DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

Kyle Hooper
Regulatory Affairs Associate
CooperSurgical, Inc.
75 Corporate Drive
Trumbull, CT 06611

RE: NDA 018680
ParaGard® T380A INTRAUTERINE COPPER CONTRACEPTIVE
MA 578

Dear Mr. Hooper:

The Office of Prescription Drug Promotion (OPDP) of the U.S. Food and Drug Administration (FDA) has reviewed a Direct-to-Consumer television advertisement (TV ad) entitled "Paragard 30 sec DTC Ad (Musical)" (US-PAR-1800079) for ParaGard® T380A INTRAUTERINE COPPER CONTRACEPTIVE (ParaGard) submitted by CooperSurgical, Inc. (CooperSurgical) under cover of Form FDA 2253. The FDA Bad Ad Program also received a complaint regarding this TV ad. This TV ad makes false or misleading representations about the risks associated with ParaGard. Thus, the TV ad misbrands ParaGard within the meaning of the Federal Food, Drug and Cosmetic Act (FD&C Act) and makes its distribution violative. 21 U.S.C. 352(n); 331(a); 321(n). 21 CFR 202.1(e)(1); (e)(5). This violation is concerning from a public health perspective because it creates a misleading impression about the safety of ParaGard.

Background

Below are the indication and summary of the most serious and most common risks associated with the use of ParaGard.[1] According to the FDA-approved product labeling (PI):

> ParaGard® is indicated for intrauterine contraception for up to 10 years.

ParaGard is contraindicated in pregnancy or suspicion of pregnancy; in women with abnormalities of the uterus resulting in distortion of the uterine cavity; acute pelvic inflammatory disease, or current behavior suggesting a high risk of pelvic inflammatory disease; postpartum endometritis or postabortal endometritis in the past 3 months; known or suspected uterine or cervical malignancy; genital bleeding of unknown etiology; mucopurulent cervicitis; Wilson's disease; allergy to any component of ParaGard; or a previously placed

[1] This information is for background purposes only and does not necessarily represent the risk information that should be included in the promotional pieces cited in this letter.

intrauterine device that has not been removed. The PI for ParaGard includes warnings regarding intrauterine pregnancy, ectopic pregnancy, pelvic infection, immunocompromise, myometrium embedment, perforation, and expulsion. The PI also includes precautions regarding vaginal bleeding; vasovagal reactions, including fainting; expulsion following placement after a birth or abortion; magnetic resonance imaging; and medical diathermy. Adverse reactions reported with use of ParaGard include anemia; backache; dysmenorrhea; dyspareunia; expulsion, complete or partial; leukorrhea; menstrual flow prolonged; menstrual spotting; pain and cramping; urticarial allergic skin reaction; and vaginitis.

False or Misleading Risk Presentation

Promotional materials misbrand a drug if they are false or misleading with respect to risk. The determination of whether promotional materials are misleading includes, among other things, not only representations made or suggested in promotional materials, but also failure to reveal facts material in light of the representations made or with respect to consequences that may result from the use of the drug as recommended or suggested in the materials.

The TV ad is misleading because it includes claims and representations about the uses and benefits of ParaGard but fails to include important risk information associated with the drug. While the TV ad includes the statement as onscreen superimposed text (SUPER), “Don’t use Paragard if you have certain cancers[,]” the TV ad fails to include any of the other contraindications for the product, such as acute pelvic inflammatory disease, or current behavior suggesting a high risk of pelvic inflammatory disease. Additionally, although the TV ad includes the statement as an audio voice over (VO), “If you experience pain, pelvic infection . . . call your healthcare provider,” it fails to adequately communicate the material fact that ParaGard is associated with an increased risk of pelvic inflammatory disease (PID) and that PID can have serious consequences. Moreover, the TV ad omits the warning for expulsion of the product. By omitting serious risks associated with ParaGard and material facts pertaining to the risks of ParaGard, the TV ad misleadingly suggests that ParaGard is safer than has been demonstrated.

Additionally, the presentation of certain risk information in the “major statement” of risks through audio and SUPERs is undermined by the simultaneous presentation of fast-paced visuals that feature choreographed dancing to instrumental background music and multiple scene changes. Specifically, many people are seen dancing through a crowded street surrounded by building fronts and street vendors and forming a pattern in the street while others hold letters that spell PARAGARD in bold blue letters. The presentation of these compelling and attention-grabbing visuals, all of which are unrelated to the risk message presented in the audio and on-screen SUPERS, in addition to the frequent scene changes and the other competing modalities such as the background music, compete for the consumers’ attention. As a result, it is difficult for consumers to adequately process and comprehend the risk information, resulting in a misleading impression of the drug’s risks.

The TV ad is also misleading because it communicates important risk information in the *visual* portion of the TV ad only, i.e., as SUPERs. TV ads must include information relating to the major side effects and contraindications of the advertised drugs in the *audio* (or audio and visual parts) of the presentation. 21 CFR 202.1(e)(1). However, the ParaGard TV ad

presents important risk information about the contraindication for certain cancers and the precaution for vaginal bleeding only visually as SUPERs.

Furthermore, the TV ad presents unrelated risk and benefit information in competing modalities that further minimizes the presentation of risk information. Specifically, the TV ad discloses important risk information about the contraindication for certain cancers in a SUPER simultaneously with audio containing unrelated risk information about calling a healthcare provider for pain, pelvic infection, or a missed period. Similarly, the TV ad discloses important risk information about the precaution for vaginal bleeding in a SUPER simultaneously with unrelated audio and visual (i.e., as SUPERs) benefit claims that ParaGard is 100% hormone free and over 99% effective at preventing pregnancy.

The overall effect of compelling and attention-grabbing visuals and other modalities competing for consumers' attention, disclosing important risk information in SUPERs only, and the simultaneous presentation of unrelated risks via SUPERs with competing audio messages undermines the communication of important risk information. As a result, the TV ad misleadingly minimizes the risks associated with the use of ParaGard. These presentations in the TV ad are especially problematic from a public health perspective given the serious and potentially life-threatening risks associated with the drug.

Further, the TV ad includes the following claims and presentations (emphasis original):

- "No hormones! I found a birth control with no hormones! Paragard's 100% hormone-free . . . !" (VO frames one and two)
- "No hormones not an ounce! With an ingredient I can pronounce." (VO frames four and five)
- "**100% HORMONE FREE**" (background visuals frames one through five; SUPER frames six and 10).
- "**1 SIMPLE ACTIVE INGREDIENT**" (background visuals frames one through five; SUPER frames six and 10)

The net impression of these claims and presentations further minimize the risks associated with ParaGard because they misleadingly suggest that, because ParaGard is, "100% HORMONE FREE[,]" and has, "No hormones not an ounce! With an ingredient I can pronounce[,]" ParaGard does not have the potential negative health effects of hormone contraceptives such as long-acting reversible contraceptives (LARC), including progesterone-containing IUDs or implants. Although it is true that ParaGard is hormone-free, the totality of the overwhelming, repetitive nature of the claims above along with the misleading omission and presentational elements of the TV ad previously described create a misleading impression of the safety profile of the drug. In fact, ParaGard is associated with many of the same serious risks as other LARC products, including risks related to pregnancy and ectopic pregnancy, and vaginal bleeding.

Moreover, because it is an intrauterine device, there are additional risks to Paragard, some of which may be fatal, which include embedment, perforation of the myometrium, migration, and pelvic inflammatory disease. In addition, its active ingredient, copper, is associated with its own risks as described in the PI, including contraindications for Wilson's disease, a genetic disease affecting copper excretion, and allergy to any component of ParaGard, which

includes the copper. Additionally, the PI describes a precaution for medical diathermy (short-wave and microwave heat therapy) in patients with a metal-containing IUD, which may cause heat injury to the surrounding tissue. Therefore, these claims and presentations are misleading with respect to ParaGard's safety and further exacerbate the minimization of ParaGard's serious and potentially life-threatening risks as described above.

Conclusion and Requested Action

For the reasons discussed above, the TV ad misbrands ParaGard within the meaning of the FD&C Act and makes its distribution violative. 21 U.S.C. 352(n); 331(a); 321(n). 21 CFR 202.1(e)(1); (e)(5).

OPDP requests that CooperSurgical immediately cease violating the FD&C Act, as discussed above. Please submit a written response to this letter on or before August 8, 2019, stating whether you intend to comply with this request, listing all promotional materials (with the 2253 submission date) for ParaGard that contain violations such as those described above, and explaining your plan for discontinuing use of such violative materials. If you believe that your products are not in violation of the FD&C Act, include your reasoning and any supporting information for our consideration.

Please direct your response to the undersigned at the **Food and Drug Administration, Center for Drug Evaluation and Research, Office of Prescription Drug Promotion, 5901-B Ammendale Road, Beltsville, Maryland 20705-1266**. A courtesy copy can be sent by facsimile to (301) 847-8444. To ensure timely delivery of your submissions, please use the full address above and include a prominent directional notation (e.g. a sticker) to indicate that the submission is intended for OPDP. Please refer to MA 578 in addition to the NDA number in all future correspondence relating to this particular matter. All correspondence should include a subject line that clearly identifies the submission as a Response to Untitled Letter. OPDP reminds you that only written communications are considered official.

The violations discussed in this letter do not necessarily constitute an exhaustive list. It is your responsibility to ensure that your promotional materials for ParaGard comply with each applicable requirement of the FD&C Act and FDA implementing regulations.

Sincerely,

{See appended electronic signature page}

Lynn Panholzer, Pharm.D.
Regulatory Review Officer
Division of Advertising & Promotion Review 2
Office of Prescription Drug Promotion

{See appended electronic signature page}

Matthew J. Falter, Pharm.D.
Team Leader
Division of Advertising & Promotion Review 2
Office of Prescription Drug Promotion

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

LYNN M PANHOLZER
07/25/2019 11:59:49 AM

MATTHEW J FALTER
07/25/2019 12:04:59 PM