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VIA HAND DELIVERY

Division of Dockets Management
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane, Room 1061
Rockville, MD 20852

CITIZEN PETITION

Sun Pharmaceutical Industries, Ltd., by its counsel, Winston & Strawn LLP, submits this petition pursuant to the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 301 *et seq.*, and in accordance with the procedural requirements specified in 21 C.F.R. § 10.30, to request that the Commissioner of Food and Drugs confirm that: (1) the FDA has not approved Ganirelix Acetate Injection for use as a female contraceptive; and (2) the FDA-labeled indication for Ganirelix is not equivalent to a method of female contraception.

In ongoing litigation, Sun and the holder of the New Drug Application ("NDA"), Organon USA Inc., have a dispute about whether the FDA has approved Ganirelix for use as a contraceptive. Organon is taking the position that the FDA-labeled indication for Ganirelix is equivalent to, or "substantially the same as," administering Ganirelix "as a method of female contraception."

But, in fact, the FDA has never approved Ganirelix for use as a female contraceptive. According to its product label, Ganirelix "is indicated for the inhibition of premature LH surges in women undergoing controlled ovarian hyperstimulation." Controlled ovarian hyperstimulation is a process used during *in vitro* fertilization—a method of *promoting* pregnancy. The FDA-approved labeling thus does not advise or encourage physicians to administer Ganirelix as a female contraceptive to *prevent* pregnancy.

To be sure, Organon is taking this extreme position in the hope of delaying generic competition through a manufactured claim of infringement. But Organon's position not only misleads a federal court, it raises significant safety concerns, including concerns about off-label

marketing for the product. The public would benefit from swift confirmation that the FDA-approved use for Ganirelix means what it says—that is, the FDA has not approved Ganirelix for use as a method of female contraception.

A. ACTION REQUESTED

Petitioner Sun respectfully requests that the FDA confirm what should be readily apparent from its unambiguous product labeling—namely, that:

1. Ganirelix is not approved by the FDA for use as a female contraceptive; and

2. The FDA-labeled indication for Ganirelix is not equivalent to a method of female contraception.

B. STATEMENT OF GROUNDS

Clarification of the scope of the FDA-approved indication is essential to correct positions taken by Organon that may significantly mislead physicians and patients as to the intended and approved use for the Ganirelix product.

1. Background

The FDA has approved NDA No. 021-057 held by Organon for the use of Ganirelix as a fertility treatment for women. As discussed, Ganirelix "is indicated for the inhibition of premature LH surges in women undergoing controlled ovarian hyperstimulation."

Sun filed Abbreviated New Drug Application ("ANDA") No. 204-246 seeking FDA approval to manufacture and sell a generic version of Ganirelix. As required, Sun's labeling is materially identical to Organon's labeling for Ganirelix.

The Orange Book currently lists two patents, including U.S. Patent Nos. 5,767,082 ("the '082 patent") held by Roche Palo Alto LLC. Organon, its parent (Merck & Co., Inc.) along with the patent holders (collectively, "Organon") have sued Sun for patent infringement, and the case is pending in the District of New Jersey, Case No. 3:12 CV 5374 (FLW) (DEA). In that lawsuit, Organon alleges that Sun's ANDA infringes both patents, which purport to cover certain methods of treatment.

The district court is currently deciding whether the asserted method in the '082 patent is limited in scope to a method of female contraception, as Sun contends. To preserve a claim of infringement under Sun's proposed construction, Organon is representing that the FDA *has* approved the use of Ganirelix for contraception.

First, Organon represented (through counsel) to Judge Douglas E. Arpert that they have a good faith basis for refusing to admit the following request for admission propounded by Sun: "Admit that Plaintiffs' Ganirelix Acetate Injection product is not approved by the FDA for use as

a contraceptive." Based on that representation, Judge Arpert refused to compel an admission to Sun's request.

Second, Organon submitted an expert report from Dr. Zev Rosenwaks—who has served as a consultant for Organon and Merck. This report offers an opinion that the FDA-approved indication for Ganirelix is equivalent to a method of female contraception. For instance, in his report, Dr. Rosenwaks says:

- "In my opinion, the function of using Sun's ganirelix acetate injection according to its label is substantially the same as the function of administering ganirelix acetate as a method of female contraception."

- "In my opinion, the way that ganirelix blocks ovulation is substantially the same when ganirelix is used in a method of inhibiting premature LH surges in women undergoing controlled ovarian hyperstimulation and in a method of female contraception."

- "In my opinion, the result achieved by administering ganirelix as a method of contraception and the result achieved by using ganirelix as a method of inhibiting premature LH surges in women undergoing controlled ovarian hyperstimulation are substantially the same."

2. The FDA Has Not Approved Ganirelix as a Method of Female Contraception.

The FDA-approved label for Ganirelix is clear—and it does not extend to a method of female contraception. Instead, it merely covers the method of inhibiting premature LH surges in women undergoing controlled ovarian hyperstimulation as a part of an *in vitro* fertilization regimen for women seeking to become pregnant. *See* Ex. 1 at Dosage and Administration.

Controlled ovarian hyperstimulation entails administering Follicular Stimulating Hormone (FSH), which stimulates the growth of ovarian follicles that develop eggs. In a natural menstrual cycle, FSH leads to the development of a single dominant follicle, which in turn leads to a progressive increase in estrogen levels. The rising estrogen levels may then lead to a sudden rise in Luteinizing Hormone levels (the LH surge), which lead to the final maturation and release of a single egg. Typically, FSH and LH work together to aid in reproduction. But administering exogenous FSH during controlled ovarian hyperstimulation may cause a surge in LH to occur too early, leading to the possible premature release of undeveloped eggs.

The FDA approved Ganirelix for the inhibition of such premature LH surges in women undergoing controlled ovarian hyperstimulation. The FDA-approved label for Ganirelix does not even mention use of the product as a contraceptive, much less designate contraception as an approved indication for the drug. Sun thus requests that the FDA confirm that Ganirelix is not approved by the FDA for use as a female contraceptive.

3. The FDA-Labeled Indication For Ganirelix Is Not Equivalent To A Method Of Female Contraception.

The FDA-approved indication for Ganirelix also is not equivalent to, nor otherwise substantially the same as, a method of female contraception. In fact, these are opposite treatments. Ganirelix is approved to help *promote* pregnancy, not *prevent* pregnancy. We thus ask the FDA to confirm this undeniable fact as well.

Again, the labeling for Ganirelix does not even use the term "contraceptive" or "contraception," much less discuss how the drug should be used for that purpose. Nor does the labeling information for Ganirelix suggest that it would be an effective contraceptive.

For example, the clinical studies reported in the label demonstrate its efficacy in promoting pregnancy rather than preventing it. *See* Ex. 1 at Clinical Studies. In a multicenter, double-blind, randomized, dose-finding study, Ganirelix was administered to 332 patients undergoing controlled ovarian hyperstimulation for *in vitro* fertilization. *Id.* at Table II. The study found that a 250 μg daily dosage of Ganirelix—the FDA-approved dosage—had the highest pregnancy and implantation rates among the patients. *Id.* The results of this clinical study clearly do not encourage physicians or patients to administer a 250 μg daily dosage of Ganirelix as a female contraceptive to prevent pregnancy but, instead, as part of a treatment regimen to induce pregnancy.

The recommended method of administration likewise anticipates using Ganirelix as a part of a treatment regimen for promoting pregnancy—not preventing pregnancy. *Id.* at Dosage and Administration. It is recommended that a Ganirelix injection be administered after initiating FSH therapy, and used to promote the growth of ovarian follicles that proceed to ovulation. The labeling further recommends co-administering FSH and Ganirelix daily until a sufficient number of follicles of adequate size are available for final maturation. Each of these steps promotes the development of mature eggs for potential fertilization, not female contraception. Thus, administering Ganirelix according to the recommended dosage and administration as set forth in the FDA-approved label would serve to enhance the opportunity for pregnancy rather than minimize the potential for pregnancy.

For these reasons, the FDA-approved labeling lends no support to Organon's claim that the FDA-approved label for Ganirelix essentially covers a method of female contraception and thus would encourage physicians to use Ganirelix as a safe and effective contraceptive. Nothing could be further from the truth. Sun thus requests that the FDA confirm that its labeled indication for Ganirelix is not equivalent to, nor substantially the same as, a method of female contraception.

4. The Broad Reading of the FDA-Approved Indication for Ganirelix Taken by Organon Raises Safety Concerns.

The logical extension of Organon's position is that the FDA has essentially reviewed and approved the use of Ganirelix for use as a female contraceptive, and thus the drug—either the branded drug or a generic—could be marketed as such. This is plainly not the case, thus raising concerns about misbranding and product safety. These concerns would be heightened if the Court were to adopt Organon's position and enter a ruling that holds the FDA-approved indication and the method of female contraception "are substantially the same." The FDA-approved label does not contain any precautions or references regarding safety and efficacy of Ganirelix as a contraceptive.

As the FDA is well aware, the Federal Food, Drug and Cosmetic Act prohibits drug manufacturers from distributing any drug that is misbranded. 21 U.S.C. § 331(a). A drug is misbranded if the labeling does not provide sufficient "directions under which the lay[person] can use a drug safely and for the purposes for which it is intended." 21 C.F.R. § 201.5. The intended purpose of a drug is a reference to the "objective intent of the persons legally responsible for labeling the drug." 21 C.F.R. § 201.128.

Organon is taking a transparently irresponsible position that the drug is labeled (or essentially labeled) for a method of female contraception. The FDA should thus clarify the limited scope of the approved indication for Ganirelix to avoid misbranding and off-label marketing.

C. ENVIRONMENTAL IMPACT

This petition involves a request for action by the FDA that is exempt from the requirement of an environmental impact statement according to 21 C.F.R. § 25.31(a), (c).

D. ECONOMIC IMPACT

Information on the economic impact of the action requested by this petition will be submitted if requested by the Commissioner pursuant to 21 C.F.R. § 10.30(b).

E. CERTIFICATION

Pursuant to 21 C.F.R. § 10.30(b), the undersigned certifies, 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 petitioner which are unfavorable to the petition.

Respectfully submitted,

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