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We are smith&nephew

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Dear Sir/Madam,

Thank you for taking the time to thoughtfully review the evidence including risks and benefits surrounding this timely subject in women's health. Smith & Nephew is a global medical technology business dedicated to helping healthcare professionals improve people's lives. We offer a number of products for women's health, including the TRUCLEAR◇ System, for hysteroscopic tissue removal.

Background

We are deeply concerned about the confusion and unintended consequences for women's health resulting from the April 17, 2014 Safety Communication titled "Laparoscopic Uterine Power Morcellation in Hysterectomy and Myomectomy."[1] In some cases, women's access to other unrelated, safe and effective minimally-invasive procedures, such as hysteroscopy, for common gynecological conditions has been restricted, even though these procedures were not meant to be addressed by the Safety Communication.

Some media reports have not helped patients in understanding the issue by providing incomplete stories, such as shortening the FDA Communication title to "Power Morcellation" and generally failing to make a distinction among procedures (laparoscopic myomectomy and hysterectomy vs. hysteroscopic polypectomy and hysteroscopic myomectomy) and corresponding products (laparoscopic morcellator and hysteroscopic morcellator). Unfortunately social media users have also been focused on the emotional aspects of the story creating further panic and concern. As a result, patients are confused.

While specialists in gynecology understand the clear and significant differences between laparoscopic and hysteroscopic morcellation, there is confusion among other healthcare professionals, including hospital administrators, risk managers, nursing staff, and other medical specialties. A small number of hospitals have mistakenly banned hysteroscopic morcellation as a result of the FDA Safety Communication. For example, a CMO at a hospital has issued a ban on "morcellation" without specifically stating laparoscopic morcellation. This resulted in cancelled patient hysteroscopy procedures, although such procedures are not the subject of the FDA Safety Communication.

Procedure and Device Inherent Differences

As the FDA is aware, there are a number of significant differences that distinguish hysteroscopic morcellation from the concerns identified in the FDA Communication on laparoscopic morcellation:

	Laparoscopic Morcellation, Targeted by FDA Safety Communication	Hysteroscopic Morcellation
Surgical Approach	• Abdominal via entry ports • Performed in operating room under anesthesia • Inside the peritoneal cavity requiring inflation of the peritoneal space with gas	• Transcervical (no incision) • May be performed in-office without anesthesia • Inside the uterus requiring inflation of the uterus with saline
Procedures/ Indications for Use	• Laparoscopic hysterectomy (removal of entire uterus – may contain fibroids) • Laparoscopic myomectomy – (subserosal and intramural fibroid removal - fibroids inside the abdomen or uterine wall)	• Hysteroscopic myomectomy (submucosal fibroid removal – fibroids inside the uterus) • Hysteroscopic polypectomy (removal of polyps inside uterus)
Clinical	• Multiple case reports and studies published on peritoneal dissemination of occult leiomyosarcoma associated with the use of laparoscopic morcellation[2]	• No case reports or studies published related to treatment, dissemination or upstage of leiomyosarcoma associated with hysteroscopic morcellation[3] • Hysteroscopic morcellation has not been linked in studies and case reports to an upstage in patients with latter proven endometrial cancer[2].
Precautions/ Labeling	• Device specific risk identified "Warning: May lead to dissemination of malignant tissue"	• No device-specific risk identified. As for all hysteroscopy procedures, contra-indicated for cervical malignancies or previously diagnosed endometrial cancer.
Device Design	• Approx. 16mm diameter • Utilization of gas to inflate the abdominal cavity therefore suction is not possible • Utilizes a grasper to pull tissue into the morcellator without suction • Cuts tissue into pieces • Pieces of tissue must be extracted by hand and may migrate within the abdomen before extraction	• 3-4mm diameter • Simultaneously cuts and removes tissue inside the uterus with suction • Removed tissue collects automatically in a trap

Clinical Evidence

Why does this confusion matter for women's health?

Hysteroscopy has long been established as a safe and effective method for diagnostic and therapeutic intervention. Uterine pathologies such as endometrial polyps and submucosal myomas are commonly removed hysteroscopically. Alternative treatments include blind curettage and definitive management via hysterectomy, each having significant drawbacks and risks for the patient.

According to a 2012 AAGL Practice Report[4], "Hysteroscopic polypectomy remains the gold standard for treatment (Level B)." It is also well established that "When hysteroscopic treatment is available, blind curettage should not be used as a diagnostic or therapeutic intervention."[4] Moreover, "Hysteroscopic removal is to be preferred to hysterectomy because of its less-invasive nature, lower cost, and reduced risk to the patient (Level C)."[4] In addition, hysteroscopic removal of polyps or submucosal myomas is recommended for the infertile patient[4]. There are a variety of devices to resect and remove tissue from the uterus hysteroscopically.

Hysteroscopic morcellation is a type of operative hysteroscopy using a device that cuts and simultaneously removes tissue via suction for collection in a tissue trap. In addition to the features common to all hysteroscopic devices, hysteroscopic morcellators offer advantages for patients over traditional resectoscopy including only a single pass through the cervix[5] and integrated aspiration for automatic removal and collection of resected tissue in a trap for analysis by pathology.

Currently there are three manufacturers of hysteroscopic morcellators marketed under different trade names in the United States. Smith & Nephew is the manufacturer of the TRUCLEAR System. Over 100,000 TRUCLEAR procedures have been performed in the United States[6]. There have not been any complaints filed[7] or reports in the literature[3] regarding the spread of cancerous tissue or the upstage of cancer related to the use of the TRUCLEAR System.

In addition, there have not been any reports in the literature regarding the spread of cancerous tissue or the upstage of cancer related to the use of other hysteroscopic morcellators available in the United States[3], the MyoSure™ Tissue Removal Device by Hologic or the Symphion™ Tissue Removal System by Boston Scientific.

The AAGL Tissue Extraction Task Force reviewed the evidence for hysteroscopic morcellation, focusing on leiomyosarcoma and concluded in May 2014 that, "Hysteroscopy remains an appropriate manner to remove symptomatic submucosal uterine myomas in premenopausal women and need not be exchanged for definitive treatment (i.e. hysterectomy) simply to avoid morcellation."[2]

When the concerns with laparoscopic morcellation were elevated recently, although Smith & Nephew did not make such a device, we took them very seriously. As a result, we requested a comprehensive independent third-party systematic review of the entire global literature on the topics of: hysteroscopy, both diagnostic and operative, leiomyosarcoma, sarcoma, cancer, resection, tissue removal, and hysteroscopic morcellation among other terms.

The systematic review concluded:

- There is no published clinical evidence supporting that hysteroscopic morcellation has been linked to an upstage in patients with latter proven endometrial cancer[2,3]
- In addition, contrary to the evidence on laparoscopic morcellation, there were no case reports or studies published related to treatment, dissemination or upstage of leiomyosarcoma associated with hysteroscopic morcellation[3]

As clinical data on operative hysteroscopy and diagnostic hysteroscopy in general is more plentiful these were also included in the literature review.

The systematic literature review notes:

- Hysteroscopy does not change the outcomes in the management of endometrial adenocarcinoma.[2,3]
- While rare[8], leiomyosarcoma (LMS) has been reported in women undergoing hysteroscopic resection of presumed submucosal myomas. At the time of subsequent hysterectomy minimal to no residual disease was documented and no women had succumbed to their disease at the time of publication.[2,3]

In conclusion, a third-party comprehensive systematic literature review did not identify any reports related to a device-specific risk factor for hysteroscopic morcellation when compared with other types of hysteroscopic tissue resection and removal. Therefore, any theoretical concerns posed regarding hysteroscopic morcellation should be examined regarding the category of diagnostic and operative hysteroscopy as a whole including traditional means of tissue resection such as resectoscopy or hysteroscopy D&C.

Conclusion

The April 17th FDA Safety Communication[1] has unintentionally led to significant confusion among healthcare professionals and women considering hysteroscopic treatments. Facts show there is little similarity between laparoscopic morcellation and hysteroscopic morcellation beyond the word morcellation. Additionally, there is no clinical evidence supporting the applicability of the issues raised in the laparoscopic morcellation discussion to hysteroscopy or hysteroscopic morcellation. While the FDA and other experts may be clear on this topic, the general community of patients and providers is confused. Therefore, we appeal to the FDA to further clarify its' statements.

First, we request that the panel and the FDA be very clear in future statements that such statements apply exclusively to laparoscopic power morcellation.

Second, the FDA has stated in an e-mail from Bonnie Alderton, Public Health Advisor, Division of Industry and Consumer Education (DICE), U.S. FDA on April 25, 2014 to Sue Dahlquist of Smith & Nephew Regulatory Affairs, that "The FDA's safety communication is focused on laparoscopic power morcellation when used for hysterectomy in women with uterine fibroids and for myomectomy. It does not address hysteroscopic power morcellation. " We request in future statements on this topic that the FDA state affirmatively and publicly that, "This communication does not apply to hysteroscopic morcellation," to reduce future potential for confusion in the patient and health care professional community.

These two short clarifying statements would go a long way towards supporting women's health by ensuring women have access to minimally invasive clinically proven technology, such as hysteroscopy and hysteroscopic morcellation, to diagnose and treat common uterine conditions. Thank you for your consideration.

Sincerely,

Andy Weymann, MD, MBA
Chief Medical Officer
Smith & Nephew Inc.

[1] "Laparoscopic Uterine Power Morcellation in Hysterectomy and Myomectomy: FDA Safety Communication," Accessed April 17, 2014. http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm393576.htm
[2] 2014 May AAGL. "Morcellation During Uterine Tissue Extraction." Special Report. Tissue Extraction Task Force.
[3] Cisterni, C. Systematic literature review of Upstaging and disseminating of uterine leiomyosarcoma, endometrial stromal sarcoma and endometrial cancer after hysteroscopic procedure. Unpublished report. June 2014.
[4] 2012 AAGL. "AAGL Practice Report: Practice Guidelines for the Diagnosis and Management of Endometrial Polyps." Journal of Minimally Invasive Gynecology. 19, 3-10.
[5] van Dongen H., Emanuel M.H., Wolterbeek R., Trimbos J.B., Jansen FW. *Hysteroscopic Morcellator for Removal of Intrauterine Polyps and Myomas: A Randomized Controlled Pilot Study among Residents in Training.* (2008). The Journal of Minimally Invasive Gynecology. **15**(4), 466-471.
[6] Smith & Nephew Internal Data. Retrieved June 30, 2014.
[7] Smith & Nephew Internal Data. Risk Management File# RM-D-0002. Retrieved June 30, 2014.
[8] 2014 May ACOG. "Power Morcellation and Occult Malignancy in Gynecologic Surgery" A Special Report.