr. Lione is the President, Associated Pharmacologists & Toxologists in Washington, DC, and is on staff at the Reproductive Toxology Center in Bethesda, MD. Dr. Lione has since issued the following comments, which we deem relevant and of importance to those concerned with Endometriosis:

"The use of menstrual retention devices, such as "The Keeper" [wwweeper.com] and its disposable version, "Mooncup" [www.softcup.com], has come into my attention as an offspring of my work as a reproductive toxicologist (see: www.reproduction.org). My two major concerns are an increased risk of toxic shock syndrome, and a difficulty in documenting, but physiologically manifest, increases in the incidence or severity of endometriosis among women who use menstrual retention devices."

As with the diaphragm, solid bodies in the vagina are likely to be a source of mechanical irritation, producing breaks and lesions in the vaginal epithelium. These sites provide a focus of growth for Staph. aureus, degenerating tissue to serve as nutrients, and a point of entry for bacillus fuscus into the systemic circulation. The association between the use of tampons during menstruation and toxic shock syndrome (TSS) has become clear enough by the late 1980's that investigators at the Centers for Disease Control addressed the risk of nonmenstrual TSS associated with barrier contraceptives such as the diaphragm and the contraceptive sponge.

I consider the referenced CDC report to be the definitive epidemiology study on the increased risk of TSS and foreign bodies in the vagina, even outside of menstruation (1). The literature suggests, however, that the risk of TSS, although increased by the use of intravaginal products, remains low. TSS has become a more recognizable and treatable condition, so to many consumers it appears to present a less formidable danger than in the past.

The concern that the use of menstrual retention devices may increase the incidence or severity of endometriosis is more difficult to present, and I will just summarize it briefly, here (a detailed discussion will be part of an FDA position on this matter that is in preparation)."

"Many of the factors that contribute to the development of endometriosis are not clearly defined, but it is generally assumed that visible fragments of the endometrium released during menstruation travel back into the abdomen and survive in some women to cause endometriosis. If clinical data suggest that the retrograde flow of menstrual debris occurs in most women, the mechanism(s) explaining why only some women have significant survival of these invading cells is what remains unclear."

The abdominal cavity has a defense system of macrophages and killer cells to eliminate or minimize the invading endometrial cells. Factors that could increase the incidence of endometriosis would be the frequency and magnitude of the challenges faced by the defense in the abdominal cavity. The occlusion of the ovary during menstruation would be expected to substantially increase the retrograde flow of menstrual debris and the potential seeding of the abdomen in women using menstrual retention devices. Since the onset of endometriosis is apparently influenced by a variety of factors, which may include diverse elements such as individual anatomy and immune function, the epidemiology of endometriosis is not clearly defined. This fact suggests that demonstrating an increase in the incidence of endometriosis in association with menstrual retention devices will be a difficult task, making caution even more important in this matter."

References:

Endometriosis Research Center

Endometriosis Center
5333 South St., SE Washington, DC 20033-4222. February 2003.

The ERC maintains that retrograde menstruation is not a sole or definite cause of Endometriosis. Dr. Lione acknowledges same. However, in the interest of Endometriosis research and to further examine various facets of the disease, the ERC will be collaborating with Dr. Lione on data collection related to menstrual cups. Although reports from our members and those in the Endometriosis community will not necessarily prove any association between the use of menstrual cups and Endometriosis, we encourage your feedback. Data collection of this nature can facilitate - and expedite - the necessary clinical studies that need to be implemented.

We hope you will join us in this interesting research project by sharing your experiences with these products.
Definition: You are invited to participate in a voluntary feedback study being conducted by the Endometriosis Research Center, an established 501(c) organization, in collaboration with Armand Lione, PhD. Participation in this research is completely voluntary. You are a possible subject if you are at least 18 years of age.

Study purpose: The goal of our study is to explore the potential increased risk of the disease Endometriosis incurred through the use of the alternative menstrual products known as "menstrual cups."

Procedure: If you choose to participate in this questionnaire, you will be asked a series of questions relating to your general health, your experience with menstrual cups, and your experience with the disease, Endometriosis. Completion of this questionnaire should take less than 10 minutes of your time.

Potential risks and discomforts: No potential risks or discomforts to the participant are anticipated.

Potential benefits to subjects and/or society at large: It is unlikely that you will benefit directly from your participation in this study. However, society at large may ultimately benefit by a.) learning more about the possible connection and/or elevated risks of Endometriosis and menstrual cups, and/or b.) by having enabled the facilitation of necessary clinical trials on said matter.

Payments and costs: You will not be paid for your participation in this questionnaire. There is no cost to participate in this questionnaire.

Confidentiality and privacy: The ERC has always maintained a strict privacy policy. We never sell, trade or otherwise share your details with any sources. All correspondence to the ERC is held confidentially, furthermore, at no time will your personal and/or identifying information be shared outside of our organization, for any reason.

Identification of Investigators: The Endometriosis Research Center in collaboration with Armand Lione, PhD.

Contact: If you have any questions or concerns about this questionnaire, please feel free to contact the ERC via email at EndoFL3@aol.com or call us toll free at 800/239-7260.

Financial Disclosure: The Endometriosis Research Center is the sole supporter of this feedback study. The ERC has no financial arrangements with any companies or individuals named herein, or their competitors.

http://ohrpp.osophs.dhhs.gov

Participant Acknowledgment: I hereby acknowledge that I have read and understood the preceding information. I am participating in, and providing my responses to, this survey on a voluntary basis.

SIGNED: ___________________________ DATE: ___________________________

PROCEED TO QUESTIONNAIRE
Health Questionnaire

Date: ____  Age: ____

CURRENT MEDICAL PROBLEMS: If you are being treated for any medical concerns, please explain:

Number of pregnancies: ____

Age menses began: ____  Number of days of menstrual flow: ____

Do you suffer from severe menstrual cramps? ____ YES  ____ NO

Do you suffer with pain associated with intercourse? ____ YES  ____ NO

Do you suffer from unexplained bleeding between periods? ____ YES  ____ NO

Please describe your experience(s) with the alternative menstrual products, "Menstrual Cups."

I have been using, or previously used, menstrual cups (any brand) for:
3 mos. or less ____  6 mos. or less ____  9 mos. or less ____  1 yr. or less ____  2+ years ____

I was diagnosed with Endometriosis PRIOR TO usage of a menstrual cup: ____

I was diagnosed with Endometriosis FOLLOWING usage of a menstrual cup: ____

Please describe how menstrual cups may have affected any pelvic pain or cramping you experience(d):

I experienced an INCREASE in pain levels after usage of a menstrual cup: ____

I experienced a DECREASE in pain levels after usage of a menstrual cup: ____

I experienced NO CHANGE in pain levels after usage of a menstrual cup: ____

Please describe any change in menses volume, if noticeable, after usage of a menstrual cup:

I experienced an INCREASE in menses volume after usage of a menstrual cup: ____

I experienced a DECREASE in menses volume after usage of a menstrual cup: ____

I experienced NO CHANGE in menses volume after usage of a menstrual cup: ____

Please describe any change in flow frequency and duration, if noticeable, after usage of a menstrual cup:

I experienced an INCREASE in flow frequency and duration after usage of a menstrual cup: ____

I experienced a DECREASE in flow frequency and duration after usage of a menstrual cup: ____

I experienced NO CHANGE in flow frequency and duration after usage of a menstrual cup: ____

Please describe the impact, if any, of menstrual cups on your fertility:

I experienced infertility PRIOR to using menstrual cup(s): ____

I did not experience infertility UNTIL using menstrual cup(s): ____

My fertility WAS NOT AFFECTED by the use of menstrual cup(s): ____

CIRCLE any illnesses/medical problems that may have (or had in the past). INDICATE WHETHER THE ILLNESS AROSE BEFORE OR AFTER YOU BEGAN USE OF A MENSTRUAL CUP:

Abnormal Pap Test prior to following

AIDS/Positive HIV prior to following

Allergies prior to following

Anemia prior to following

Anxiety prior to following

Asthma prior to following

Bacterial Vaginosis prior to following

Bleeding Disorder prior to following

Bleeding gums prior to following

Blood clot in Leg or Lung prior to following

Blood in stools prior to following

Blood in urine prior to following

Cancer prior to following

Change in appetite prior to following

Change in color of mole prior to following

Change in vision prior to following

Change in weight prior to following

Changes in bowel habits prior to following

Chest Pain prior to following

Chills/Fever prior to following

Chlamydia prior to following

Colitis prior to following

Convulsions or Seizures prior to following

Depression prior to following

Diabetes prior to following

Difficulty swallowing prior to following

Discharge from nipple prior to following

Dizziness prior to following

Double vision prior to following

Easy bruising prior to following

Eating Disorder prior to following

Endometriosis prior to following

Excessive hunger prior to following

Excessive thirst prior to following

Eye pain prior to following

Fainting spells prior to following

Fatigue prior to following

Fibroids prior to following

Frequent urination prior to following

Frequent, severe headaches prior to following

Generalized Pain prior to following

Genital Herpes prior to following

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Gonorrhea prior to following
Heart Disease prior to following
Heart Murmur prior to following
Heart murmur prior to following
Hepatitis prior to following
High Blood Pressure prior to following
High Cholesterol prior to following
Hearing loss prior to following
HPV/Genital Warts prior to following
Indigestion/Heartburn prior to following
Insomnia prior to following
Irregular heartbeat prior to following
Irregular bowel disease prior to following
Kidney stones prior to following
Kidney/Bladder Disease prior to following
Loss of coordination prior to following
Loss of hearing prior to following
Low Blood Pressure prior to following
Lumps in breast prior to following
Memory loss prior to following
Mental Illness prior to following
Migraine Headaches prior to following
Mononucleosis prior to following
Narcolepsy prior to following
Nasal stuffiness or runny nose prior to following
Nervousness/anxiety prior to following
Night sweats prior to following
Numbness prior to following
Pain burning on urination prior to following
Palpitations (heart racing) prior to following
Pelvic infection prior to following
Persistent cough prior to following
Pneumonia prior to following
Positive TB test prior to following
Previous infections prior to following
Problem with periods prior to following
Rash or hives prior to following
Rheumatic Fever prior to following
Ringing in ears prior to following
Seizures prior to following
Sexually Transmitted Disease prior to following
Shortness of breath prior to following
Sinus pressure/infection prior to following
Sore throat prior to following
Spitting up blood prior to following
Stiffness prior to following
Stomach pain/abdominal pain prior to following
Stomach/Duodenal Ulcers prior to following
Swelling prior to following
Swollen lymph nodes prior to following
Tachycardia prior to following
Thyroid Problem prior to following
Toxic Shock prior to following
Trichomoniasis prior to following
Tuberculosis prior to following
Twitching prior to following
Vaginal discharge prior to following
Vaginal itching or burning prior to following
Vaginitis prior to following
Vomiting/Nausea prior to following
Varicose veins prior to following
Weakness prior to following
Wheezing prior to following
Yeast prior to following

Please describe your family's medical history. Do you have a history of any of the following on either side?
Blood Disease/Clings Cancer Diabetes Epilepsy Heart Disease
High Blood Pressure High Cholesterol Mental Illness Stroke Thyroid Disease

MEDICATIONS: List all medications you take, including those you buy over the counter; i.e., aspirin or cold tablets:

ALLERGIES AND SENSITIVITIES: List anything you are allergic to; i.e., certain foods, medications, dust, chemicals, perfumes, soaps, household items, pollen, bee stings, iodine, etc.:

SOCIAL HABITS:
Do you smoke cigarettes? No If yes, packs per day? # years you have smoked?
If you previously smoked, have you quit one or more years ago?

EXERCISE, DIET & NUTRITION:
Do you consume caffeine (coffee, tea, cola)? No If yes, amount:
Do you consume alcoholic beverages? No If yes, amount:
Do you exercise 2 times per week? Yes No

Would you recommend Menstrual Cups to your family or friends?
YES NO

THANK YOU FOR YOUR PARTICIPATION.
The Endometriosis Research Center
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Citizen Petition

The undersigned submit this petition under 21 CFR 10.30 of the Federal Food, Drug, and Cosmetic Act to request Dr. Mark McClellan, the Commissioner of Food and Drugs, revoke the approval for the marketing of the devices categorized as menstrual cups (21CFR 884.5400) because there is a high likelihood that the use of these devices as directed will endanger a woman's reproductive health by inducing endometriosis.

Action Requested

The FDA administrative record for the two menstrual cups currently marketed shows that neither was required to submit clinical data regarding their safety (see FDA Freedom of Information (FOI) Files: The Keeper: Record K870803, 1987; Instead, softcup: Record K971303, 1997 (abridged versions attached(Addendum A)). Until the manufacturers of the menstrual cups can submit suitable animal and clinical data to support that these devices can be safely used as directed without increasing the risk or severity of endometriosis, we hereby request the approval for the sale of menstrual cups be revoked.
Statement of Grounds

Summary

Menstrual cups, when used as currently recommended, can be worn for 12 hour periods during menstruation. They are designed to fit either over the cervix or within the vagina tightly enough so no menstrual debris is released from the body while a cup is in place.

Obstructions of the cervix and vagina are commonly recognized as important factors in inducing endometriosis. The cervical outlet obstruction inherent in the use of menstrual cups is likely to increase the incidence and severity of endometriosis among women who use these products.

Detailed Statement of Grounds

Menstrual Cups and Endometriosis

A. Menstrual Cups: Approval History and Current Use

Currently there are two menstrual cups approved for sale by the FDA: 1. The Keeper (www.keeper.com), a flexible rubber cone, that sits intravaginally to occlude menstrual discharge, and 2. Instead (www.Softcup.com), a plastic diaphragm-shaped disc that covers the mouth of the cervix with an impermeable barrier. The Keeper is a reusable product. Instead is intended for one time use and disposal. The package inserts for both products recommend they be used for periods of time not to exceed 12 hours. The possible effect of these products on the risk of endometriosis is not mentioned in the package inserts.
The approval records for both products show that neither manufacturer was required to submit any clinical data to demonstrate their safety when used as directed (FOI Files[attached]). Thus the possible effects of these products on reproductive health have not been reviewed by the Food & Drug Administration.

Among the possible reproductive effects of the menstrual cups, there is a physiologically credible mechanism whereby their use would increase the incidence or severity of endometriosis.

B. Endometriosis

Endometriosis is a chronic condition that is typically diagnosed clinically because of severe dysmenorrhea. Asymptomatic cases of endometriosis are often diagnosed during peritoneal surgery. In rare cases, endometriotic growths are found outside the peritoneum and the reproductive tract. Since endometriosis develops over an extended time period, the origins of this condition are subject to hypothetical explanations, and no one hypothesis appears to explain all manifestations of the disease (Guarnaccia et al, 2000; Evers, 1996; Cramer & Missmer, 2002). However, a diverse assortment of clinical and animal data are consistent with the Sampson (menstrual reflux) hypothesis for explaining the origins of peritoneal endometriosis (Sampson, 1927; Guarnaccia et al, 2000; Evers, 1996; Cramer & Missmer, 2002; D’Hooghe & Debrock, 2002). Sampson suggested that peritoneal endometriosis develops when fragments of functional endometrium are released from the surface of the uterus during menstruation and refluxed back through the Fallopian tubes to reach the peritoneal cavity. Some endometrial fragments attach to peritoneal surfaces,
growing and degenerating, cyclically, in conjunction with the menstrual cycle. These ectopic endometrial growths sometimes cause inappropriate adhesions between peritoneal tissues and organs, producing debilitating pain. When endometrial tissues occlude the fimbriated ends of the fallopian tubes, endometriosis can cause infertility.

There are several sources of clinical and experimental data that support the Sampson hypothesis and the role that “out flow obstruction” can play in the induction of endometriosis. (figure 1)

![Diagram of endometriosis pathogenesis](image)

**Figure 1.** Model for pathogenesis of endometriosis involving retrograde menstruation.

First, the collected anatomical analyses of the distribution of endometriotic growths in the peritoneum are consistent with the fallopian tubes as a source for the seeding tissue (Guarnaccia et al, 2000).

Second, women born with congenital defects of their reproductive tract which prevent menstrual debris from being discharged through the cervix or vagina typically develop severe forms of endometriosis (Pinsonneault O, Goldstein DP, 1985; Hanton et al, 1966; Olive &
Henderson, 1987; Geary & Weed, 1973; Farber M, Marchant, 1975; Maciulla et al, 1978; Niver et al, 1980; Nunley & Kitchin, 1980; SanFilippo et al, 1986). Some clinicians have also analyzed this population sufficiently to report that women without functional endometrial tissues (another aspect of their developmental abnormalities) do not develop endometriosis (Olive & Henderson, 1987).

Third, several observations in the baboon model for endometriosis (D'Hooghe et al, 1994; D'Hooghe et al, 1995; D'Hooghe et al., 1996) appear to support the Sampson hypothesis, and the role of out flow obstruction in the induction of endometriosis. These observations include a demonstration of the increased incidence of retrograde menstruation in baboons with spontaneous endometriosis (D'Hooghe et al., 1996); intrapelvic injection of menstrual endometrium causing experimental endometriosis similar to that observed in spontaneous disease (D'Hooghe et al. 1995); and surgically induced cervical occlusion leading to retrograde menstruation and endometriosis (D'Hooghe et al, 1994).

Retrograde menstruation appears to occur in most women (Halme & Hall, 1984). This has been demonstrated in a variety of ways, including the detection of endometrial cells in the dialysate of peritoneal dialysis patients (Blumenkrantz et al., 1981). Since retrograde menstruation is relatively common, but endometriosis appears to occur in a fraction of menstruating women, multiple factors apparently interact to produce symptomatic endometriosis. In an animal model of endometriosis, one group of researchers has demonstrated that the successful survival and growth of endometrial cells correlated directly with the amount of tissue (represented by
its weight) injected into the peritoneum (D'Hoooghe et al., 1995). Additional research is being focused on the possible role that immune factors may play on the elimination of menstrual debris. In some women a defect in immunosurveillance may play a role in the clearing of menstrual debris, suggesting that women unable to clear menstrual debris go on to develop disease (Cramer & Missmer, 2002).

Epidemiological data has shown that women with early menarche, short menstrual cycles or longer periods of menstruation are more likely to suffer from endometriosis (7,8,20,22-24). These findings are consistent with the Sampson reflux hypothesis for the origin of peritoneal endometriosis. On one hand, the more frequent the challenge (i.e. in women with early onset of menstruation and those with shorter cycles) or the larger the challenge (i.e. in women with longer periods of menstruation), the more likely it is that a woman will develop endometriosis. Some clinicians also have drawn attention to epidemiological data showing a lower incidence of endometriosis among women who have given birth and suggested that the enlargement of the cervical opening (and corresponding reduction in resistance to menstrual outflow) to explain this finding (Cramer & Missmer, 2002). Dysmenorrhea is a strong risk factor for endometriosis, but it has generally been considered to represent a symptom of existing disease, since it is easy to imagine that monthly bleeding from pelvic lesions is painful. However, some data suggest that dysmenorrhea may correlate with stronger uterine contractility (Schulman et al., 1983), and one reviewer has suggested an alternate interpretation: dysmenorrhea may be associated with some degree of outflow.
obstruction, caused by stronger uterine cramping, and an increased propensity to retrograde menstruation (Cramer & Missmer, 2002).

Consistent with these observations, the mechanical occlusion of the cervix or vagina during menstruation would be expected to substantially increase the retrograde flow of menstrual discharge. This mechanical occlusion would thereby increase the seeding of the peritoneal cavity with endometrial cells. Menstrual cups are, in essence, removable cervical and vaginal occlusion devices. Thus, the increased menstrual retention produced by the use of the menstrual cups is likely to have endometriosis-promoting effects.

C. Potential for Reflux With Menstrual Cups and Other Menstrual Products

A clear distinction can be made between the menstrual occlusion that results from the use of menstrual cups and the occlusive potential of absorbent menstrual products such as tampons. Simply described, a menstrual absorbent product, such as a tampon, can retain the menstrual discharge within its structure until its absorbent capacity is exceeded. When a tampon is saturated, it too can become an obstructive device that would increase the reflux of endometrial tissues. However, the saturation of a tampon would also produce vaginal leakage, prompting its removal.

In contrast, menstrual cups are composed of impervious, non-absorptive materials. Since fluids are non-compressible, any discharge being held in the cavity of a menstrual cup can be readily refluxed back into the uterine cavity, as well as the fallopian tubes and eventually into the peritoneum. It should also be noted that
clinical studies using menstrual cups have shown that the debris they collect does contain viable endometrial cells (Koks et al., 1997). Although quantitative data on their effect on endometrial reflux has not yet been collected, it can be anticipated that a woman wearing a menstrual cup might inadvertently apply compressive forces and promote endometrial reflux when assuming a number of routine positions that compress the vaginal space or apply pressure to the cervical os. One of the available products (Softcup) is recommended for use during sexual intercourse. The mechanical effects on menstrual reflux in this situation also await evaluation.

In the research literature on endometriosis, one reviewer has suggested that larger fragments of endometrium may have higher invasive potential, once they enter the peritoneal cavity (Evers, 1996). Therefore, future research also needs to address whether cervical or vaginal occlusion during menstruation generates increased fluid reflux through the uterus, altering the size distribution of dislodged endometrial tissue. Available research techniques have monitored endometrial cells in peritoneal fluid during menstruation in women and in animal studies (Bartosik et al., 1986; Kruitwagen et al., 1991; D’Hooghe et al., 2001). This approach could be used to evaluate the role played by menstrual cups.

D. Endometriosis Risk in Specialized Populations

Given the concerns expressed above about how the use of menstrual cups might increase the risk of endometriosis, this adverse effect would not be expected among women who had ligated fallopian tubes. However, a review of the one adverse report involving the menstrual
cups and endometriosis in the CEDER/MAUDE database (Addendum B(attached)) shows that it involved problems apparently resulting from menstrual obstruction associated with the use of the Keeper, in a woman with ligated fallopian tubes. In this case the reporting physician described the patient’s uterus as "completely endometrial" and hysterectomy was recommended.

Endometriosis is a relatively common problem in teenage women. The superficial convenience of the menstrual cups for young women active in athletic competitions would make them an attractive choice for use during menstruation. However, as discussed above, until data is collected on effects of mechanical forces on the endometrial reflux associated with the use of menstrual cups, their use during strenuous activities, such as athletic competitions, is a prominent point of concern.

E. Epidemiological Monitoring

Since the onset of endometriosis is apparently influenced by a variety of factors, which include diverse elements such as individual anatomy and immune function, the epidemiology of endometriosis is not clearly defined (Cramer & Mischner, 2002). This fact suggests that the clinical demonstration of an increase in the incidence of endometriosis in association with menstrual retention devices will be a complex task, making caution even more important in this matter, while research data is being collected.
Conclusion

Based on the theoretical concerns discussed above and the limited clinical reports in the FDA databases, current users of menstrual cups should be informed of the possible risk of endometriosis associated with these products, and the sale of menstrual cups as OTC devices should be discontinued until sufficient data on their safety has been collected and analyzed.

Environmental impact

The petitioners claim a categorical exclusion from this requirement under Secs. 25.30 - 25.34 of 21(1) CFR.
Certification

The undersigned certify, that, to the best knowledge and belief of
the undersigned, this petition includes all information and views on
which the petition relies, and that it includes representative data
and information known to the petitioners which are unfavorable to the
petition.

For Associated Pharmacologists & Toxicologists*:

(Signature) 

Armand Lione, Ph.D., President, APT

(Name of petitioner) Associated Pharmacologists & Toxicologists

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For The Endometrosis Research Center:

(Signature) 

Heather C. Guindone, Director of Operations, ERC

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* To whom correspondence about filing this petition should be
addressed.
References


CEDER Adverse Event Report*: MDR Text Key: 892088; 02/11/2000.(see addendum B, below)


USFDA Freedom of Information (FOI) Files (abridged)*: The Keeper; Record K870803, 1987; Instead, softcup: Record K971303. (See Addendum A, below)

*Reference enclosed
Addendum B:  
CEDER Adverse Event Report:  
Menstrual Cups,  
APT Citizen Petition  
CEDER/MAUDE Database Adverse Report

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<tr>
<th>BRAND NAME</th>
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<td>TYPE OF DEVICE</td>
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<tr>
<td>MANUFACTURER (Section D)</td>
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<td>3244 N. HENDRICKSON AVE.</td>
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1 DEVICE WAS INVOLVED IN THE EVENT

1 PATIENT WAS INVOLVED IN THE EVENT

DATE FDA RECEIVED 02/11/2000

IS THIS AN ADVERSE EVENT REPORT? YES

IS THIS A PRODUCT PROBLEM REPORT? NO

DEVICE OPERATOR HEALTH PROFESSIONAL

WAS DEVICE AVAILABLE FOR EVALUATION? NO

PATIENT OUTCOME HOSPITALIZATION

ADVERSE EVENT OR PRODUCT PROBLEM DESCRIPTION

REPORT DATE: 02/10/2000  MDR TEXT KEY: 892088  Patient Sequence Number: 1

PT HAD A RECENT SURGERY. PT HAS BEEN USING THE KEEPER CUP FOR ABOUT SIX YEARS. ACCORDING TO PT IT'S A MENSTRUAL CUP THAT'S WORN INTERNALLY; IT'S SOLD THROUGH MAGAZINE CLASSIFIEDS ESPECIALLY THE HERB COMPANION AND
NOW AT THEIR WEBSITE WWW.KEEPER.COM. CLICK TO USAGE TO SEE A PICTURE OF THE DEVICE. PT HAS INCREASING MONTHLY PAIN FOR THE LAST 3 YEARS. THE PAIN IS MUCH DIFFERENT FROM CRAMPS. SOMETIMES ULTRAM AND FLEXERIL DON’T EVEN "DENT" THE PAIN. LAST MONTH PT HAD ENDOMETRIOSIS SURGERY AS PART OF AN ENDOMETRIOSIS STUDY. PT’S DR FOUND VERY LITTLE ENDOMETRIOSIS; JUST WHAT HAD SLIPPED OUT AROUND THE TUBAL LIGATION PT HAD NINE YEARS AGO. WHAT PT DID FIND WAS THAT UTERUS HAS BECOME COMPLETELY ENDOMETRIAL, AS CONFIRMED BY LAB RESULTS. DR DESCRIBED UTERUS AS BLANCHING WHEN TOUCHED, LIKE YOU COULD WRITE ON IT AND SEE THE WORDS. THE DIAGNOSIS IS "ADNOMYOSIS" AND PT WAS ASKED TO START CONSIDERING A HYSTERECTOMY TO RELIEVE THE PAIN. PT WROTE THE KEEPER CUP CO. THEY SAY THIS PRODUCT HAS NEVER BEEN EVALUATED FOR ENDOMETRIOSIS. SINCE PT SEES THEM ADVERTISING A LITTLE MORE EACH YEAR, PT HOPES NO ONE ELSE HAS THE SAME OUTCOME. PT ASKS FDA TO PLEASE CONSIDER LOOKING INTO THIS. PT IS ALL FOR ALTERNATIVE HEALTHCARE WHEN IT DOES GOOD AND NO HARM.
Armand Lione, PhD, President
Associated Pharmacologists and Toxicologists
533 4th Street, SE
Washington, DC 20003-4222

03P0166 – Citizen Petition on Menstrual Cups & Endometriosis
Dated: April 16, 2003
Received: April 17, 2003

Dear Dr. Lione:

The purpose of this letter is to respond to your above-referenced Citizen Petition on menstrual cups. Specifically, your petition asks the Food and Drug Administration (FDA) to “...revoke the approval for the marketing of the devices... because there is a high likelihood that the use of these devices as directed will endanger a woman's reproductive health by inducing endometriosis.”

In support of your petition, you state that manufacturers of menstrual cups were not required to submit clinical data demonstrating safety and efficacy of their devices. It is true that products FDA clears through the pre-market notification process do not ordinarily contain cleared data. Menstrual cups are pre-amendments medical devices, which means they were on the market before the Medical Device Amendments were enacted in 1976. Upon the recommendation of the Obstetrics and Gynecology Device Classification Panel, an FDA advisory committee, the agency classified menstrual cups in 1980 into Class II because we believed that intermediate level of regulatory controls would provide sufficient assurance of safety and effectiveness of this type of device. (I have enclosed the proposed and final rules on the classification of menstrual cups, including a summary of the classification panel recommendation). Because it is a Class II preamendments device, manufacturers may introduce menstrual cups to the market in the U.S following FDA’s clearance of a 510(k) premarket notification. Premarket notifications typically do not contain results from clinical studies. These submissions do contain information to demonstrate that the device is as safe and effective as a similar product that is already legally on the market. Data in 510 (k) submissions for menstrual cups ordinarily include descriptive and design information, performance characteristics, biomaterial safety information, and labeling.

While we agree that endometriosis is an important women's health issue, FDA does not believe that there are sufficient grounds to “withdraw the approval” of these devices, as you request.

We agree with the assertion in your petition that it is physiologically plausible that use (and misuse) of the menstrual cup might increase the risk of endometriosis by creating an obstruction
to the flow of menstrual effluent (blood and cells) out of the uterus, re-directing menstrual effluent into the peritoneal cavity via the fallopian tubes (retrograde menstruation). However, you have not submitted and we have not identified sufficient evidence to show this is more than theoretical.

To determine whether there might be other data available to support the Citizen Petition (besides what you included), we searched our MAUDE database for reports of adverse events associated with the use of a menstrual cup. Our search identified a total of sixteen reports. Only one report suggests a possible association between a menstrual cup and endometriosis (and adenomyosis). This is the same report you cite in your Citizen Petition.

We also performed a literature search on this topic and identified one case report of endometriosis and adenomyosis where use of a menstrual cup is listed as a potential cause (Gynecol Obstet Invest 706, Spechler et al., in press). Again, this case report appears to be the same case that appears in FDA’s MAUDE database. Regarding the menstrual cup and other menstrual collecting devices, the abstract for this case report states that such devices may theoretically increase the likelihood of developing endometriosis or adenomyosis. This single case report does not constitute an adequate basis for FDA to issue an order to stop distribution of this product or withdraw approval. Additional information might warrant a review of menstrual cup labeling to determine whether an additional precaution or warning is needed, as well as whether menstrual cup wear time should be re-examined. However, in the absence of results from a well-designed clinical study, it would be inappropriate to make any statements about whether menstrual cups (or other menstrual fluid collecting devices) increase the risk of either endometriosis or adenomyosis.

If you have any questions regarding this letter, you may contact Mr. Colin Pollard, Chief of the Obstetrics and Gynecology Devices Branch, at (301) 594-1180.

Sincerely yours,

Linda S. Kahan,
Deputy Director
Center for Devices and Radiological Health

Attachments
cc: HFZ-215 (B. Noland, J. Sheehan)
    HFZ-404 (POS, H. Rosecrans)
    HFZ-470 (M. Byrne, J. Corrado, C. Pollard)
    HFA-305

Draft: M. Byrne, C. Pollard – 9/16/03
Revised: L. Kahan 10-24-03
Classification and Premarket Notification

The Federal Food, Drug, and Cosmetic Act (21 U.S.C. 301 et seq.) (the act), as amended by the 1976 amendments (Public Law 94-295), the Safe Medical Devices Act of 1990 (SMDA) (Public Law 101-629), the Food and Drug Administration Modernization Act of 1997 (FDAMA) (Public Law 105-115), and The User Fee and Modernization Act of 2002 (MDUFMA) (Public Law 107-250), established a comprehensive system for the regulation of medical devices intended for human use. Section 513 of the act (21 U.S.C. 360c) established three categories (classes) of devices, depending on the regulatory controls needed to provide reasonable assurance of their safety and effectiveness. The three categories of devices are class I (general controls), class II (special controls), and class III (premarket approval).

Under Section 513 of the act, devices that were in commercial distribution before May 28, 1976 (the date of enactment of the 1976 amendments), generally referred to as preamendments devices, are classified after FDA has: (1) Received a recommendation from a device classification panel (an FDA advisory committee); (2) published the panel’s recommendation for comment, along with a proposed regulation classifying the device; and (3) published a final regulation classifying the device. FDA classified menstrual cups in class II under these procedures.

A premarket notification (510(k)) is a premarket submission made to FDA to demonstrate that the device to be marketed is as safe and effective, that is, substantially equivalent (SE), to a legally marketed device that is not subject to premarket approval (PMA). Applicants must compare their 510(k) device to one or more similar devices currently on the U.S. market and make and support their substantial equivalency claims. A legally marketed device is a device that was legally marketed prior to May 28, 1976 (preamendments device), or a device which has been reclassified from Class III to Class II or I, a device which has been found to be substantially equivalent to such a device through the 510(k) process, or one established through Evaluation of Automatic Class III Definition. The legally marketed device(s) to which equivalence is drawn is known as the “predicate” device(s).

Applicants must submit descriptive data and, when necessary, performance data to establish that their device is SE to a predicate device. Again, the data in a 510(k) is to show comparability, that is, substantial equivalency (SE) of a new device to a predicate device. Therefore, an applicant must submit clinical data in a 510(k) only when it is necessary to determine whether a device is substantially equivalent to a predicate device.

Withdrawal of Approval of Menstrual Cups

You request in your petition that FDA “withdraw the approval” of menstrual cups because manufacturers of the presently marketed menstrual cups have not submitted clinical data to demonstrate their safety and effectiveness. As discussed above, menstrual cups are marketed through the premarket notification process which only requires the applicant to demonstrate
substantial equivalence to other legally marketed devices. Therefore, FDA cannot withdraw the approval of these devices as such. FDA could remove these devices from the market through a cease distribution and notification order under section 518(e) of the act or by banning them under section 516 of the act.

**Cease Distribution and Notification Order.** Section 518(e) of the act (21 U.S.C. 360(h)(e)) provides that, if FDA finds that there is a reasonable probability that a device intended for human use would cause serious, adverse health consequences or death, the agency may issue a cease distribution and notification order requiring the person named in the order to immediately:

1. Cease distribution of the device;
2. Notify health professionals and device user facilities of the order; and
3. Instruct these professionals and device user facilities to cease use of the device.

**Banning.** The criteria for banning a device are set out in section 516 of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 360f) as follows:

**SEC. 516. [360f] (a) Whenever the Secretary finds, on the basis of all available data and information, that -**

(a) (1) a device intended for human use presents substantial deception or an unreasonable and substantial risk of illness or injury; and
(2) in the case of substantial deception or an unreasonable and substantial risk of illness or injury which the Secretary determined could be corrected or eliminated by labeling or change in labeling and with respect to which the Secretary provided written notice to the manufacturer specifying the deception or risk of illness or injury, the labeling or change in labeling to correct the deception or eliminate or reduce such risk, and the period within which such labeling or change in labeling was to be done, such labeling or change in labeling was not done within such period, he may initiate a proceeding to promulgate a regulation to make such device a banned device.

In the regulations implementing section 516, FDA states that, in determining whether the risk of illness or injury is substantial, FDA will consider whether the risk is important, material, or significant in relation to the benefit to the public health from the continued marketing of the device (21 CFR 895.21(a)(1)).
Classification of Menstrual Cup

AGENCY: Food and Drug Administration.

ACTION: Proposed rule.

SUMMARY: The Food and Drug Administration (FDA) is issuing for public comment a proposed regulation classifying menstrual cups into class II (performance standard). The FDA is also publishing the recommendation of the Obstetrical and Gynecological Device Classification Panel that the device be classified into class II. The effect of classifying a device into class II is to provide for the future development of one or more performance standards to assure the safety and effectiveness of the device. After considering public comments, FDA will issue a final regulation classifying the device. These actions are being taken under the Medical Device Amendments of 1990.

DATES: Comments due by June 6, 1997. The Commissioner of Food and Drugs proposes that the final regulation based on this proposal become effective 30 days after the date of its publication in the Federal Register.

ADDRESSES: Written comments to the Office of the Hearing Clerk (HFA–305), Food and Drug Administration, Docket No. 97N–010, 5600 Fisher's Lane, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Lillian L. Yin, Bureau of Medical Devices (HFM–470), Food and Drug Administration, Department of Health, Education, and Welfare, 5637 Georgia Avenue, Silver Spring, MD 20910, 301–427–2750.

SUPPLEMENTARY INFORMATION:

Final Recommendation

A proposal elsewhere in this issue of the Federal Register provides background information concerning the development of the proposed regulation. The Obstetrical and Gynecological Device Classification Panel, an FDA advisory committee, made the following recommendation with respect to the classification of menstrual cups:

1. Identification: A menstrual cup is a receptacle placed in the vagina to collect menstrual flow.

2. Recommended classification: Class II (performance standard). The Panel recommends that establishing a performance standard for this device be a high priority.

3. Summary of reasons for recommendation: The Panel believes that menstrual cups should be classified into class II performance standards because the device is likely to cause serious injury or death if it fails to perform as intended and because the device is intended to replace the uterus and thus has the potential to cause serious injury or death if it fails to perform as intended.

Interested persons may, on or before June 6, 1997, submit to the Hearing Clerk (HFA–305), Food and Drug Administration, Docket No. 97N–010, 5600 Fisher’s Lane, Rockville, MD 20852, written comments regarding this proposal. Four copies of all comments shall be submitted, except that individuals may submit single copies of comments, and shall be identified with the docket number.

[31 CFR part 884]

Federal Register / Vol. 55, No. 55 / Tuesday, April 1, 1997 / Proposed Rules
submit single copies of comments, and shall be identified with the Hearing Clerk docket number found in brackets in the heading of this document.

Received comments may be seen in the above office between the hours of 9 a.m. and 4 p.m., Monday through Friday.


William A. Rawlence,
Acting Assistant Commissioner for Regulatory Affairs.

[70 FR 36573, July 28, 2005] [Remainder of document redacted]

[21 CFR Part 864]

Classification of Scented Deodorized Menstrual Pads

AGENCY: Food and Drug Administration.

ACTION: Proposed Rule.

SUMMARY: The Food and Drug Administration (FDA) is issuing for public comment a proposed regulation classifying scented deodorized menstrual pads into class II (performance standards). The FDA is also publishing the recommendation of the Obstetric and Gynecological Device Classification Panel that the device be classified into class II. The effect of classifying a device into class II is to provide for the future development of one or more performance standards to assure the safety and effectiveness of the device. After considering public comments, FDA will issue a final regulation classifying the device. These actions are being taken under the Medical Device Amendments of 1976.

DATES: Comments by June 4, 1979. The Commissioner of Food and Drugs proposes that the final regulation based on this proposal become effective 90 days after the date of its publication in the Federal Register.

ADDRESSE: Written comments to the Hearing Clerk (DFA-805), Food and Drug Administration, Room 4-65, 5000 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: Lillian L. Yin, Bureau of Medical Devices (HFA-470), Food and Drug Administration, Department of Health, Education, and Welfare, 8757 Georgia Ave., Silver Spring, MD 20993; Telephone: 301-443-7855.

SUPPLEMENTARY INFORMATION:

Panel Recommendation

A proposal elsewhere in this issue of the Federal Register provides background information concerning the development of the proposed regulation. The Obstetric and Gynecological Device Classification Panel, an FDA advisory committee, made the following recommendation with respect to the classification of scented deodorized menstrual pads:

1. Identification: A scented deodorized menstrual pad is an absorbent cotton or synthetic material pad with fragrant chemicals added for the purpose of deodorizing or for sanitary purposes. The device is used to absorb menstrual or other vaginal discharge. This generic type of device does not include devices with added drugs or antimicrobial agents.

2. Recommended classification Class II (performance standards). The Panel recommends that establishing a performance standard for this device be a low priority.

3. Summary of reasons for recommendation: The Panel recommends that scented deodorized menstrual pads be classified into class II (performance standards) because the Panel believes that the device materials comprising the body should meet a biocompatibility standard to prevent an adverse tissue reaction. The Panel believes that general controls alone will not provide sufficient control over this characteristic. The Panel also recommends that the caution, "Discontinue use of sensitivity or irritation occurs" be stated on the device labeling and be prominently displayed on the outside of the package. The Panel believes that a performance standard will provide reasonable assurance of the safety and effectiveness of the device and that there is sufficient information to establish a standard to provide such assurance.

4. Summary of data on which the recommendation is based: The Panel based its recommendation on clinical experience with these pads. The Panel reviewed the complaint file of the only manufacturer of this device at the time of its meeting (November 2, 1976). The complaints dealt with irritation associated with the cosmetic used for deodorizing.

5. Risks to health: Adverse tissue reaction: Materials in the device could cause a systemic or local tissue reaction when the device comes in contact with the patient.

Proposed Classification

The Commissioner agrees with the Panel recommendation and is proposing that scented deodorized menstrual pads be classified into class II (performance standards). The Commissioner believes that a performance standard is necessary for this device because general controls by themselves are insufficient to control the risks to health. A performance standard would provide reasonable assurance of the safety and effectiveness of the device. The Commissioner also believes that there is sufficient information to establish a standard to provide reasonable assurance of the safety and effectiveness of the device.

Therefore, under the Federal Food, Drug, and Cosmetic Act (sect. 513, 701(a), 52 Stat. 1065, 90 Stat. 543-546 [21 U.S.C. 351(a)] and under authority delegated to him (21 CFR 3.1), the Commissioner proposes to amend Part 864 to Subpart P by adding new § 864.5125 as follows:

§ 864.5125 Scented deodorized menstrual pad.

(a) Identification. A scented deodorized menstrual pad is an absorbent cotton or synthetic material pad with fragrant chemicals added for the purpose of deodorizing. The device is used to absorb menstrual or other vaginal discharge. This generic type of device does not include devices with added drugs or antimicrobial agents.

(b) Classification. Class II (performance standards).

Interested persons may, on or before June 4, 1979, submit to the Hearing Clerk (HFA-805), Food and Drug Administration, Room 4-65, 5000 Fishers Lane, Rockville, MD 20857, written comments regarding this proposal. Four copies of all comments shall be submitted, except that individuals may submit single copies of comments, and shall be identified with the Hearing Clerk docket number found in brackets in the heading of this document. Received comments may be seen in the above office between the hours of 9 a.m. and 4 p.m., Monday through Friday.


William F. Randolph,
Acting Assistant Commissioner for Regulatory Affairs.

[FR Doc.79-10547 Filed 4-4-79; 8:45 am]

[21 CFR Part 865]

Classification of Untreated Menstrual Pads

AGENCY: Food and Drug Administration.

ACTION: Proposed Rule.

SUMMARY: The Food and Drug Administration (FDA) is issuing for public comment a proposed regulation classifying untreated menstrual pads into class I (general controls). The FDA is also publishing the recommendation of the Obstetric and Gynecological Device Classification Panel that the device be classified into class I. The effect of classifying a device into class I is to require that the device meet only the general controls applicable to all devices. After considering public comments, FDA will issue a final regulation classifying the device. These actions are being taken under the Medical Device Amendments of 1976.

DATES: Comments by June 4, 1979. The Commissioner of Food and Drugs proposes that the final regulation based on this proposal become effective 90 days after the date of its publication in the Federal Register.

ADDRESSE: Written comments to the Hearing Clerk (HFA-805), Food and Drug Administration, Room 4-65, 5000 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: Lillian L. Yin, Bureau of Medical Devices (HFA-470), Food and Drug Administration, Department of Health, Education, and Welfare, 8757 Georgia Ave., Silver Spring, MD 20993; Telephone: 301-443-7855.

SUPPLEMENTARY INFORMATION:

Panel Recommendation

A proposal elsewhere in this issue of the Federal Register provides background information concerning the development of the proposed regulation. The Obstetric and Gynecological Device Classification Panel, an FDA advisory committee, made the following
Federal Register / Vol. 45, No. 33 / Tuesday, February 28, 1980 / Rules and Regulations 12713

21 CFR Part 884

Ostetrical and Gynecological Devices; Classification of Menstrual Cups

AGENCY: Food and Drug Administration.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is issuing a final rule classifying menstrual cups into class II (performance standards). The effect of classifying a device into class II is to provide for the future development of one or more performance standards to assure the safety and effectiveness of the device. This action is being taken under the Medical Device Amendments of 1976.

EFFECTIVE DATE: March 27, 1980.

FOR FURTHER INFORMATION CONTACT: Lillian L. Yin, Bureau of Medical Devices (HFE-470), Food and Drug Administration, Department of Health, Education, and Welfare, 8777 Georgia Ave., Silver Spring, MD 20910, 301-427-7521.

SUPPLEMENTARY INFORMATION: FDA published in the Federal Register of April 3, 1979 (44 FR 18695), a proposed regulation explaining the development of the proposed regulations classifying obstetrical and gynecological devices, the medical device classification procedures, and the activities of the Obstetrical and Gynecological Device Classification Panel. FDA also published in that issue of the Federal Register (44 FR 18699) a proposed regulation to classify menstrual cups into class II (performance standards). A period of 60 days was provided for interested persons to submit written comments to FDA.

No written comments have been received regarding the proposed regulation to classify this device. Accordingly, the proposed regulation is being adopted without change.

Therefore, under the Federal Food, Drug, and Cosmetic Act (secs. 513, 701(d), 52 Stat. 1053, 92 Stat. 540-546 [21 U.S.C. 360c, 371(d)]) and under authority delegated to him (21 CFR 5.1), the Commissioner of Food and Drugs is amending Part 884 in Subpart F by adding new §884.5420, to read as follows:

§884.5420 Menstrual cup.

(a) Identification. A menstrual cup is a receptacle placed in the vagina to collect menstrual flow.

(b) Classification. Class II (performance standards).

Effective date: This regulation shall be effective March 27, 1980.

(Secs. 513, 701(d), 52 Stat. 1053, 92 Stat. 540-546 [21 U.S.C. 360c, 371(d)])

Dated January 23, 1980,

William P. Randolph,
Acting Associate Commissioner for Regulatory Affairs

BILLING CODE 4160-01-M

21 CFR Part 884

Ostetrical and Gynecological Devices; Classification of Scented Menstrual Pads

AGENCY: Food and Drug Administration.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is issuing a final rule classifying scented menstrual pads into class II (performance standards). The effect of classifying a device into class II is to provide for the future development of one or more performance standards to assure the safety and effectiveness of the device. This action is being taken under the Medical Device Amendments of 1976.

EFFECTIVE DATE: March 29, 1980.

FOR FURTHER INFORMATION CONTACT: Lillian L. Yin, Bureau of Medical Devices (HFE-470), Food and Drug Administration, Department of Health, Education, and Welfare, 8777 Georgia Ave., Silver Spring, MD 20910, 301-427-7521.

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No written comments have been received regarding the proposed regulation to classify this device. Accordingly, the proposed regulation is being adopted without change.

Therefore, under the Federal Food, Drug, and Cosmetic Act (secs. 513, 701(d), 52 Stat. 1053, 92 Stat. 540-546 [21 U.S.C. 360c, 371(d)]) and under authority delegated to him (21 CFR 5.1), the Commissioner of Food and Drugs is amending Part 884 in Subpart F by adding new §884.5430, to read as follows:

§884.5430 Menstrual pad.

(a) Identification. A menstrual pad is a receptacle placed in the vagina to collect menstrual flow.

(b) Classification. Class II (performance standards).

Effective date: This regulation shall be effective March 29, 1980.

(Secs. 513, 701(d), 52 Stat. 1053, 92 Stat. 540-546 [21 U.S.C. 360c, 371(d)])

Dated January 23, 1980,

William P. Randolph,
Acting Associate Commissioner for Regulatory Affairs

BILLING CODE 4160-01-M

21 CFR Part 884

Ostetrical and Gynecological Devices; Classification of Scented Menstrual Pads

AGENCY: Food and Drug Administration.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is issuing a final rule classifying scented menstrual pads into class II (performance standards). The effect of classifying a device into class II is to provide for the future development of one or more performance standards to assure the safety and effectiveness of the device. This action is being taken under the Medical Device Amendments of 1976.

EFFECTIVE DATE: March 29, 1980.

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No written comments have been received regarding the proposed regulation to classify this device. Accordingly, the proposed regulation is being adopted without change.

Therefore, under the Federal Food, Drug, and Cosmetic Act (secs. 513, 701(d), 52 Stat. 1053, 92 Stat. 540-546 [21 U.S.C. 360c, 371(d)]) and under authority delegated to him (21 CFR 5.1), the Commissioner of Food and Drugs is amending Part 884 in Subpart F by adding new §884.5430, to read as follows:

§884.5430 Menstrual pad.

(a) Identification. A menstrual pad is a receptacle placed in the vagina to collect menstrual flow.

(b) Classification. Class II (performance standards).

Effective date: This regulation shall be effective March 29, 1980.

(Secs. 513, 701(d), 52 Stat. 1053, 92 Stat. 540-546 [21 U.S.C. 360c, 371(d)])

Dated January 23, 1980,

William P. Randolph,
Acting Associate Commissioner for Regulatory Affairs

BILLING CODE 4160-01-M
The Keeper®, a Menstrual Collection Device, as a Potential Cause of Endometriosis and Adenomyosis

Stacey Spechler a, Lynnette K. Nieman b, Ahalya Premkumar b
Pamela Stratton a

aPediatric and Reproductive Endocrinology Branch, National Institute of Child Health and Human Development, Bethesda, Md., and bDepartment of Radiology, Clinical Center, National Institutes of Health, Bethesda, Md., USA

Key Words
Keeper®, Menstrual collection device - Endometriosis - Adenomyosis

Abstract
Barrier contraceptive devices like the cervical cap and diaphragm and menstrual collecting devices may block menstrual flow, increase retrograde menstruation, and thus theoretically increase the likelihood of developing endometriosis or adenomyosis. We describe the case of a woman with a prior tubal ligation who after 4 years of regular use of the Keeper®, a menstrual collecting device, developed adenomyosis and endometriosis.

Introduction

In 1927, Sampson [1] proposed that retrograde menstruation causes endometriosis. More recently, others [2] have shown that menstrual endometrium can implant and grow outside the uterus within the peritoneal cavity. Thus, factors such as contraceptive method or menstrual product use that influence the amount of menses may in turn influence the development of endometriosis. Methods that cause amenorrhea or lighten menstrual flow, like Depo Provera, the levonorgestrol intrauterine device, and birth control pills, may decrease the endometriosis risk [3, 4]. Similarly, after tubal ligation, women presumably are less likely to have endometriosis because menses cannot flow into the peritoneal cavity [5]. By contrast, heavy menses may increase the risk [6]. Although studies have not reported an increased incidence of endometriosis with diaphragm or cervical cap use, it is possible that these female barrier contraceptives or new menstrual collecting devices block menstrual flow, increase retrograde menstruation, and thereby increase the likelihood of developing endometriosis.

Despite a hypothetical association, few data have been gathered concerning any association between endometriosis and vaginal products. This report concerns the Keeper® (Health Keeper, Kitchener, Canada), a small rubber cup which holds up to an ounce of menstrual fluid. The Keeper is structurally similar to the cervical cap and fits closely to the cervix. Compared to tampons and pads, the Keeper prevents leakage and is more convenient and acceptable, as it is emptied only once every 6–12 h. Because the Keeper can only hold a certain amount of fluid and does not leak, when it is full, menses theoretically may either stay in the endometrial cavity or spill into the peritoneal cavity, rather than accumulate in the vagina.
na. If a blood clot blocks the flow of menses through the cervix, retrograde menstruation may be even more likely.

We describe a 41-year-old woman who developed adenomyosis and endometriosis 4 years after regular use of the Keeper, despite previous tubal ligation.

**Case Report**

This healthy 41-year-old woman presented to the NIH as part of a study of pain caused by endometriosis. She had a tubal ligation 10 years earlier and began using the Keeper 4 years before presentation. Over the previous 2 years, she began to have dysmenorrhea and intermittent pelvic pain, symptoms suggestive of endometriosis. She denied having painful menses at any other time, including prior to the tubal ligation. On preoperative magnetic resonance imaging, diffuse thickening of the endometrial-myometrial junctional zone was considered consistent with adenomyosis (fig. 1) [8]. At laparoscopy, the fallopian tubes were normal except for surgically absent midsegments and tubal occlusion at the previous surgical sites (fig. 2). The ovaries were normal. The uterus was enlarged and boggy, also consistent with adenomyosis. A single 0.5-mm area of endometriosis was seen about 2 cm from the occluded end of the proximal fallopian tube and was surgically excised. The rest of the pelvic anatomy was normal without evidence of adhesions. Histological evaluation of an endometrial biopsy specimen was normal, and the peritoneal biopsy specimen confirmed endometriosis. After laser laparoscopic removal of endometriosis and discontinuing use of the Keeper, the patient experienced a dramatic decrease in pelvic pain, and 2 years later, she has only mild dysmenorrhea.

**Discussion**

We presented the case of a woman who experienced new, severe, chronic pelvic pain while using a menstrual collection device after tubal ligation. Preoperative magnetic resonance imaging and surgical findings were con-

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**Fig. 1.** T2-weighted magnetic resonance image of the uterus. The arrows point to the diffuse thickening of the endometrial-myometrial junctional zone which is consistent with adenomyosis.

**Fig. 2.** Line drawing of the pelvic findings at laparoscopy. The arrow points to a small black area of endometriosis. The uterus appears boggy, consistent with the magnetic resonance imaging findings of adenomyosis.
sistent with adenomyosis and stage I endometriosis and confirmed previous tubal ligation. We speculate that the Keeper prevented menstrual flow, forcing menstrual effluent into the myometrium and through the occluded fallopian tube. This could account for the presence of endometriosis at a site where retrograde menses could have spilled from the proximal fallopian tube and for the presumed adenomyosis. This hypothesis is consistent with the unusual timing of pelvic symptoms which occurred after age 40 years and only after tubal ligation followed by years of use of the Keeper.

Clinicians have wondered whether female barrier devices or menstrual collection devices increase the risk of endometriosis or adenomyosis. Indeed, the recommendation against menstrual use of diaphragms and cervical caps may reflect a desire to prevent retrograde menstruation. However, it is not known whether these products actually increase the risk of either adenomyosis or endometriosis, because the association has not been systematically evaluated. We speculate that the Keeper may block menstrual flow while being used as recommended. As a result, retrograde menstruation may be more common for all women using the Keeper, and adenomyosis or endometriosis rates might be increased in susceptible women. Furthermore, when used in a woman after tubal ligation, we speculate that the Keeper may so successfully block menstrual flow that menses can be forced into the uterine wall. The observations in our patient suggest that it may be useful to inquire about use of these devices in women with pelvic pain or endometriosis. If the association is confirmed in others, it may be prudent to advise women using the Keeper to empty it more often than every 6–12 h, especially after tubal ligation or if menses are heavy.

Acknowledgment

We would like to thank Dr. James Segars for his assistance in the operating room.

References

1 Sampson JA: Peritoneal endometriosis due to the menstrual dissemination of endometrial tissue into the peritoneal cavity. Am J Obstet Gynecol 1927;14:422-469.
Addendum A: Citizen Petition, Menstrual Cups

FDA Records for the Approval of

The Menstrual Cups:
(abridged)

The Keeper, K870803/A

and

Instead, K971303

Acquired through the FDA Freedom Of Information Office, 11/13/02 and 01/30/03

For additional information, contact:

Armand Lione, Ph.D.
202.544.0711
ArmandLione@hotmail.com

533 Fourth St., SE Washington, DC 20003-4222 202.544.0711
Re: K870803/A

THE KEEPER

Dated: March 16, 1987
Received: March 20, 1987
Regulatory Class: II
21 CFR 884.5400

Mr. Lou Crawford
The Keeper Company
P.O. Box 20823
Cincinnati, Ohio 45220

Dear Mr. Crawford:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent to devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments. You may, therefore, market the device, subject to the general controls provisions of the Federal Food, Drug, and Cosmetic Act (Act). The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, and labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Performance Standards) or class III (Premarket Approval) it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 995. In addition, the Food and Drug Administration (FDA) may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligations you might have under the Radiation Control for Health and Safety Act of 1968, or other Federal Laws or Regulations.

This letter immediately will allow you to begin marketing your device as described. An FDA finding of substantial equivalence of your device to a pre-Amendments device results in a classification for your device and permits your device to proceed to the market, but it does not mean that FDA approves your device. Therefore, you may not promote or in any way represent your device or its labeling as being approved by FDA. If you desire specific advice on the labeling for your device please contact the Division of Compliance Operations, Regulatory Guidance Branch (HFZ-323) at (301) 427-8040. Other general information on your responsibilities under the Act, may be obtained from the Division of Small Manufacturers Assistance at their toll free number (800) 638-2041 or at (301) 443-6297.

Sincerely yours,

[Signature]

Lillian Yin, Ph.D.
Director, Division of OB-GYN, ENT.
and Dental Devices
Office of Device Evaluation
Center for Devices and Radiological Health
MARCH 20, 1987
THE KEEPER COMPANY
ATTN: LOU CRAWFORD
P.O. BOX 20023
CINCINNATI, OH 45220

D.C. Number : K870803
Received : 03-20-87
Product : THE KEEPER

The additional information you have submitted has been received.

We will notify you when the processing of your submission has been completed or if any additional information is required. You are required to wait ninety (90) days after the received date shown above or until receipt of a 'substantially equivalent' letter before placing the product into commercial distribution. I suggest that you contact us if you have not been notified in writing at the end of this ninety (90) day period before you begin marketing your device. Written questions concerning the status of your submission should be sent to:

Food and Drug Administration
Center for Devices and Radiological Health
Office of Device Evaluation
Document Mail Center (HFZ-401)
8757 Georgia Avenue
Silver Spring, Maryland 20910

If you have procedural or policy questions, please contact the Division of Small Manufacturers Assistance at their toll-free number (800) 638-2041 or me at (301) 427-8162.

Sincerely yours,

Robert I. Chissler
Premarket Notification Coordinator
Office of Device Evaluation
Center for Devices and Radiological Health
OB-GYN BRANCH 510(k) REVIEW FORM

CMC Dated: 3/20/87           Date received by reviewer: 3/24/87
Control #: K870803

original  30 day limit: 4/19/87
A amendment  90 day limit: 6/18/87

Device Name: The Keeper - Menstrual Cup
Manufacturer: The Keeper Co.

Device Description:
The device is identifiable as a latex rubber cup intended for vaginal insertion to collect menstrual fluid.

Review Summary:
The product is equivalent to the Tenesse & prometral device.
This amendment responds to our March 11, 1987 letter requesting the chemical composition, copies of proposed product instructions and statement that the device will include the information on TSS warnings identified @ 21CFR § 801.430.

Recommendation: Substantially equivalent

Product Code: 85 MHE
Classification: II @ §884.5400

Michael Kirsch, C. 4/15/87
Reviewer

Branch Chief  4/19
Kirsch

1-1 concur 1/1 do not concur

6/4 CP: 19
Kuchariska
K870803/A

THE RECORD

It is my recommendation that the subject 510(k) Notification:

(A) Is substantially equivalent to marketed devices.

(B) Requires premarket approval. NOT substantially equivalent to marketed devices.

(C) Requires more data.

(D) Is an incomplete submission. (See Submission Sheet).

Additional Comments:

I checked with M. Kuchariska on effectiveness. Mike believed the "it is o.k." in 5/4/87.

The submitter requests:

No Confidentiality

Confidentiality for 90 days

Continued Confidentiality exceeding 90 days

REVIEW: [Signature]
(BRANCH/CHIEF) 5/4/87

FINAL REVIEW: [Signature]
(DIVISION DIRECTOR) 5/4/87
DEPARTMENT OF HEALTH & HUMAN SERVICES

JUN - 6 1997

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

Utriglum, Inc.
Re: K971303

% Mr. Peter S. Reichertz
Arent Fox Kinstler Plotkin & Kahn
1050 Connecticut Avenue, N.W.
Washington, D.C. 20036-5339

INSTEAD® Softcup - Feminine Protection Cup

Dear Mr. Reichertz:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the Good Manufacturing Practice for Medical Devices: General (GMP) regulation (21 CFR Part 820) and that, through periodic GMP inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 511 through 542 of the Act for devices under the Electronic Product Radiation Control (EPiRC) provisions, or other Federal laws or regulations.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4616. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "http://www.fda.gov/CDRH/demansain.html".

Sincerely yours,

Lillian Yin, Ph.D.
Director, Division of Reproductive, Abdominal, Ear, Nose and Throat, and Radiological Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure
DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

Memorandum

From: Reviewer(s) - Name(s) ELSA D. HARVEY

Subject: 510(k) Number K971303

To: The Record - It is my recommendation that the subject 510(k) Notification:

☐ Refused to accept.
☐ Requires additional information (other than refuse to accept).
☒ Accepted for review 4/15
☒ Is substantially equivalent to marketed devices.
☐ NOT substantially equivalent to marketed devices.
☐ Other (e.g., exempt by regulation, not a device, duplicate, etc.)

☐ YES ☐ NO
Is this device subject to Postmarket Surveillance?

☐ YES ☐ NO
Is this device subject to the Tracking Regulation?

☐ YES ☐ NO
Was clinical data necessary to support the review of this 510(k)?

☐ YES ☐ NO
Is this a prescription device?

☐ YES ☐ NO
Was this 510(k) reviewed by a Third Party?

This 510(k) contains:

☐ Truthful and Accurate Statement ☐ Requested ☑ Enclosed
(required for originals received 3-14-95 and after)

☐ A 510(k) summary OR ☑ A 510(k) statement

☐ The indication for use form (required for originals received 1-1-96 and after)

The submitter requests under 21 CFR 807.95 (does not apply for SEs):

☐ No Confidentiality ☐ Confidentiality for 90 days ☐ Continued Confidentiality exceeding 90 days

Predicate Product Code with panel and class: Additional Product Code(s) with panel (optional):

WA 85 HPE 21 CFR 884: C400

Review: Colin M. Reardon OGB 6/14/97
(Branch Chief) (Branch Code) (Date)

Final Review: (Division Director) 6/14/97

Revised 11-28-96
Re: K870803/A

THE KEEPER

Dated: March 16, 1987
Received: March 20, 1987
Regulatory Class: II
21 CFR 884.5400

Mr. Lou Crawford
The Keeper Company
P.O. Box 20023
Cincinnati, Ohio 45220

Dear Mr. Crawford:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent to devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments. You may, therefore, market the device, subject to the general controls provisions of the Federal Food, Drug, and Cosmetic Act (Act). The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, and labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Performance Standards) or class III (Premarket Approval) it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. In addition, the Food and Drug Administration (FDA) may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under the Radiation Control for Health and Safety Act of 1968, or other Federal Laws or Regulations.

This letter immediately will allow you to begin marketing your device as described. An FDA finding of substantial equivalence of your device to a pre-Amendments device results in a classification for your device and permits your device to proceed to the market, but it does not mean that FDA approves your device. Therefore, you may not promote or in anyway represent your device or its labeling as being approved by FDA. If you desire specific advice on the labeling for your device please contact the Division of Compliance Operations, Regulatory Guidance Branch (HFZ-323) at (301) 427-8040. Other general information on your responsibilities under the Act, may be obtained from the Division of Small Manufacturers Assistance at their toll free number (800) 638-2041 or at (301) 443-6597.

Sincerely yours,

[Signature]

Lillian Yin, Ph.D.
Director, Division of OB-GYN, ENT, and Dental Devices
Office of Device Evaluation
Center for Devices and Radiological Health
OB-GYN BRANCH 510(k) REVIEW FORM

DMC Dated: 3/20/87 Date received by reviewer: 3/24/87
Control #: K870803

_____ original 30 day limit: 4/19/87
A amendment 90 day limit: 6/18/87

Device Name: The Keeper - Menstrual Cup
Manufacturer: The Keeper Co.

Device Description:
The device is identified as a latex rubber cup intended for vaginal insertion to collect menstrual flow.

Review Summary:
The product is equivalent to the Tassette is preamendment device.
This amendment responds to our March 11, 1987 letter requesting the chemical composition, copies of proposed product instructions, and statement that the device will include the information on TSS warning identified at 21 CFR § 801.430.

Recommendation:
Substantially equivalent

Product Code: 85 HHE
Classification: II
@ 5884.5400

Signature: Michael Kushner
Date: 4/15/87

Branch Chief: 11 concur 11 do not concur
6/4
MARCH 20, 1987

THE KEEPER COMPANY
ATTN: LOU CRAWFORD
P.O. BOX 20023
CINCINNATI, OH 45220

D.C. Number : KB70803
Received : 03-20-87
Product : THE KEEPER

The additional information you have submitted has been received.

We will notify you when the processing of your submission has been
completed or if any additional information is required. You are required
to wait ninety (90) days after the received date shown above or until
receipt of a "substantially equivalent" letter before placing the product
into commercial distribution. I suggest that you contact us if you have
not been notified in writing at the end of this ninety (90) day period
before you begin marketing your device. Written questions concerning the
status of your submission should be sent to:

Food and Drug Administration
Center for Devices and
Radiological Health
Office of Device Evaluation
Document Mail Center (HFZ-401)
8757 Georgia Avenue
Silver Spring, Maryland 20910

If you have procedural or policy questions, please contact the Division of
Small Manufacturers Assistance at their toll-free number (800) 638-2041 or
me at (301) 427-8162

Sincerely yours,

Robert I. Chisler
Premarket Notification Coordinator
Office of Device Evaluation
Center for Devices and
Radiological Health
It is my recommendation that the subject 510(k) Notification:

- [ ] (A) Is substantially equivalent to marketed devices.
- [ ] (B) Requires premarket approval. NOT substantially equivalent to marketed devices.
- [ ] (C) Requires more data.
- [ ] (D) Is an incomplete submission. (See Submission Sheet).

Additional Comments:

I checked with M. Kuchinski by phone. He believed that it is O.K. in May 1987.

The submitter requests:

- [ ] No Confidentiality
- [X] Confidentiality for 90 days
- [ ] Continual Confidentiality exceeding 90 days

Class Code w/Panel:

85 HHE Class II
8534-5700

REVIEW: [Signature] [Date]

FINAL REVIEW: [Signature] [Date]
Utrufem, Inc.
% Mr. Peter S. Reichertz
Arent Fox Kintner Plotkin & Kahn
1050 Connecticut Avenue, N.W.
Washington, D.C. 20036-5339

Re: K971303
INSTEAD® Softcup - Feminine Protection Cup

Dated: April 7, 1997
Received: April 8, 1997
Regulatory class: II
21 CFR §884.5400/Product code: 85 HHE

Dear Mr. Reichertz:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the Good Manufacturing Practice for Medical Devices: General (GMP) regulation (21 CFR Part 820) and that, through periodic GMP inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 331 through 542 of the Act for devices under the Electronic Product Radiation Control (EPRC) provisions, or other Federal laws or regulations.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4616. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulations entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll-free number (800) 638-2041 or (301) 443-4597 or at its Internet address "http://www.fda.gov/cdrh/dsmasmain.html."

Sincerely yours,

Lillian Vin, Ph.D.
Director, Division of Reproductive
Abdominal, Ear, Nose and Throat,
and Radiological Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure
From:  Reviewer(s) - Name(s)  ELISA D. HARRIET  9/16

Subject:  510(k) Number  K971303

To:  The Record - It is my recommendation that the subject 510(k) Notification:

☐ Refused to accept.
☐ Requires additional information (other than refuse to accept).
☒ Accepted for review  4/15
☒ Is substantially equivalent to marketed devices.
☐ NOT substantially equivalent to marketed devices.
☐ Other (e., exempt by regulation, not a device, duplicate, etc.)

Is this device subject to Postmarket Surveillance?  ☐ YES ☒ NO

Is this device subject to the Tracking Regulation?  ☐ YES ☒ NO

Was clinical data necessary to support the review of this 510(k)?  ☐ YES ☒ NO

Is this a prescription device?  ☐ YES ☒ NO

Was this 510(k) reviewed by a Third Party?  ☐ YES ☒ NO

This 510(k) contains:

☐ Truthful and Accurate Statement ☒ Requested ☒ Enclosed
(required for original received 3-14-95 and after)

☐ A 510(k) summary OR ☒ A 510(k) statement

☐ The required certification and summary for class III devices  NA

☒ The indication for use form (required for original received 1-1-96 and after)

The submitter requests under 21 CFR 807.95 (does not apply for SEs):
☐ No Confidentiality  ☒ Confidentiality for 90 days  ☐ Continued Confidentiality exceeding 90 days

Predicate Product Code with panel and class:  Additional Product Code(s) with panel (optional):

85 85H1E 21 CFR 884 5440

Review:  Colleen M. Gouds  OGB  6/4/97
(Branch Chief) (Branch Code) (Date)

Final Review:  [Signature] (Division Director)  6/4/97
(Date)

Revised 11-20-96