Questions and Answers:

Minerva Surgical's Allegations Regarding the Retrospective Comparative Study of the NovaSure and Minerva Endometrial Ablation Devices Published in the International Journal of Women's Health[1]

Minerva Surgical, Inc. ("Minerva") has been engaging in a widespread, highly unethical campaign to discredit a recently published Hologic-sponsored study that compared Hologic's NovaSure endometrial ablation device to Minerva's device. While Minerva may view this as a mere commercial dispute, Hologic takes these false and deceptive allegations very seriously, and we strongly believe that Minerva's actions threaten the health of women who rely on their physician's access to accurate scientific information in order to make critical clinical decisions.

Below please find questions and answers relating to the study and Minerva's allegations. Should you have any further questions about this matter, please contact Jane G. Mazur, Vice President, Divisional Communications at 508.263.8764.

1. **What study publication is at issue?**

On April 18, 2018, the International Journal of Women's Health ("IJWH") published a manuscript for a Hologic-sponsored study titled, *Efficacy and patient satisfaction after NovaSure and Minerva endometrial ablation for treating abnormal uterine bleeding: a retrospective comparative study* (available at dovepress.com). Apparently due to their concerns about the study results pertaining to their device, Minerva has engaged in a widespread, highly unethical campaign to falsely discredit the study, Hologic, and the highly esteemed study investigators. Of greatest concern, Minerva's attempt to gain business advantage via these false claims threatens the health of women who rely on their physician's access to accurate scientific information in order to make critical clinical decisions.

2. **What were the study objectives and design?**

The primary objective of the retrospective study was to compare amenorrhea rate, menstrual symptoms, patient satisfaction, and adverse events in women who underwent endometrial ablation with the NovaSure device versus the Minerva device. The investigators reviewed 189 premenopausal women (mean 40.8±6.2 years old) who underwent endometrial ablation for abnormal uterine bleeding using the NovaSure (n=97) or Minerva (n=92) systems, at four private U.S. gynecology clinics, and whose procedure date was after July 2015, with follow-up ≥3 months. Women were surveyed an average of 11.3±3.9 months (range 137–532 days) after ablation.

[1] **Please note that this Q&A is not intended to promote any Hologic product. It is provided in response to the false allegations made by Minerva Surgical with respect to the study in question, and is intended solely as scientific exchange communication.**

3. **Why did Hologic sponsor the study?**

Hologic identified a scientific/medical need to conduct this study in order to identify potential clinical differences and patient outcomes for each device, and thereby add to the peer-reviewed scientific information available to physicians for clinical decision making. Hologic's sponsorship was fully consistent with all applicable laws, Good Clinical Practices (GCPs) and publication standards. The investigators carried out their duties in a manner that was fully consistent with the protocol that was approved by the institutional review board (IRB).

4. **What were the results of the study?**

In this retrospective, comparative study, the subject-reported amenorrhea rate was 52% higher in NovaSure subjects than Minerva subjects (64% and 42%, respectively; p=0.004). Age and bleeding cyclicity did not affect amenorrhea rate in either group. Normal-to-no bleeding was reported by >90% of subjects after either treatment. The NovaSure procedure was significantly more effective than Minerva at reducing pad/tampon use in women with any residual bleeding (2.4±5.2 items/day versus 4.7±5.5 items/day, p=0.049). The NovaSure procedure was significantly more effective than Minerva at reducing premenstrual syndrome (PMS) symptoms (p=0.019) and menstrual pain (p=0.003), and more NovaSure subjects (94%) than Minerva subjects (78%) were satisfied with clinical outcomes (p=0.003). Adverse events did not differ by treatment; three women in each group progressed to hysterectomy.

5. **What publication standards does IJWH follow?**

IJWH is a peer-reviewed scientific and medical journal that is a member of and subscribes to the principles of the Committee on Publication Ethics ("COPE"). IJWH also endorses the International Committee of Medical Journal Editors (ICMJE) Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals as well as the GPP3 guidelines regarding authorship. All manuscripts submitted to Dove Medical Press journals, such as the IJWH, undergo single blind peer review.

6. **Was the Hologic study subject to these IJWH publication and ethical standards?**

Yes. The Hologic study was subject to IJWH's independent peer review process and was accepted for publication.

7. **Did IJWH investigate the study based on Minerva's allegations?**

In January 2018, Minerva, without appropriate authorization, obtained confidential information regarding the study and submitted a complaint to IJWH alleging that Hologic and/or the investigators conducted the study in a manner that did not comply with applicable research standards and was skewed to prejudice Minerva's product. IJWH conducted an independent investigation into these allegations, in which Hologic fully cooperated, and the IJWH determined that Minerva's allegations had no merit. Unfortunately, Minerva has continued to engage in a widespread, highly unethical campaign to discredit Hologic and the study investigators with false

allegations, including additional outreach to IJWH. Hologic will continue to fully cooperate with IJWH in its review of Minerva's complaints, and we are confident that IJWH will again conclude that Minerva's allegations have no merit.

8. **What specifically is Minerva alleging about the study?**

Minerva makes several allegations, all of which are false or have no merit. Below we have included each allegation and Hologic's response.

a) **Minerva Allegation: Hologic and/or investigators skewed the results of the study by "hand picking" NovaSure patients, and failed to include certain Minerva patients.**

Hologic Response: The study protocol required investigators to identify patients who had undergone ablation with the NovaSure or Minerva device whose procedure date was after July 2015. Consistent with the study protocol, investigators were first required to identify such patients and then obtain their informed consent. After the investigators had a sufficient number of consented eligible patients for statistical analysis per the protocol, the retrospective study commenced. During the informed consent and eligibility screening process, Hologic personnel never determined which specific patients to include in the study, and investigators were directed to utilize only neutral criteria, such as date of treatment. In fact, other than initial site qualification visits to certain sites, Hologic did not conduct any site visits or monitoring of the investigators, as required under the study protocol, until after the investigators had already selected all of their eligible patients. Notably, all Minerva patients that consented and met inclusion/exclusion criteria per the protocol were enrolled by the investigators.

b) **Minerva Allegation: Hologic and/or investigators skewed the study results by "cherry picking" patients based on 2-3 month bleeding status.**

Hologic Response: The IJWH study protocol was designed and executed in a manner that strictly prohibited Hologic's selection of specific patients. Hologic personnel did not access 2-3 month post-procedure bleeding status information during the informed consent or screening process, and certainly did not make any decisions on patient inclusion based on bleeding status or any other criteria. Only investigators selected eligible patients for inclusion, in accordance with the criteria in the IRB-approved protocol.

c) **Minerva Allegation: Hologic omitted 2-3 months follow up visit data from the IJWH manuscript because it somehow showed bias in favor of the NovaSure group in the study.**

Hologic Response: Minerva's allegation that the exclusion of 2-3 month bleeding status data from the IJWH publication somehow skewed the publication against Minerva is scientifically misguided. Based on feedback from the peer review process, Hologic and the authors determined that the focus in the IJWH publication should be on the clinically meaningful 11-12 months postoperative time point. The omission of the 2-3 month

bleeding status data is consistent with the clear consensus in the medical community that such data is not clinically meaningful or predictive of outcomes in endometrial ablation.

d) **Minerva Allegation: There were clinically significant differences in the patient groups in the study due to differences in (1) uterine sound lengths; and (2) intra-cavitary pathology (fibroids), and those differences prejudiced Minerva's device.**

Hologic Response:

- Uterine sounding length:
    - Both the NovaSure and Minerva device are only cleared by FDA for use in patients with a uterine sounding length equal to or less than 10cm.
    - As expressly listed in Table 2 of the study, the mean uterine *sounding length* for the NovaSure and Minerva cohorts were 8.2±1.8 and 8.6±0.9, respectively; and the medians were 9 (6-10) and 8 (6-10), respectively. Thus, in those patients who had a recorded uterine sounding, there were no clinically significant differences in the patient groups with respect to uterine sound lengths, which is the only measurement identified in the device instructions for use and relevant to this procedure.
    - Minerva apparently mistakenly cited to differences in the ultrasound measurement of *uterine length* listed under the diagnostics assessments, which has no clinical significance to the study or use of the devices in endometrial ablation.

- Intra-cavitary pathology: There were no statistically significant differences in the patient groups with respect to intra-cavitary pathology, and thus those outcomes did not prejudice Minerva in any way.

e) **Minerva Allegation: Important conflicts of interests were not disclosed in association with the publication of the IJWH study.**

Hologic Response: The IJWH study expressly acknowledged that the study was "funded by Hologic Inc." and included a disclosure statement that expressly acknowledged the material fact that "*All* authors were principal investigators in the current study and received compensation from Hologic for participation." Other investigator financial interests were submitted by the investigators directly to the IJWH in accordance with the journal's guidelines. None were material to the study in question.

For example, Minerva has complained that one of the investigators, Dr. Stankiewicz, received payments from Hologic in 2016 that were not listed in the study's disclosure statement. These payments were disclosed directly to IJWH in compliance with the journal's policies but were not identified for inclusion in the disclosure statement, likely

because they were deemed an immaterial addition to the already clear acknowledgement of a financial relationship between Hologic and the investigators.

9. **Is it true that the Journal of Minimally Invasive Gynecology ("JMIG) rejected a prior version of the manuscript? If so, what does that mean for the IJWH study publication?**

   Hologic initially submitted an earlier version of the study manuscript to JMIG for publication. Although JMIG did not accept the manuscript for publication, scientific journals decide not to accept manuscripts for various reasons, and not all journals publish company-sponsored retrospective studies of this type. JMIG's decision was not a judgment on the integrity or quality of the conduct of the study by Hologic or the investigators. As noted above, Hologic incorporated JMIG's feedback and ultimately decided that the peer-reviewed IJWH would be a more appropriate publication for the revised manuscript.

Given the above, it is clear that Minerva is engaging in a false and highly unethical marketing campaign based on an intentional mischaracterization of the actions of Hologic and the investigators. These findings confirm the findings of the IJWH that the study was conducted with integrity and was appropriate for publication.