U.S. FOOD & DRUG ADMINISTRATION

VIA UNITED PARCEL SERVICE

Paddock Laboratories, LLC
Attention: Maureen Rath
U.S. Agent for Perrigo Israel Pharmaceuticals Ltd.
Associate Director, Regulatory Affairs
3940 Quebec Avenue North
Minneapolis, Minnesota 55427

Dear Dr. Rath:

The U.S. Food and Drug Administration (FDA) has determined that Perrigo Israel Pharmaceuticals Ltd. ("Perrigo") failed to comply with the milestone dates in the timetable for completion of a postmarketing requirement (PMR) for Testosterone Gel 1%, under New Drug Application (NDA) 203098 (Testosterone Gel). Failure to comply with these milestone dates without demonstrating good cause for noncompliance is a violation of section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act (the Act) [21 U.S.C. 355] and renders Testosterone Gel misbranded under section 502(z) [21 U.S.C. 352(z)] of the Act.

This violation is concerning from a public health perspective, because failure to conduct the PMR impedes the evaluation of important information regarding the serious safety risk of major adverse cardiovascular events (MACE) associated with the use of your drug for testosterone replacement therapy (TRT) in men.

On February 9, 2015, FDA notified you of the requirement to complete the following PMR (originally, PMR (b) (4); now (b) (4)):

(b) (4) (b) (4)

TIMETABLE FOR COMPLETION

Final Protocol Submission:	June 2016
Trial Completion:	June 2021
Final Report Submission:	June 2022

U.S. Food & Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20903
www.fda.gov

Background

On February 9, 2015, FDA issued letters to all holders of NDAs approved for TRT products, notifying them of the requirement to conduct a PMR to assess the risk of MACE associated with TRT under section 505(o)(3) of the Act. Specifically, FDA determined that a clinical trial was needed to further evaluate the signal of a serious risk for MACE associated with the class of TRT products in men. FDA encouraged Perrigo to work with other holders of NDAs for TRT products to complete this required clinical trial/PMR.

On April 14, 2015, you responded to FDA and conveyed Perrigo's commitment to completing the postmarketing requirement.

In September 2017, FDA became aware of Perrigo's decision not to join the TRT Consortium.

On October 20, 2017, FDA notified Perrigo of its failure to comply with the Final Study Protocol Submission date; requested an explanation for Perrigo's noncompliance with the PMR timetable for completion; and reminded you of Perrigo's responsibility to complete the PMR, whether independent of the TRT Consortium or as part of the Consortium.

On November 20, 2017, FDA received your response to the Notification of Missed PMR Milestones Letter. Your written response requested that FDA "waive" Perrigo's responsibility for its PMR. You based your request on the following assertions:

- Membership in the TRT Consortium would pose an undue financial burden on Perrigo.

- Completion of (b) (4) independent of the TRT Consortium would pose an undue financial burden on Perrigo.

- Because Testosterone Gel is an AB-rated product, you assert that your product is equivalent to a generic and is not subject to this FDAAA PMR requirement; and that you should be responsible for labeling changes only, once the PMR is fulfilled by the TRT Consortium.

On January 19, 2018, FDA issued a letter notifying Perrigo of its failure to demonstrate good cause for noncompliance with the timetable of completion for (b) (4), because (1) the circumstance for the delay was under your control, and (2) the circumstance underlying the PMR noncompliance is not directly related to the milestone that was missed.

Conclusion and Requested Action

As the NDA holder of Testosterone Gel, your firm is subject to PMR (b) (4), including each of the milestones that constitute a timetable for completion, until a formal request to withdraw your NDA has been submitted and withdrawal of the NDA is published in the Federal Register.

Section 505(o)(3) applies to "an application under [section 505(b) of the Act] for a drug that is subject to section 503(b)" of the Act. Your NDA was submitted under section 505(b) of the Act and is for a drug that is subject to section 503(b) of the Act; therefore, you are subject to PMR (b) (4). Section 505(o)(3) is applicable to your product even if your product is therapeutically equivalent to another listed drug.

Your firm has failed to comply with the timetable for completion under section 505(o)(3)(E)(ii) of the Act, and has failed to demonstrate good cause for noncompliance with PMR (b) (4). Under section 502(z) of the Act, Testosterone Gel is considered misbranded within the meaning of the Act. The required postmarketing trial described above is considered to be in delayed status. The statuses of all postmarketing requirements are on the FDA Postmarketing Requirement and Commitments Web site at http://www.accessdata.fda.gov/scripts/cder/pmc/index.cfm.

Prominently identify your submission to your NDA with the following wording in bold, capital letters at the top of the first page, as follows:

PMR/PMC CORRESPONDENCE/GENERAL CORRESPONDENCE
OSI/RESPONSE TO UNTITLED LETTER

Please send a hard copy of the cover letter from your written response to the following address:

Attention: Hee (Sheila) Lianos
Office of Scientific Investigations
Food and Drug Administration
Building 51, Room 5337
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

If you have any questions regarding this letter, please call Hee Lianos, the PMR compliance officer for the Office of Scientific Investigations.

Sincerely yours,

{See appended electronic signature page}

David Burrow, Pharm.D., J.D.
Director
Office of Scientific Investigations
Office of Compliance
Center for Drug Evaluation and Research
Food and Drug Administration

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

DAVID C BURROW
06/15/2018