



JAN 19 2000

WARNING LETTER

VIA FEDERAL EXPRESS  
VIA FACSIMILE

CryoGen, Inc.  
David R. Murray  
President and CEO  
11065 Sorrento Valley Court  
San Diego, California 92121

Dear Mr. Murray:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has reviewed some promotional materials distributed by CryoGen, Inc. (CryoGen) and your Internet site found at [www.cryogen-inc.com](http://www.cryogen-inc.com). These materials promote the use of the First Option™ Uterine Cryoblation Therapy™ (First Option™) system for endometrial ablation, the treatment of abnormal uterine bleeding, and as an alternative to hysterectomy. The First Option™ is a device as defined within the meaning of section 201(h) of the Federal Food, Drug and Cosmetic Act (the Act).

The intended use of the First Option™ system that was cleared in CryoGen's 510(k) premarket notification submissions designated K964971 and K972662 was "for the ablation of tissue by the application of extreme cold in the areas of dermatology, general surgery, neurosurgery, thoracic surgery, E.N.T., gynecology, oncology, proctology and urology." CryoGen did not provide the agency with data or receive clearance supporting the use of the First Option™ for the treatment of a specific medical condition.

Although CryoGen made a commitment to the agency in its October 25, 1999, letter to stop using the term endometrial ablation and to discontinue its promotion of the First Option™ device as an alternative to hysterectomy, our review of both your web site and recently distributed promotional materials shows that CryoGen has continued to make these representations. Examples of these claims and representations include:

The title of CryoGen's "home page", "Improving therapy for menstrual abnormalities through cryosurgery," found at [www.CryoGen-inc.com/](http://www.CryoGen-inc.com/). The site contains references to the treatment of menorrhagia or abnormal uterine bleeding. The target patient population is described as "women diagnosed with Abnormal Uterine Bleeding."

At [www.CryoGen-inc.com/forwomen.html](http://www.CryoGen-inc.com/forwomen.html), CryoGen's representations promote the use of the First Option™ device as an alternative to hysterectomy. Under the banner "for women – overview" you state that traditional methods of treatment for heavy menstrual bleeding such as dilation and curettage or drug therapy are not always effective and "a hysterectomy has been one of the only available permanent options." Following this you state that the "treatment [Intra-uterine Cryoblation] is generally completed under local anesthetic and may provide the relief you desire without resorting to a hysterectomy.

At [www.CryoGen-inc.com/fw\\_about.html](http://www.CryoGen-inc.com/fw_about.html), a picture entitled "for women-about the procedure" depicts the probe freezing the uterine lining. The text that accompanies the picture informs the reader that the "patient who undergoes Intra-uterine Cryoblation can expect her periods to return to a normal bleeding level or less and in some cases, no bleeding will recur after the initial discharge has stopped."

A flier distributed at the International Congress of Gynecologic Endoscopy/American Academy of Gynecologic Laparoscopists' 28<sup>th</sup> Annual Meeting, held in Las Vegas, Nevada November 8-11<sup>th</sup> 1999 entitled, "What's 'Way COOLER' Than a Hysterectomy?" The flier states, "Cryoblation System just may be the 'COOLEST' way to treat menstrual abnormalities."

Another flier, reportedly distributed at the same conference, entitled "Cryoblation Therapy that's quick, easy and thorough. (No wonder we call it FIRST OPTION™)," promotes the device as an effective tool to ablate 9 to 12 mm of uterine tissue and as an effective tool for the complete destruction of the endometrium and uterine fibroids. These claims are inappropriate because CryoGen has not provided data to the agency related to a zone of ablation or data that this degree of ablation is effective in treating or eliminating uterine fibroids.

CryoGen's First Option™ device is not cleared to be used as a tool for endometrial ablation, as a device to treat menorrhagia, or as an alternative to hysterectomy. We reviewed your arguments, made in your October 25<sup>th</sup> letter, concerning the various terms you believe should be allowed to describe your device or its use. Your conclusions appear to be based on the agency's clearance of your device as an intra-uterine probe, your belief that the clinical community uses the probe for endometrial ablation, and Dr. Burlington's letter of January 23, 1998, in which he referred to your device as an endometrial probe.

As we have previously explained, we disagree with your conclusions. When you represent your device as a viable treatment for abnormal uterine bleeding, an alternative to hysterectomies, an endometrial probe, or imply that it is intended to be used for "cryoblation of the uterus," and "cryoblation of endometrial tissue," you are promoting the device for an unapproved use.

Claims that imply that First Option™ can be used for endometrial ablation, treatment of abnormal uterine bleeding, menstrual abnormalities or other uterine conditions, or as an alternative to hysterectomy have misbranded and adulterated the device within the meanings of sections 502(o) and 501 (f)(1)(B) of the Act. The First Option™ system is misbranded because a notice or other information respecting the device was not provided to the FDA as required by section 510(k) and it has not been found to be substantially equivalent to a predicate device for the uses claimed. The device is adulterated because it is a class III device under section 513(f) and does not have approved applications for premarket approval in effect pursuant to section 515(a) or approved applications for investigational device exemptions under section 520(g).

FDA's regulations at 21 CFR 801.4 provide that the term "intended uses" of a device refers to the objective intent of the persons legally responsible for the labeling of a device. That intent may be shown by labeling claims or advertising matter or oral or written statements by such persons or their representatives. Making claims that your device can be used as an alternative to hysterectomy, for endometrial ablation, or to treat menorrhagia, change the intended use for which the First Option™ device was cleared. Pursuant to section 510(k) of the Act and as provided in 21 CFR 807.81(a)(3)(ii), claims that constitute a major change in the cleared intended use of a device require the submission of premarket notification to FDA.

The specific violations in this letter may represent practices used in other promotional or advertising materials used by your firm. You are responsible for investigating and reviewing these materials to ensure compliance with applicable regulations.

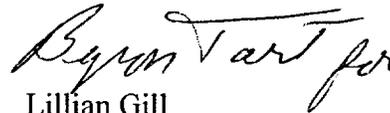
You should take prompt action to correct these violations. Failure to promptly correct these violations may result in regulatory action being initiated by FDA without further notice. These actions include, but are not limited to, seizure, injunctions and/or civil penalties. This letter is not intended to be an all-inclusive list of deficiencies associated with the First Option™ system.

Please notify this office in writing within 15 working days of your receipt of this letter of the specific steps you have taken to correct the cited violations. Your response should include steps being taken to address misleading information currently in the marketplace and actions to prevent similar violations in the future. If corrective actions cannot be completed within 15 working days, state the reason for the delay and the time within which the corrections will be completed.

Send your response to Terri Garvin, Regulatory Counsel, Promotion and Advertising Policy Staff, Office of Compliance (HFZ-302), Center for Devices and Radiological Health, 2098 Gaither Road, Rockville, Maryland 20850.

A copy of this letter is being sent to FDA's Los Angeles District Office. Please send a copy of your response to the District Director, Los Angeles District Office (HFR-PA-240), 19900 MacArthur Boulevard, Suite 300, Irvine, California 92715.

Sincerely,

A handwritten signature in cursive script, appearing to read "Lillian Gill for".

Lillian Gill  
Director  
Office of Compliance  
Center for Devices and  
Radiological Health

Prepared: 11/16/99  
Reviewed: 11/17/99:BT  
Revised: 12/1/99:LK  
Revised: 12/2/99:BT  
Revised:12/9/99:LK  
Reviewed:12/21/99BT  
Revised:12/21/99  
Revised: 12/23/99BT  
Reviewed:1/13/00:LK  
Revised:1/14/00  
Reviewed:1/18/00:CP  
Reviewed:1/18/00:BT  
Final:1/19/00  
Bcc:  
HFA-224  
HFZ-302  
HFZ-305  
HFZ-1(D.W. Feigal)  
HFZ-300(L. Gill)  
HFZ-470(C. Pollard)  
HFZ-470(D. Schultz)  
HFZ-2(L. Kahan)  
HFR-PA-240