CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

202763Orig1s000

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

TEVA PHARMACEUTICALS

Philip Erickson, R.Ph.
Vice President, Regulatory Affairs

PATENT CERTIFICATION

TESTOSTERONE GEL, 1%

The undersigned certifies that to the best of our knowledge and in Teva Pharmaceuticals USA's opinion there is 1 listed patent which claims the reference drug Androgel® (Testosterone Gel) 1 %.

U.S. Patent #	Expiration Date	PED Expiration Date
#6,503,894	August 30, 2020	March 1, 2021

Paragraph IV Certification

The undersigned hereby certifies, pursuant to Section 505(b)(2)(A)(iv) of the Federal Food, Drug, and Cosmetic Act, as amended, that U.S. Patent 6,503,894 which was filed for Androgel® (Testosterone Gel) 1 %, is invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of the drug product for which this application is submitted. Teva Pharmaceuticals USA, the applicant, will give notice as required by 505(b)(3)(A)(i) and (ii) to Abbott Prods as the holder of NDA 021015 for Androgel® (Testosterone Gel) 1 % and to the assignee of the patent. This notice will include a detailed statement of the factual and legal basis of the applicant's opinion that the patent is invalid, unenforceable, or will not be infringed.

Philip Erickson
Vice President, Regulatory Affairs

December 30, 2010
Date

1090 Horsham Road, P.O. Box 1090, North Wales, PA 19454-1090
Phone: 215.591.3141 Fax: 215.591.8813 Email: philip.erickson@tevausa.com
www.tevausa.com

EXCLUSIVITY SUMMARY

NDA # 202763 SUPPL # HFD #

Trade Name N/A

Generic Name testosterone gel

Applicant Name Teva Pharmaceuticals, USA

Approval Date, If Known Febuary 14, 2012

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, and all efficacy supplements. Complete PARTS II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following questions about the submission.

a) Is it a 505(b)(1), 505(b)(2) or efficacy supplement?

YES ☒ NO ☐

If yes, what type? Specify 505(b)(1), 505(b)(2), SE1, SE2, SE3,SE4, SE5, SE6, SE7, SE8

505 (b) (2)

c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")

YES ☒ NO ☐

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

N/A

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

N/A

d) Did the applicant request exclusivity?

YES ☐ NO ☒

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

e) Has pediatric exclusivity been granted for this Active Moiety?

YES ☒ NO ☐

If the answer to the above question in YES, is this approval a result of the studies submitted in response to the Pediatric Written Request?

No

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS AT THE END OF THIS DOCUMENT.

2. Is this drug product or indication a DESI upgrade?

YES ☐ NO ☒

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES
(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES ☒ NO ☐

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA# *Please see attachment after the last page of this document

NDA#

NDA#

2. Combination product.

If the product contains more than one active moiety(as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES ☐ NO ☐

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA#

NDA#

NDA#

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. (Caution: The questions in part II of the summary should only be answered "NO" for original approvals of new molecular entities.)
IF "YES," GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDAs AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2 was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES ☒ NO ☐

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES ☒ NO ☐

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 8:

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES ☐ NO ☒

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES ☐ NO ☒

If yes, explain:

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES ☐ NO ☒

If yes, explain:

(c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

BE study #70343
Study # CRI-00018704: Hand washing study
Study # M1FX10001: Transfer study
Study # 10936025:Skin irritation study

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1	YES ☐	NO ☒
Investigation #2	YES ☐	NO ☒
Investigation #3	YES ☐	NO ☒
Investigation #4	YES ☐	NO ☒

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

b) For each investigation identified as "essential to the approval", does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1	YES ☐	NO ☒
Investigation #2	YES ☐	NO ☒
Investigation #3	YES ☐	NO ☒

Investigation #4 YES ☐ NO ☒

If you have answered "yes" for one or more investigation, identify the NDA in which a similar investigation was relied on:

c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

BE study #70343
Study # CRI-00018704: Hand washing study
Study # M1FX10001: Transfer study
Study # 10936025:Skin irritation study

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1 !
!
IND # YES ☒ ! NO ☐
! Explain:

Investigation #2 !
!
IND # YES ☐ ! NO ☐
! Explain:

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1 !

YES ☐	NO ☐
Explain:	Explain:
Investigation #2	
YES ☐	NO ☐
Explain:	Explain:

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES ☐ NO ☒

If yes, explain:

==========

Name of person completing form: Jeannie Roule
Title: Regulatory Health Project Manager
Date: February 14, 2012

Name of Office/Division Director signing form: Audrey Gassman, M.D.
Title: Acting Deputy Director

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05

Appl No	Proprietary Name
A083976	TESTRED
A080767	METHYLTESTOSTERONE
A084310	METHYLTESTOSTERONE
A086450	ANDROID 10
A087147	ANDROID 25
N020489	ANDRODERM
N021015 N022309	ANDROGEL 1% ANDROGEL 1.62%
N021454	TESTIM
A080911	TESTOPEL
N022504	AXIRON
N021463	FORTESTA
N021543	STRIANT
A090387	TESTOSTERONE CYPIONATE
A090387	TESTOSTERONE CYPIONATE
A040530	TESTOSTERONE CYPIONATE
A085635	DEPO-TESTOSTERONE
A085635	DEPO-TESTOSTERONE
A040615	TESTOSTERONE CYPIONATE
A040615	TESTOSTERONE CYPIONATE
A040652	TESTOSTERONE CYPIONATE
A086030	TESTOSTERONE CYPIONATE
N009165	DELATESTRYL
A040575	TESTOSTERONE ENANTHATE
A040647	TESTOSTERONE ENANTHATE
A085598	TESTOSTERONE ENANTHATE

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

/s/

JEANNIE M ROULE
02/14/2012

AUDREY L GASSMAN
02/14/2012

PEDIATRIC PAGE
(Complete for all filed original applications and efficacy supplements)

NDA/BLA#: 202763 Supplement Number: _____ NDA Supplement Type (e.g. SE5): _____

Division Name: DRUP PDUFA Goal Date: 11-14-11 Stamp Date: 01-14-11

Proprietary Name: _____

Established/Generic Name: testosterone gel 1%

Dosage Form: gel

Applicant/Sponsor: Teva Pharmaceuticals

Indication(s) *previously approved* (please complete this question for supplements and Type 6 NDAs only):
(1) _____
(2) _____
(3) _____
(4) _____

Pediatric use for each pediatric subpopulation must be addressed for each indication covered by current application under review. A Pediatric Page must be completed for each indication.

Number of indications for this pending application(s): 1
(Attach a completed Pediatric Page for each indication in current application.)

Indication: __ Replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone, including primary hypogonadism and hypogonadotropic or secondary hypogonadism.

Q1: Is this application in response to a PREA PMR? Yes ☐ Continue
No ☒ Please proceed to Question 2.

If Yes, NDA/BLA#: _____ Supplement #: _____ PMR #: _____

Does the division agree that this is a complete response to the PMR?

☐ Yes. Please proceed to Section D.

☐ No. Please proceed to Question 2 and complete the Pediatric Page, as applicable.

Q2: Does this application provide for (If yes, please check all categories that apply and proceed to the next question):

(a) NEW ☐ active ingredient(s) (includes new combination); ☐ indication(s); ☐ dosage form; ☐ dosing regimen; or ☐ route of administration?*

(b) ☒ No. PREA does not apply. **Skip to signature block.**

**** Note for CDER: SE5, SE6, and SE7 submissions may also trigger PREA.***

Q3: Does this indication have orphan designation?

☐ Yes. PREA does not apply. **Skip to signature block.**

☐ No. Please proceed to the next question.

Q4: Is there a full waiver for all pediatric age groups for this indication (check one)?

☐ Yes: (Complete Section A.)

☐ No: Please check all that apply:

☐ Partial Waiver for selected pediatric subpopulations (Complete Sections B)

☐ Deferred for some or all pediatric subpopulations (Complete Sections C)

☐ Completed for some or all pediatric subpopulations (Complete Sections D)

☐ Appropriately Labeled for some or all pediatric subpopulations (Complete Sections E)

☐ Extrapolation in One or More Pediatric Age Groups (Complete Section F)

existing appropriate labeling, this Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.

Section F: Extrapolation from Other Adult and/or Pediatric Studies (for deferred and/or completed studies)

Note: Pediatric efficacy can be extrapolated from adequate and well-controlled studies in adults and/or other pediatric subpopulations if (and only if) (1) the course of the disease/condition AND (2) the effects of the product are sufficiently similar between the reference population and the pediatric subpopulation for which information will be extrapolated. Extrapolation of efficacy from studies in adults and/or other children usually requires supplementation with other information obtained from the target pediatric subpopulation, such as pharmacokinetic and safety studies. Under the statute, safety cannot be extrapolated.

Pediatric studies are not necessary in the following pediatric subpopulation(s) because efficacy can be extrapolated from adequate and well-controlled studies in adults and/or other pediatric subpopulations:

Population		minimum	maximum	Extrapolated from:	
				Adult Studies?	Other Pediatric Studies?
☐	Neonate	__ wk. __ mo.	__ wk. __ mo.	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐
☐	All Pediatric Subpopulations	0 yr. 0 mo.	16 yr. 11 mo.	☐	☐

Are the indicated age ranges (above) based on weight (kg)? ☐ No; ☐ Yes.

Are the indicated age ranges (above) based on Tanner Stage? ☐ No; ☐ Yes.

Note: If extrapolating data from either adult or pediatric studies, a description of the scientific data supporting the extrapolation must be included in any pertinent reviews for the application.

If there are additional indications, please complete the attachment for each one of those indications. Otherwise, this Pediatric Page is complete and should be signed and entered into DFS or DARRTS as appropriate after clearance by PeRC.

This page was completed by:

{See appended electronic signature page}
Jeannie Roule *January 2011*
Regulatory Project Manager

(Revised: 6/2008)

1.3.3 Debarment Certification

Amendment Table of Contents

1.3.3 Debarment Certification
• Cipla Ltd.
• Teva Pharmaceuticals USA

TEVA PHARMACEUTICALS

Robert S. Vincent
Director, Regulatory Affairs

DEBARMENT CERTIFICATION

Teva Pharmaceuticals USA, hereby certifies that they did not and will not use in any capacity the services of any person debarred under subsection (a) or (b) [section 306 (a) or (b)], in connection with this application. [Section 306 (k) (1) of the Federal Food, Drug and Cosmetic Act {21 U.S.C. 335 a (k) (1)}.]

Teva Pharmaceuticals USA, hereby certifies that neither the applicant nor any affiliated person(s) responsible for the development or submission of this application have been convicted of any relevant crime or offense for which they are subject to debarment.

Robert S. Vincent
Director, Regulatory Affairs

March 24, 2011
Date

400 Chestnut Ridge Road, Woodcliff Lake, NJ 07677
Phone: 201.930.3610 Fax: 201.489.1403 Email: rob.vincent@tevausa.com
www.tevausa.com

Cipla
Cipla Ltd.
Mumbai Central
Mumbai 400 008. India

DEBARMENT CERTIFICATION

Section 306 (k) (1) Requirement

I, the undersigned, do hereby certify that Cipla Limited did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug & Cosmetic Act in connection with this application of **Testosterone gel 1% w/w.**

Section 306 (k) (2) Requirement

Cipla Limited has no relevant convictions to report for any persons (including contracted affiliations) responsible for the development of data or other information used to support this application of **Testosterone gel 1% w/w.**

Dr. S.M.Purandare

Head – Regulatory Affairs

24/03/2011

Date

Phone : (9122) 23082891, 23095521 Fax : (9122) 23070013, 23070393, 23070385, 23020297
E-mail : prc@cipla.com

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION[1]

NDA # 202763 BLA #	NDA Supplement # BLA STN #	If NDA, Efficacy Supplement Type:
Proprietary Name: N/A Established/Proper Name: testosterone gel Dosage Form: gel		Applicant: Teva Pharmaceuticals Agent for Applicant (if applicable):
RPM: Jeannie Roule		Division: Reproductive and Urologic Products

NDAs:
NDA Application Type: ☐ 505(b)(1) ☒ 505(b)(2)
Efficacy Supplement: ☐ 505(b)(1) ☐ 505(b)(2)

(A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). Consult page 1 of the 505(b)(2) Assessment or the Appendix to this Action Package Checklist.)

505(b)(2) Original NDAs and 505(b)(2) NDA supplements:
Listed drug(s) relied upon for approval (include NDA #(s) and drug name(s)):

Androgel 1%

Provide a brief explanation of how this product is different from the listed drug.

Different penetration enhancer

If no listed drug, explain.
- ☐ This application relies on literature.
- ☐ This application relies on a final OTC monograph.
- ☒ Other (explain) This drug relied on a RLD and literature

Two months prior to each action, review the information in the 505(b)(2) Assessment and submit the draft to CDER OND IO for clearance. Finalize the 505(b)(2) Assessment at the time of the approval action.

On the day of approval, check the Orange Book again for any new patents or pediatric exclusivity.

☒ No changes ☐ Updated Date of check:

If pediatric exclusivity has been granted or the pediatric information in the labeling of the listed drug changed, determine whether pediatric information needs to be added to or deleted from the labeling of this drug.

❖ Actions	
• Proposed action • User Fee Goal Date is February 14, 2012	☒ AP ☐ TA ☐ CR
• Previous actions *(specify type and date for each action taken)*	☐ None Review extension: 9/21/11

[1] The **Application Information** section is (only) a checklist. The **Contents of Action Package** section (beginning on page 5) lists the documents to be included in the Action Package.

❖ If accelerated approval or approval based on efficacy studies in animals, were promotional materials received? Note: Promotional materials to be used within 120 days after approval must have been submitted (for exceptions, see http://www fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf). If not submitted, explain _____	☐ Received
❖ Application Characteristics [2]	

Review priority: ☒ Standard ☐ Priority
Chemical classification (new NDAs only):

☐ Fast Track
☐ Rolling Review
☐ Orphan drug designation
☐ Rx-to-OTC full switch
☐ Rx-to-OTC partial switch
☐ Direct-to-OTC

NDAs: Subpart H
☐ Accelerated approval (21 CFR 314.510)
☐ Restricted distribution (21 CFR 314.520)
Subpart I
☐ Approval based on animal studies

BLAs: Subpart E
☐ Accelerated approval (21 CFR 601.41)
☐ Restricted distribution (21 CFR 601.42)
Subpart H
☐ Approval based on animal studies

☐ Submitted in response to a PMR
☐ Submitted in response to a PMC
☐ Submitted in response to a Pediatric Written Request

REMS: ☐ MedGuide
☐ Communication Plan
☐ ETASU
☐ REMS not required

Comments:

❖ BLAs only: Ensure *RMS-BLA Product Information Sheet for TBP* and *RMS-BLA Facility Information Sheet for TBP* have been completed and forwarded to OPI/OBI/DRM (Vicky Carter)	☐ Yes, dates
❖ BLAs only: Is the product subject to official FDA lot release per 21 CFR 610.2 *(approvals only)*	☐ Yes ☐ No
❖ Public communications *(approvals only)*	
• Office of Executive Programs (OEP) liaison has been notified of action	☒ Yes ☐ No
• Press Office notified of action (by OEP)	☒ Yes ☐ No
• Indicate what types (if any) of information dissemination are anticipated	☒ None ☐ HHS Press Release ☐ FDA Talk Paper ☐ CDER Q&As ☐ Other

[2] Answer all questions in all sections in relation to the pending application, i.e., if the pending application is an NDA or BLA supplement, then the questions should be answered in relation to that supplement, not in relation to the original NDA or BLA. For example, if the application is a pending BLA supplement, then a new *RMS-BLA Product Information Sheet for TBP* must be completed.

❖ Exclusivity	
• Is approval of this application blocked by any type of exclusivity?	☒ No ☐ Yes
• NDAs and BLAs: Is there existing orphan drug exclusivity for the "same" drug or biologic for the proposed indication(s)? *Refer to 21 CFR 316.3(b)(13) for the definition of "same drug" for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification.*	☒ No ☐ Yes If, yes, NDA/BLA # and date exclusivity expires:
• (b)(2) NDAs only: Is there remaining 5-year exclusivity that would bar effective approval of a 505(b)(2) application)? *(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)*	☒ No ☐ Yes If yes, NDA # and date exclusivity expires:
• (b)(2) NDAs only: Is there remaining 3-year exclusivity that would bar effective approval of a 505(b)(2) application? *(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)*	☒ No ☐ Yes If yes, NDA # and date exclusivity expires:
• (b)(2) NDAs only: Is there remaining 6-month pediatric exclusivity that would bar effective approval of a 505(b)(2) application? *(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)*	☒ No ☐ Yes If yes, NDA # and date exclusivity expires:
• NDAs only: Is this a single enantiomer that falls under the 10-year approval limitation of 505(u)? *(Note that, even if the 10-year approval limitation period has not expired, the application may be tentatively approved if it is otherwise ready for approval.)*	☒ No ☐ Yes If yes, NDA # and date 10-year limitation expires:
❖ Patent Information (NDAs only)	
• Patent Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought. If the drug is an old antibiotic, skip the Patent Certification questions.	☒ Verified ☐ Not applicable because drug is an old antibiotic.
• Patent Certification [505(b)(2) applications]: Verify that a certification was submitted for each patent for the listed drug(s) in the Orange Book and identify the type of certification submitted for each patent.	21 CFR 314.50(i)(1)(*i*)(A) ☒ Verified 21 CFR 314.50(i)(1) ☐ (ii) ☐ (iii)
• [505(b)(2) applications] If the application includes a **paragraph III** certification, it cannot be approved until the date that the patent to which the certification pertains expires (but may be tentatively approved if it is otherwise ready for approval).	☒ No paragraph III certification Date patent will expire
• [505(b)(2) applications] For **each paragraph IV** certification, verify that the applicant notified the NDA holder and patent owner(s) of its certification that the patent(s) is invalid, unenforceable, or will not be infringed (review documentation of notification by applicant and documentation of receipt of notice by patent owner and NDA holder). *(If the application does not include any paragraph IV certifications, mark "N/A" and skip to the next section below (*Summary Reviews*)).*	☐ N/A (no paragraph IV certification) ☒ Verified

Version: 8/25/10

- [505(b)(2) applications] For **each paragraph IV** certification, based on the questions below, determine whether a 30-month stay of approval is in effect due to patent infringement litigation.

  Answer the following questions for **each** paragraph IV certification:

  (1) Have 45 days passed since the patent owner's receipt of the applicant's notice of certification? ☒ Yes ☐ No

  (Note: The date that the patent owner received the applicant's notice of certification can be determined by checking the application. The applicant is required to amend its 505(b)(2) application to include documentation of this date (e.g., copy of return receipt or letter from recipient acknowledging its receipt of the notice) (see 21 CFR 314.52(e))).

  *If "**Yes**," skip to question (4) below. If "**No**," continue with question (2).*

  (2) Has the patent owner (or NDA holder, if it is an exclusive patent licensee) submitted a written waiver of its right to file a legal action for patent infringement after receiving the applicant's notice of certification, as provided for by 21 CFR 314.107(f)(3)? ☐ Yes ☐ No

  *If "**Yes**," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip the rest of the patent questions.*

  *If "**No**," continue with question (3).*

  (3) Has the patent owner, its representative, or the exclusive patent licensee filed a lawsuit for patent infringement against the applicant? ☐ Yes ☐ No

  (Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2))).

  *If "**No**," the patent owner (or NDA holder, if it is an exclusive patent licensee) has until the expiration of the 45-day period described in question (1) to waive its right to bring a patent infringement action or to bring such an action. After the 45-day period expires, continue with question (4) below.*

  (4) Did the patent owner (or NDA holder, if it is an exclusive patent licensee) submit a written waiver of its right to file a legal action for patent infringement within the 45-day period described in question (1), as provided for by 21 CFR 314.107(f)(3)? ☐ Yes ☒ No

  *If "**Yes**," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (*Summary Reviews*).*

  *If "**No**," continue with question (5).*

(5) Did the patent owner, its representative, or the exclusive patent licensee bring suit against the (b)(2) applicant for patent infringement within 45 days of the patent owner's receipt of the applicant's notice of certification? (Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)). If no written notice appears in the NDA file, confirm with the applicant whether a lawsuit was commenced within the 45-day period). *If "**No**," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (*Summary Reviews*).* *If "**Yes**," a stay of approval may be in effect. To determine if a 30-month stay is in effect, consult with the OND ADRA and attach a summary of the response.*	☒ Yes ☐ No

CONTENTS OF ACTION PACKAGE

❖ Copy of this Action Package Checklist[3]	2/14/12
Officer/Employee List	
❖ List of officers/employees who participated in the decision to approve this application and consented to be identified on this list *(approvals only)*	☒ Included
Documentation of consent/non-consent by officers/employees	☒ Included
Action Letters	
❖ Copies of all action letters *(including approval letter with final labeling)*	Action(s) and date(s)
Labeling	
❖ Package Insert *(write submission/communication date at upper right of first page of PI)*	
• Most recent draft labeling. If it is division-proposed labeling, it should be in track-changes format.	2/10/12
• Original applicant-proposed labeling	January 14, 2011
• Example of class labeling, if applicable	N/A

[3] Fill in blanks with dates of reviews, letters, etc.
Version: 8/25/10

❖ Medication Guide/Patient Package Insert/Instructions for Use/Device Labeling *(write submission/communication date at upper right of first page of each piece)*	☒ Medication Guide ☐ Patient Package Insert ☐ Instructions for Use ☐ Device Labeling ☐ None
• Most-recent draft labeling. If it is division-proposed labeling, it should be in track-changes format.	2/10/12
• Original applicant-proposed labeling	January 14, 2011
• Example of class labeling, if applicable	N/A
❖ Labels (**full color** carton and immediate-container labels) *(write submission/communication date on upper right of first page of each submission)*	
• Most-recent draft labeling	2/13/12
❖ Proprietary Name • Acceptability/non-acceptability letter(s) *(indicate date(s))* • Review(s) *(indicate date(s))*	N/A
❖ Labeling reviews *(indicate dates of reviews and meetings)*	☐ RPM ☒ DMEPA 11/4/11 ☒ DRISK 1/20/12 ☒ DDMAC 1/30/12 ☒ CSS 9/16/11 ☒ Other reviews SEALD 2/10/12
Administrative / Regulatory Documents	
❖ Administrative Reviews *(e.g., RPM Filing Review[4]/Memo of Filing Meeting) (indicate date of each review)*	RPM Filing review: 5/6/11
❖ All NDA (b)(2) Actions: Date each action cleared by (b)(2) Clearance Cmte ❖ NDA (b)(2) Approvals Only: 505(b)(2) Assessment *(indicate date)*	☐ Not a (b)(2) ☐ Not a (b)(2) 2/13/12
❖ NDAs only: Exclusivity Summary *(signed by Division Director)*	☒ Included
❖ Application Integrity Policy (AIP) Status and Related Documents http://www fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm	
• Applicant is on the AIP	☐ Yes ☒ No
• This application is on the AIP o If yes, Center Director's Exception for Review memo *(indicate date)* o If yes, OC clearance for approval *(indicate date of clearance communication)*	☐ Yes ☐ No ☒ Not an AP action
❖ Pediatrics *(approvals only)* • Date reviewed by PeRC _____ If PeRC review not necessary, explain: PREAA does not apply to this application • Pediatric Page/Record *(approvals only, must be reviewed by PERC before finalized)*	☒ Included
❖ Debarment certification (original applications only): verified that qualifying language was not used in certification and that certifications from foreign applicants are cosigned by U.S. agent *(include certification)*	☒ Verified, statement is acceptable

[4] Filing reviews for scientific disciplines should be filed behind the respective discipline tab.
Version: 8/25/10

❖ Outgoing communications *(letters (except action letters), emails, faxes, telecons)*	2/6/12, 2/3/12, 2/1/12, 1/13/12, 12/19/11, 11/8/11, 9/6/11, 8/4/11, 8/2/11, 7/28/11, 7/19/11, 4/13/11, 3/28/11, 1/25/11
❖ Internal memoranda, telecons, etc.	N/A
❖ Minutes of Meetings	
• Regulatory Briefing *(indicate date of mtg)*	☒ No mtg
• If not the first review cycle, any end-of-review meeting *(indicate date of mtg)*	☒ N/A or no mtg
• Pre-NDA/BLA meeting *(indicate date of mtg)*	☒ No mtg
• EOP2 meeting *(indicate date of mtg)*	☒ No mtg
• Other milestone meetings (e.g., EOP2a, CMC pilots) *(indicate dates of mtgs)*	N/A
❖ Advisory Committee Meeting(s)	☒ No AC meeting
• Date(s) of Meeting(s)	
• 48-hour alert or minutes, if available *(do not include transcript)*	
Decisional and Summary Memos	
❖ Office Director Decisional Memo *(indicate date for each review)*	☒ None
Division Director Summary Review *(indicate date for each review)*	☒ None 2/14/12
Cross-Discipline Team Leader Review *(indicate date for each review)*	☒ None 2/10/12
PMR/PMC Development Templates *(indicate total number)*	☐ None One PMR 2/14/12
Clinical Information[5]	
❖ Clinical Reviews	
• Clinical Team Leader Review(s) *(indicate date for each review)*	2/10/12 (see CDTL)
• Clinical review(s) *(indicate date for each review)*	2/25/11, 1/26/12
• Social scientist review(s) (if OTC drug) *(indicate date for each review)*	☐ None
❖ Financial Disclosure reviews(s) or location/date if addressed in another review OR If no financial disclosure information was required, check here ☐ and include a review/memo explaining why not *(indicate date of review/memo)*	
❖ Clinical reviews from immunology and other clinical areas/divisions/Centers *(indicate date of each review)*	☒ None
❖ Controlled Substance Staff review(s) and Scheduling Recommendation *(indicate date of each review)*	☐ Not applicable 9/16/11
❖ Risk Management • REMS Documents and Supporting Statement *(indicate date(s) of submission(s))* • REMS Memo(s) and letter(s) *(indicate date(s))* • Risk management review(s) and recommendations (including those by OSE and CSS) *(indicate date of each review and indicate location/date if incorporated into another review)*	1/14/11 and 2/03/12 ☐ None
❖ DSI Clinical Inspection Review Summary(ies) *(include copies of DSI letters to investigators)*	☒ None requested

[5] Filing reviews should be filed with the discipline reviews.

Clinical Microbiology ☐ None	
❖ Clinical Microbiology Team Leader Review(s) *(indicate date for each review)*	☒ None
Clinical Microbiology Review(s) *(indicate date for each review)*	☒ None
Biostatistics ☐ None	
❖ Statistical Division Director Review(s) *(indicate date for each review)*	☐ None
Statistical Team Leader Review(s) *(indicate date for each review)*	☐ None
Statistical Review(s) *(indicate date for each review)*	☐ None 1/24/12 and 3/7/11
Clinical Pharmacology ☐ None	
❖ Clinical Pharmacology Division Director Review(s) *(indicate date for each review)*	☐ None
Clinical Pharmacology Team Leader Review(s) *(indicate date for each review)*	☐ None
Clinical Pharmacology review(s) *(indicate date for each review)*	☒ None 2/9/12, 1/19/12 and 3/15/11
❖ DSI Clinical Pharmacology Inspection Review Summary *(include copies of DSI letters)*	☐ None 7/1/11
Nonclinical ☐ None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) *(indicate date for each review)*	☐ None
• Supervisory Review(s) *(indicate date for each review)*	☐ None
• Pharm/tox review(s), including referenced IND reviews *(indicate date for each review)*	☒ None 9/30/11 and 2/25/11
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer *(indicate date for each review)*	☐ None
❖ Statistical review(s) of carcinogenicity studies *(indicate date for each review)*	☒ No carc
❖ ECAC/CAC report/memo of meeting	☐ None Included in P/T review, page
❖ DSI Nonclinical Inspection Review Summary *(include copies of DSI letters)*	☒ None requested
Product Quality ☐ None	
❖ Product Quality Discipline Reviews	
• ONDQA/OBP Division Director Review(s) *(indicate date for each review)*	☐ None
• Branch Chief/Team Leader Review(s) *(indicate date for each review)*	☐ None
• Product quality review(s) including ONDQA biopharmaceutics reviews *(indicate date for each review)*	☐ None 2/9/12, 12/14/11, 9/11/11, 3/9/11
❖ Microbiology Reviews ☐ NDAs: Microbiology reviews (sterility & pyrogenicity) (OPS/NDMS) *(indicate date of each review)* ☐ BLAs: Sterility assurance, microbiology, facilities reviews (DMPQ/MAPCB/BMT) *(indicate date of each review)*	☒ Not needed
❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer *(indicate date of each review)*	☒ None

❖ Environmental Assessment (check one) (original and supplemental applications)	
☒ Categorical Exclusion *(indicate review date)(all original applications and all efficacy supplements that could increase the patient population)*	Quality Review 12/14/11
☐ Review & FONSI *(indicate date of review)*	
☐ Review & Environmental Impact Statement *(indicate date of each review)*	
❖ Facilities Review/Inspection	
☐ NDAs: Facilities inspections (include EER printout) *(date completed must be within **2 years** of action date) (only original NDAs and supplements that include a new facility or a change that affects the manufacturing sites[6])*	Date completed: ☐ Acceptable ☐ Withhold recommendation ☒ Not applicable
☐ BLAs: TB-EER *(date of most recent TB-EER must be within **30 days** of action date) (original and supplemental BLAs)*	Date completed: ☐ Acceptable ☐ Withhold recommendation
❖ NDAs: Methods Validation *(check box only, do not include documents)*	☒ Completed ☐ Requested ☐ Not yet requested ☐ Not needed (per review)

[6] I.e., a new facility or a change in the facility, or a change in the manufacturing process in a way that impacts the Quality Management Systems of the facility.

Appendix to Action Package Checklist

An NDA or NDA supplemental application is likely to be a 505(b)(2) application if:

(1) It relies on published literature to meet any of the approval requirements, and the applicant does not have a written right of reference to the underlying data. If published literature is cited in the NDA but is not necessary for approval, the inclusion of such literature will not, in itself, make the application a 505(b)(2) application.
(2) **Or** it relies for approval on the Agency's previous findings of safety and efficacy for a listed drug product and the applicant does not own or have right to reference the data supporting that approval.
(3) **Or** it relies on what is "generally known" or "scientifically accepted" about a class of products to support the safety or effectiveness of the particular drug for which the applicant is seeking approval. (Note, however, that this does not mean *any* reference to general information or knowledge (e.g., about disease etiology, support for particular endpoints, methods of analysis) causes the application to be a 505(b)(2) application.)

Types of products for which 505(b)(2) applications are likely to be submitted include: fixed-dose combination drug products (e.g., heart drug and diuretic (hydrochlorothiazide) combinations); OTC monograph deviations(see 21 CFR 330.11); new dosage forms; new indications; and, new salts.

An efficacy supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2).

An efficacy supplement is a 505(b)(1) supplement if the supplement contains all of the information needed to support the approval of the change proposed in the supplement. For example, if the supplemental application is for a new indication, the supplement is a 505(b)(1) if:

(1) The applicant has conducted its own studies to support the new indication (or otherwise owns or has right of reference to the data/studies).
(2) **And** no additional information beyond what is included in the supplement or was embodied in the finding of safety and effectiveness for the original application or previously approved supplements is needed to support the change. For example, this would likely be the case with respect to safety considerations if the dose(s) was/were the same as (or lower than) the original application.
(3) **And** all other "criteria" are met (e.g., the applicant owns or has right of reference to the data relied upon for approval of the supplement, the application does not rely for approval on published literature based on data to which the applicant does not have a right of reference).

An efficacy supplement is a 505(b)(2) supplement if:

(1) Approval of the change proposed in the supplemental application would require data beyond that needed to support our previous finding of safety and efficacy in the approval of the original application (or earlier supplement), and the applicant has not conducted all of its own studies for approval of the change, or obtained a right to reference studies it does not own. For example, if the change were for a new indication AND a higher dose, we would likely require clinical efficacy data and preclinical safety data to approve the higher dose. If the applicant provided the effectiveness data, but had to rely on a different listed drug, or a new aspect of a previously cited listed drug, to support the safety of the new dose, the supplement would be a 505(b)(2).
(2) **Or** the applicant relies for approval of the supplement on published literature that is based on data that the applicant does not own or have a right to reference. If published literature is cited in the supplement but is not necessary for approval, the inclusion of such literature will not, in itself, make the supplement a 505(b)(2) supplement.
(3) **Or** the applicant is relying upon any data they do not own or to which they do not have right of reference.

If you have questions about whether an application is a 505(b)(1) or 505(b)(2) application, consult with your ODE's ADRA.

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

/s/

JEANNIE M ROULE
02/16/2012

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: February 13, 2012

TO: NDA 202763

THROUGH: Jeannie Roule

SUBJECT: Carton and Container edits

APPLICATION NUMBER: NDA 202763 (testosterone gel)

The Sponsor agreed that their February 7th version of their cartons and containers would be used for the Divisions final edits.

The final edits and other correspondences are attached.

Comments from DMEPA and CMC concerning the cartons and containers were emailed to the Sponsor.

Please see attached email correspondences for all of the details.

From:	Jane Frahn
To:	Roule, Jeannie
Cc:	Robert Vincent; Aglaye Metellus; Virginia Hogan
Subject:	Testosterone - NDA 202763
Date:	Friday, February 10, 2012 4:21:56 PM

Hi Jeannie:

After a discussion with my colleagues and per our conversation, please disregard the carton and packet labeling sent to you yesterday, February 9th. We are in agreement that the labeling sent to you previously, on February 7th, is the correct labeling to be considered for review.

Enjoy your weekend,

Jane

Jane A. Frahn
Teva Pharmaceuticals USA
Senior Manager, Regulatory Affairs

(201) 930-2231 Work
jane.frahn@tevapharm.com

400 Chestnut Ridge Road
Woodcliff Lake, NJ 07677

3 Pages of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

---

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

/s/

JEANNIE M ROULE
02/14/2012

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: February 6, 2012

TO: NDA 202763

THROUGH: Jeannie Roule

SUBJECT: Agreement to PMR dates

APPLICATION NUMBER: NDA 202763 (testosterone gel)

The Sponsor has agreed to the dates for the application site trial that will be completed as a PMR.

An application site washing clinical trial following application of testosterone gel to measure the amount of residual testosterone before and after washing the primary user's application site.

The timetable you submitted February 6, 2012, states that you will conduct this clinical trial according to the following schedule:

Final Protocol Submission:	May 2012
Trial Completion:	August 2012
Final Report Submission:	November 2012

Please see attached email correspondences for all of the details.

From: Aglaye Metellus [Aglaye.Metellus@tevapharm.com]
Sent: Monday, February 06, 2012 11:54 AM
To: Roule, Jeannie
Cc: Robert Vincent; Jane Frahn
Subject: RE: Testosterone draft labeling - ANDA 202763

Hi Jeannie,

I verified the dates with our Biopharm team & they confirmed the PMR dates listed below are acceptable. The CRO is currently working on the protocol - having the study complete and finalized report by November will not be a problem.

The requested labeling information will be sent in a separate email. Thanks

Regards,

Aglaye Metellus
Sr. Manager, Regulatory Affairs
Teva Pharmaceuticals USA
400 Chestnut Ridge Road
Woodcliff Lake, NJ 07677
Phone: (201) 930-2247
Fax: (201) 489-1350
E-mail: aglaye.metellus@tevapharm.com

From: Roule, Jeannie [mailto:Jeannie.Roule@fda.hhs.gov]
Sent: Monday, February 06, 2012 10:09 AM
To: Aglaye Metellus
Cc: Robert Vincent; Jane Frahn
Subject: RE: Testosterone draft labeling - ANDA 202763

Thank you. Most importantly, I need to know if the PMR dates for May 2012, August 2012 and November 2012 are okay. I am going to assume that because Teva originally agreed to 3, 6 and 9 months from the approval dates.

Regards,
Jeannie

From: Aglaye Metellus [mailto:Aglaye.Metellus@tevapharm.com]
Sent: Monday, February 06, 2012 10:05 AM
To: Roule, Jeannie
Cc: Robert Vincent; Jane Frahn
Subject: RE: Testosterone draft labeling - ANDA 202763

Hi Jeannie,

We will give you a call shortly to discuss the draft labeling.

Regards,

Aglaye Metellus
Sr. Manager, Regulatory Affairs
Teva Pharmaceuticals USA
400 Chestnut Ridge Road

Woodcliff Lake, NJ 07677
Phone: (201) 930-2247
Fax: (201) 489-1350
E-mail: aglaye.metellus@tevapharm.com

From: Robert Vincent [mailto:Robert.Vincent@tevapharm.com]
Sent: Monday, February 06, 2012 9:23 AM
To: Philip Erickson; Jill Pastore; Jean Zwicker; John Derstine; Aglaye Metellus; Demeitrius Sawickij; David DeCicco; Arthur Lawn; Cory Wohlbach; Jennifer Nikolaou; Jan Sluzalis; John Kovaleski
Subject: FW: Testosterone draft labeling - ANDA 202763

From: Roule, Jeannie[SMTP:JEANNIE.ROULE@FDA.HHS.GOV]
Sent: Monday, February 06, 2012 9:23:16 AM
To: Jane Frahn; Aglaye Metellus; Robert Vincent; FDA SharedMailbox
Subject: RE: Testosterone draft labeling - ANDA 202763
Auto forwarded by a Rule

Hello,

Would one of you kindly call me. I need to discuss a few things with you as soon a s possible.

Regards,
Jeannie

From: Jane Frahn [mailto:Jane.Frahn@tevapharm.com]
Sent: Friday, February 03, 2012 4:15 PM
To: Roule, Jeannie
Subject: Testosterone draft labeling - ANDA 202763

Hi Jeannie:

Here is the revised draft PI and its side-by-side to our previous draft labeling (WORD and pdf).

With best regards,

Jane

From: Roule, Jeannie [mailto:Jeannie.Roule@fda.hhs.gov]
Sent: Thursday, February 02, 2012 1:54 PM
To: Aglaye Metellus; Robert Vincent
Subject: Label and medguide

Reference ID: 3083103

Aglaye,

Please review the attached Label and Medguide. We are hoping that this will be the last round of negotiations so please make sure that the formatting is exact.

We would like this back no later than close of business on Monday, February 6 (or sooner).

Please confirm receipt of this email.

Thanks,
Jeannie

Jeannie Roule
Regulatory Project Manager
Division of Reproductive and Urologic Products
Center for Drug Evaluation and Research
Food and Drug Administration
Phone: (301) 796-2130 (main)
Direct Line: (301) 796-3993
Fax: (301) 796-9897
Email: jeannie.roule@fda.hhs.gov

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

/s/

JEANNIE M ROULE
02/06/2012
PMR dates agreed upon

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: February 3, 2012

TO: NDA 202763

THROUGH: Jeannie Roule

SUBJECT: DRISK comments/ REMS document

APPLICATION NUMBER: NDA 202763 (testosterone gel)

Comments from DRISK concerning the REMS document wee emailed to the Sponsor.

Please see attached email correspondences for all of the details.

The Division of Risk Management (DRISK) has completed their review of your proposed Risk Evaluation Mitigation Strategy (REMS) for the New Drug Application (NDA) 202763 submitted by Teva Pharmaceuticals January 13, 2011.

Your agreed upon REMS document is attached.

A Supporting Document was not provided in this proposed REMS submission.

Regarding your Assessment Plan:

Submit for review the detailed plan you propose to use to evaluate patients' understanding about the safe use of testosterone gel. You may submit the proposed plan after approval of the REMS, however submit it at least 90 days before you conduct the evaluation. Code the submission "REMS Correspondence." If the plan is to conduct the required assessment using a survey, make sure the submission includes all methodology and instruments used to evaluate the knowledge about the risks associated with and safe use of testosterone gel.

1. Recruit respondents using a multi-modal approach. For example, you might recruit respondents through physicians' offices, pharmacies, managed care providers, consumer panels, or on-line.

   Explain how often you perform non-respondent follow-up or reminders. If you use an incentive or honorarium, provide details on what is offered and the estimated dollar value.

   Explain how you select recruitment sites.

   Submit for review any recruitment advertisements.

2. Define the sample size and confidence interval associated with that sample size. Describe the rationale for your sample size.

3. Define the expected number of people to be contacted to obtain the proposed sample size, and how the sample is determined (selection criteria).

4. Ensure the sample is demographically representative of the population who use the drug (patients), regardless of the condition for which they use or prescribe it.

5. When possible and appropriate, ensure the sample is diverse in terms of age, race, ethnicity, sex, socio-economic status, education level, and geographically.

6. List the inclusion criteria for patients. For example, eligible *patient* respondents must be:

- Age 18 or older
- Currently taking testosterone gel or have taken the drug in the past 3 months
- Not currently participating in a clinical trial involving testosterone gel

Submit any screener instruments, and describe any quotas of sub-populations used.

7. Explain how you administer surveys and the intended frequency.
   Offer respondents multiple options for completing the survey. Be sure to include an option for the lower literacy population. For example, respondents might complete surveys online or through email, in writing or by mail, over the phone, and in person.

   Explain how you train surveyors.

8. Explain how you control for limitations or bias associated with the methodology and survey instrument(s).

9. Submit for review the introductory text used to inform respondents about the purpose of the survey.

   Tell potential respondents that their answers will not affect their ability to receive or take (patients testosterone gel, and that their answers and personal information will be kept confidential and anonymous.

10. Clarify in your methodology that respondents are eligible for one wave of the survey only.

11. Analyze results on an item-by-item or variable-by-variable basis. You may present the data using descriptive statistics, such as sample size, mean, standard deviation, median, minimum and maximum (for continuous variables), and frequency distributions (for categorical variables).

    You may stratify the data by any relevant variable, and also in aggregate.

12. Submit all methodology and instruments utilized with your assessments.

WITH REGARD TO THE PATIENT SURVEY INSTRUMENT:

13. The assessment evaluates the effectiveness of the REMS in achieving the goal by evaluating patients' knowledge of the serious risks associated with use of the drug. The assessment does not evaluate consumer comprehension of the Medication Guide.

14. Respondents should not be offered an opportunity to read or see the Medication Guide, Package Insert, or any other related educational materials again prior to taking the survey.

15. Submit for review the survey instruments (questionnaires and/or moderator's guide), including any background information on testing survey questions and correlation to the messages in the Medication Guide.

16. Ensure the patient knowledge survey includes questions that ask about the specific risks or safety information conveyed in the Medication Guide to determine if the patient understands the information and knows what to do if they experience an adverse event.

    Derive the risk-specific questions from information located in the "What is the Most Important Information I should know about testosterone gel?" section of the Medication Guide.

    Ensure the risk-specific questions are not biased or leading, and that multiple choice questions include an instruction to "select all that apply." Answer options should include an appropriate number of foils. Ensure that each question has an "I don't know" answer option.

    Randomize the order of the multiple choice responses on each survey.

17. Order questions so the risk-specific questions are asked first, followed by questions about receipt of the Medication Guide. Collect demographic questions last or as part of any screener questions.

    Do not allow respondents the opportunity or ability to go back to previous questions in the survey.

    Explain if and when any education will be offered for incorrect responses.

18. Include questions about receipt of the Medication Guide in the patient survey as a way to fulfill the obligation to report on the distribution of the Medication Guide.

19. Prior to the questions about receipt of the Medication Guide, include text that describes a Medication Guide. For example, Now we are going to ask you some questions about the Medication Guide you may have received with testosterone gel. The Medication Guide is a paper handout that contains important information about the risks associated with use of testosterone gel and how to use testosterone gel safely. Medication Guides always include the title "Medication Guide" followed by the word testosterone gel and its pronunciation. The Medication Guide usually has sections titled "What is the most important information I should know about testosterone gel," "What is testosterone gel," and "Who should not take testosterone gel."

20. Use the following (or similar) questions to assess receipt and use of the Medication Guide.

- Who gave you the Medication Guide for testosterone gel? (Select all that apply)
  - a) My doctor or someone in my doctor's office
  - b) My pharmacist or someone at the pharmacy
  - c) Someone else - please explain: _____
  - d) I did not get a Medication Guide for [Testosterone gel]

- Did you read the Medication Guide?
  - a) All,
  - b) Most,
  - c) Some,
  - d) None

- Did you understand what you read in the Medication Guide?
  - a) All,
  - b) Most,
  - c) Some,
  - d) None

- Did someone offer to explain to you the information in the Medication Guide?
  - a) Yes, my doctor or someone in my doctor's office
  - b) Yes, my pharmacist or someone at the pharmacy
  - c) Yes, someone else – please explain: _____
  - d) No

- Did you accept the offer? Yes or No

- Did you understand the explanation that was given to you?
  - a) All,
  - b) Most,
  - c) Some,
  - d) None

- Did or do you have any questions about the Medication Guide? Yes or No (If Yes, list your question(s) below) Note: Group/code this open text field prior to submitting to FDA

From: Roule, Jeannie
Sent: Friday, February 03, 2012 3:04 PM
To: 'Jane Frahn'; 'Aglaye Metellus'; Robert Vincent
Subject: REMS comments

Attachments: REMS comments from DRISK to Sponsor Feb 2012.doc; REMS doc from Sponsor Feb 2 2012.doc

Hello,

I have attached a word document that contains the comments concerning your REMS document that you have agreed to.
I have attached that document as well. The version that you sent back to me had deleted the top line. I have included it in this version.

Please accept the change and return the REMS document (only) back to me as soon as possible

Regards,
Jeannie


REMS comments from DRISK to Sp...


REMS doc from Sponsor Feb 2 20...

Jeannie Roule
Regulatory Project Manager
Division of Reproductive and Urologic Products
Center for Drug Evaluation and Research
Food and Drug Administration
Phone: (301) 796-2130 (main)
Direct Line: (301) 796-3993
Fax: (301) 796-9897
Email: jeannie.roule@fda.hhs.gov

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

/s/

JEANNIE M ROULE
02/03/2012

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: February 1, 2012

TO: NDA 202763

THROUGH: Jeannie Roule

SUBJECT: Comments from DMEPA and CMC reviewers concerning carton/container

APPLICATION NUMBER: NDA 202763 (testosterone gel)

The DMEPA and CMC reviewers requested that I send the attached comments to the Applicant concerning the carton and container.

Please see attached email correspondences for all of the details.

From: Roule, Jeannie
Sent: Wednesday, February 01, 2012 4:03 PM
To: Aglaye Metellus; Robert Vincent
Subject: NDA 202763 Carton and container

Dear Aglaye,

After some further review and discussion, we have some additional changes that need to be made to your carton/container. Please send the revised art work to me via email as soon as possible. Once there is a final agreement, you can submit them formally.

These comments are from CMC and DMEPA:

Regards,
Jeannie

Jeannie Roule
Regulatory Project Manager
Division of Reproductive and Urologic Products
Center for Drug Evaluation and Research
Food and Drug Administration
Phone: (301) 796-2130 (main)
Direct Line: (301) 796-3993
Fax: (301) 796-9897
Email: jeannie.roule@fda.hhs.gov

APPEARS THIS
WAY ON
ORIGINAL

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

/s/

JEANNIE M ROULE
02/01/2012

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: January 13, 2012

TO: NDA 202763

THROUGH: Jeannie Roule

SUBJECT: PMR dates from Applicant regarding Application site trial.

APPLICATION NUMBER: NDA 202763 (testosterone gel)

Please see attached email correspondences for all of the details.

From: Roule, Jeannie
Sent: Wednesday, January 04, 2012 2:39 PM
To: 'Robert Vincent'
Subject: NDA 202763 and Post Marketing Requirement (PMR)

Rob,

As a refresher this is what the Division had told you in your Filing letter:

> We note that there was no application site washing study conducted. We believe that a study evaluating the effect of washing on removing residual testosterone from the application site is necessary in addition to the hand-washing study. We believe that the application
> site washing study, conducted at 2 hours after application of the product, is needed to support labeling language indicating that washing the application site will limit the potential for interpersonal transfer. You may propose to conduct this study under the terms of a post
> marketing requirement.

The Division is requesting Teva Pharmaceutical's agreement to the following dates for the planned PMR:

Final Protocol Submission: 3 months from the approval date
Study/Trial Completion: 6 months from the approval date
Final Report Submission: 12 months from the approval date

Please let me know if this is acceptable.

Regards,
Jeannie

Jeannie Roule
Regulatory Project Manager
Division of Reproductive and Urologic Products
Center for Drug Evaluation and Research
Food and Drug Administration
Phone: (301) 796-2130 (main)
Direct Line: (301) 796-3993
Fax: (301) 796-9897
Email: jeannie.roule@fda.hhs.gov

From: Roule, Jeannie
Sent: Wednesday, January 11, 2012 1:06 PM
To: 'Robert Vincent'
Subject: NDA 202763

Rob,

Please see below regarding the application site study. Let me know if you have any questions.

Regards,
Jeannie

The Division believes that a study evaluating the effect of washing on removing residual testosterone from the application site is necessary in addition to the hand-washing study submitted. The application site washing study is needed to support labeling indicating that washing the application site will limit the potential for interpersonal transfer. In this study, post-dose control samples before washing should be collected (e.g., use one side as the control and the opposite side as the test) and the recovered testosterone before and after washing should be reported, respectively.

Jeannie Roule
Regulatory Project Manager
Division of Reproductive and Urologic Products
Center for Drug Evaluation and Research
Food and Drug Administration
Phone: (301) 796-2130 (main)
Direct Line: (301) 796-3993
Fax: (301) 796-9897
Email: jeannie.roule@fda.hhs.gov

From: Robert Vincent [Robert.Vincent@tevapharm.com]
Sent: Thursday, January 12, 2012 6:26 PM
To: Roule, Jeannie; FDA SharedMailbox
Cc: Gregg DeRosa; Yatindra Joshi; Philip Erickson
Subject: RE: NDA 202763 and Post Marketing Requirement (PMR)

Importance: High

Jeannie,

Regarding the Post Marketing Requirement delineated below, Teva agrees to perform this study and to adhere to the time line set forth in your e-mail. To reiterate, Teva will prepare and submit a final study protocol no later than 3 months from the issuance of final approval of NDA 202763. Additionally, the requisite study is to be completed no later than 6 months and the final study report to be submitted to the application no later than 12 months, each taken from the date of final approval of NDA 202763.

As previously discussed, response to this e-mail message was requested. If a formal submission/amendment to the NDA is desired, please let me know and a written correspondence will be provided.

Regards,

Rob

From: Roule, Jeannie [mailto:Jeannie.Roule@fda.hhs.gov]
Sent: Wednesday, January 04, 2012 2:39 PM
To: Robert Vincent; FDA SharedMailbox
Subject: NDA 202763 and Post Marketing Requirement (PMR)

Rob,

As a refresher this is what the Division had told you in your Filing letter:

e note that there was no application site washing study conducted. We believe that a study evaluating the effect of washing on removing residual testosterone from the application site is necessary in addition to the hand-washing study. We believe that the application
e washing study, conducted at 2 hours after application of the product, is needed to support labeling language indicating that washing the application site will limit the potential for interpersonal transfer. You may propose to conduct this study under the terms of a post
arketing requirement.

The Division is requesting Teva Pharmaceutical's agreement to the following dates for the planned PMR:

Final Protocol Submission: 3 months from the approval date
Study/Trial Completion: 6 months from the approval date

Final Report Submission: 12 months from the approval date

Please let me know if this is acceptable.

Regards,
Jeannie

Jeannie Roule
Regulatory Project Manager
Division of Reproductive and Urologic Products
Center for Drug Evaluation and Research
Food and Drug Administration
Phone: (301) 796-2130 (main)
Direct Line: (301) 796-3993
Fax: (301) 796-9897
Email: jeannie.roule@fda.hhs.gov

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

/s/

JEANNIE M ROULE
01/13/2012

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: December 19, 2011

TO: NDA 202763

THROUGH: Jeannie Roule

SUBJECT: IR request from DMEPA and CMC reviewers

APPLICATION NUMBER: NDA 202763 (testosterone gel)

The DMEPA and CMC reviewers requested that I send the attached Information Request to the Applicant concerning the carton and container.

Please see attached email correspondences for all of the details.

Roule, Jeannie

From: Robert Vincent [Robert.Vincent@tevapharm.com]
Sent: Monday, December 19, 2011 2:47 PM
To: Roule, Jeannie
Cc: Jan Sluzalis; Regulatory_To_Legal
Subject: RE: Carton and Container

Jeannie,

By way of this e-mail I am confirming receipt of the comments from DMEPA and CMC reviewers concerning the carton and container.

Regards,

Rob

Robert Vincent
Director, Regulatory Affairs
Tel NW 215 591 3144
Email:
robert.vincent@tevapharm.com

From: Roule, Jeannie [mailto:Jeannie.Roule@fda.hhs.gov]
Sent: Monday, December 19, 2011 2:32 PM
To: Robert Vincent; FDA SharedMailbox
Subject: Carton and Container

Rob,

The DMEPA and CMC reviewers have a few more comments concerning your carton and container.
Please confirm receipt of this email.

Summary
Improve the strength differentiation and prominence of the strength statement by utilizing the colors (red or green) to highlight the different strengths.

(b) (4)

[redacted]

Regards,
Jeannie

Jeannie Roule
Regulatory Project Manager
Division of Reproductive and Urologic Products
Center for Drug Evaluation and Research
Food and Drug Administration
Phone: (301) 796-2130 (main)
Direct Line: (301) 796-3993
Fax: (301) 796-9897
Email: jeannie.roule@fda.hhs.gov

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

/s/

JEANNIE M ROULE
12/19/2011

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 202763 **INFORMATION REQUEST**

Teva Pharmaceuticals USA
Attention: Robert S. Vincent
Director, Regulatory Affairs
400 Chestnut Ridge Road
Woodcliff Lake, NJ 07677

Dear Mr. Vincent:

Please refer to your New Drug Application (NDA) dated January 13, 2011, received January 14, 2011, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for testosterone gel 1%.

In collaboration with the Division of Medication Errors Prevention and Assessment (DMEPA) in the Office of Surveillance and Epidemiology (OSE), we have the following comments related to your proposed container/carton labeling. Your prompt response to these comments is requested.

1. For both Container Labels and Carton Labeling:

   a. Revise the presentation of the established name (b) (4) Title Case to improve readability. In addition, revise the presentation of the strength, (b) (4) to *xx mg of testosterone per packet*. Thus the presentation of the established name and strength should appear as follows:

      Testosterone Gel
      xx mg of testosterone per packet*

      *Each packet contains x g of gel

   b. Add a statement to the principal display panel that Testosterone Gel is not interchangeable with other topical testosterone products.

   c. (b) (4)

2. For the Container Label, only:

   a. Revise the statement, *Used packets should be discarded* (b) (4), to read as follows:

      Discard used packets in household trash

   b. Add the statement, *For Topical Use Only*, to the principal display panel.

   c. Add a bar code to be in compliance with 21 CFR 201.25.

3. For the Carton Labeling, only:

   a. Relocate the statement, *For Topical Use Only*, (b) to the principal display panel.

   b. Revise the Medication Guide Statement to read:

      Dispense the enclosed Medication Guide to each patient.

If you have any questions, call Jeannie Roule, Regulatory Project Manager at (301) 796-3993.

Sincerely,

{See appended electronic signature page}

Jennifer Mercier
Chief, Project Management Staff
Division of Reproductive and Urologic Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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

/s/

JENNIFER L MERCIER
11/08/2011

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: October 12, 2011

TO: NDA 202763

THROUGH: Jeannie Roule

SUBJECT: IR request from Clinical Pharmacology reviewer

APPLICATION NUMBER: NDA 202763 (testosterone gel)

The Clinical Pharmacology reviewer requested that I send the attached Information Request to the Applicant.

Please see attached email correspondences for all of the details.

Roule, Jeannie

From: Roule, Jeannie
Sent: Wednesday, October 12, 2011 9:51 AM
To: 'Robert Vincent'; 'Aglaye Metellus'
Subject: NDA 202763 and request for information

Dear Rob and Aglaye,

Please respond to the question below as soon as possible.

Thanks,
Jeannie

*In the September 14, 2011 response, it was noted that you did not report the pharmacokinetics (PK) and bioequivalence (BE) analysis results for the baseline **uncorrected** testosterone based on the reintegration of the chromatograms with the exclusion of the 6 subjects under question.*

The Division requests that you do the following:

- *Submit the PK and statistical results for the baseline **uncorrected** testosterone based on the reintegration of the chromatograms for **all** subjects that completed the study*
- *Submit the BE analysis results for baseline **uncorrected** testosterone based on the reintegration of the chromatograms with exclusion of the 6 subjects under question*

Jeannie Roule
Regulatory Project Manager
Division of Reproductive and Urologic Products
Center for Drug Evaluation and Research
Food and Drug Administration
Phone: (301) 796-2130 (main)
Direct Line: (301) 796-3993
Fax: (301) 796-9897
Email: jeannie.roule@fda.hhs.gov

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

/s/

JEANNIE M ROULE
10/19/2011

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: September 21, 2011

TO: NDA 202763

THROUGH: Jeannie Roule

SUBJECT: IR request from CMC reviewer

APPLICATION NUMBER: NDA 202763 (testosterone gel)

The CMC reviewer requested that I send the attached Information Request to the Applicant.

Please see attached email correspondences for all of the details.

Roule, Jeannie

From: Roule, Jeannie
Sent: Wednesday, September 21, 2011 3:33 PM
To: 'Robert Vincent'
Cc: 'Aglaye Metellus'
Subject: NDA 202763

Dear Rob,

Below is a request from the CMC reviewer. Please confirm receipt.

- In the amendment submitted on Sep 14, 2011, it is noted that the drug product specification has been revised to include an acceptance criterion for (b) (4) to be NMT (b) (4) Since historical batch data provided in the NDA shown that the maximum individual related substance in the drug product is less than (b) (4) please revise the acceptance criterion for (b) (4) to be (b) (4)

Thanks,
Jeannie

Jeannie Roule
Regulatory Project Manager
Division of Reproductive and Urologic Products
Center for Drug Evaluation and Research
Food and Drug Administration
Phone: (301) 796-2130 (main)
Direct Line: (301) 796-3993
Fax: (301) 796-9897
Email: jeannie.roule@fda.hhs.gov

Roule, Jeannie

From: Roule, Jeannie
Sent: Wednesday, September 21, 2011 3:30 PM
To: Ge, Zhengfang
Subject: RE: NDA 202763: request fro the change of DP specification

I will send this to the Sponsor

From: Ge, Zhengfang
Sent: Wednesday, September 21, 2011 3:19 PM
To: Roule, Jeannie
Cc: Christner, Donna; Rhee, Moo Jhong
Subject: FW: NDA 202763: request fro the change of DP specification

Hi, Jeannie:

Please send the following attached CMC request to the sponsor. Thanks

Zhengfang Ge, Ph.D.
ONDQA/DNDQAII/Branch IV
Food and Drug Administration
10903 New Hampshire Ave, Bldg 22, Rm 1483
Silver Spring, MD 20993-0002
Phone: 301-796-1358
Email: zhengfang.ge@fda.hhs.gov

From: Rhee, Moo Jhong
Sent: Wednesday, September 21, 2011 2:52 PM
To: Ge, Zhengfang
Subject: RE: NDA 202763: request fro the change of DP specification

Please proceed.

From: Ge, Zhengfang
Sent: Wednesday, September 21, 2011 1:39 PM
To: Rhee, Moo Jhong
Subject: NDA 202763: request fro the change of DP specification

Hi, Moo-Jhong:

I would like to ask Jeanie to send the following to the sponsor. Please let me know your comment. Thanks

- In the amendment submitted on Sep 14, 2011, it is noted that the drug product specification has been revised to include an acceptance criterion for (b) (4) to be NMT (b) (4) Since historical batch data provided in the NDA shown that the maximum individual related substance in the drug product is less than (b) (4) please revise the acceptance criterion for (b) (4) to be NMT (b) (4)

Zhengfang Ge, Ph.D.
ONDQA/DNDQAII/Branch IV
Food and Drug Administration
10903 New Hampshire Ave, Bldg 22, Rm 1483
Silver Spring, MD 20993-0002
Phone: 301-796-1358
Email: zhengfang.ge@fda.hhs.gov

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

/s/

JEANNIE M ROULE
09/21/2011

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 202763

REVIEW EXTENSION – MAJOR AMENDMENT

Teva Pharmaceuticals USA
Attention: Robert S. Vincent
Director, Regulatory Affairs
400 Chestnut Ridge Road
Woodcliff Lake, NJ 07677

Dear Mr. Vincent:

Please refer to your January 13, 2011, New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for testosterone gel 1%.

On September 14, 2011, we received your solicited major amendment to this application. This amendment contains a new clinical and statistical report for the pivotal bioequivalence study 70343, entitled "*Randomized, open-label, 2-way crossover, bioequivalence study of testosterone 1% topical gel formulation and Androgel (reference) following a 100 mg dose in hypogonadal volunteers".* The receipt date is within three months of the user fee goal date. Therefore, we are extending the goal date by three months to provide time for a full review of the submission. The extended user fee goal date is February 14, 2012.

In addition, we are establishing a new timeline for communicating labeling changes and/or postmarketing requirements/commitments in accordance with "PDUFA REAUTHORIZATION PERFORMANCE GOALS AND PROCEDURES – FISCAL YEARS 2008 THROUGH 2012." If major deficiencies are not identified during our review, we plan to communicate proposed labeling and, if necessary, any postmarketing requirement/commitment requests by January 14, 2012.

If you have any questions, call Jeannie Roule, Regulatory Project Manager at (301) 796-3993.

Sincerely,

{See appended electronic signature page}

Jennifer Mercier
Chief, Project Management Staff
Division of Reproductive and Urologic Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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

/s/

JENNIFER L MERCIER
09/21/2011

3 Page has been Withheld in Full as b4 (CCI/TS) immediately following this page

---

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

/s/

JENNIFER L MERCIER
09/06/2011
for Dr. Scott Monroe

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: August 2, 2011

TO: NDA 202763

THROUGH: Jeannie Roule

SUBJECT: IR request from the Clinical Review team

APPLICATION NUMBER: NDA 202763 (testosterone gel)

The Clinical reviewer requested that the attached Information Request be emailed to the Applicant.

Please see attached email correspondences for all of the details.

Roule, Jeannie

From: Hirsch, Mark S
Sent: Tuesday, August 02, 2011 11:01 AM
To: Roule, Jeannie
Cc: Fang, Guodong; Ge, Zhengfang; Christner, Donna
Subject: guodongBatchX045(MHAug2).doc

Attachments: guodongBatchX045(MHAug2).doc

guodongBatchX0
5(MHAug2).doc (

Hello Jeannie:
Dr. Fang and I have another information request for TEVA. It concerns clarifying the specific batches used in the skin irritiation study. Our request is attached. Please send this request to Sponsor ASAP and ask that they respond ASAP.

Thank you very much,
Mark

Roule, Jeannie

From: Roule, Jeannie
Sent: Tuesday, August 02, 2011 11:39 AM
To: 'Aglaye Metellus'; Robert Vincent
Subject: Information request

Aglaye and Rob,

We have a question for you regarding the batches used in the **Skin Irritation and Sensitization Study (Study 10936025)**

The final study report for the skin irritation and sensitization study (Study 10936025) states (on page 4 of the study synopsis) that Batch X045 was used in the study.

However, in your July 29, 2011, submission (eCTD submission 007), in response to our Comment #2, you state that Batch X028 and Batch X145 were used in the clinical studies, and that Batch X045 was not used in any studies that support the NDA.

In order to resolve this discrepancy, we request that you submit evidence from source documents to clarify which batches were used in Study 10936025. If the study report for Study 10936025 erroneously lists Batch X045 as the clinical material used in the study, please state clearly that the study report is in error.

Please confirm receipt of this email and respond as soon as possible.

Regards,
Jeannie

Jeannie Roule
Regulatory Project Manager
Division of Reproductive and Urologic Products
Center for Drug Evaluation and Research
Food and Drug Administration
Phone: (301) 796-2130 (main)
Direct Line: (301) 796-3993
Fax: (301) 796-9897
Email: jeannie.roule@fda.hhs.gov

Roule, Jeannie

From: Aglaye Metellus [Aglaye.Metellus@tevapharm.com]
Sent: Thursday, August 04, 2011 8:13 AM
To: Roule, Jeannie
Subject: RE: Confirm receipt

Hi Jeannie,

I received the below email notification. Thanks

Regards,

Aglaye Metellus
Sr. Manager, Regulatory Affairs
Teva Pharmaceuticals USA
400 Chestnut Ridge Road
Woodcliff Lake, NJ 07677
Phone: (201) 930-2247
Fax: (201) 489-1350
E-mail: aglaye.metellus@tevapharm.com

From: Roule, Jeannie [mailto:Jeannie.Roule@fda.hhs.gov]
Sent: Wednesday, August 03, 2011 3:27 PM
To: Aglaye Metellus
Subject: Confirm receipt

Dear Aglaye,

Would you kindly confirm receipt of the email (see below) that I sent you yesterday.

Thanks,
Jeannie

ıie
ust 02, 2011 11:39 AM
ıs'; Robert Vincent
ation request

Aglaye and Rob,

We have a question for you regarding the batches used in the **Skin Irritation and Sensitization Study (Study 10936025)**

The final study report for the skin irritation and sensitization study (Study 10936025) states (on page 4 of the study synopsis) that Batch X045 was used in the study.

However, in your July 29, 2011, submission (eCTD submission 007), in response to our Comment #2, you state that Batch X028 and Batch X145 were used in the clinical studies, and that Batch X045 was not used in any studies that support the NDA.

In order to resolve this discrepancy, we request that you submit evidence from source documents to clarify which batches were used in Study 10936025. If the study report for Study 10936025 erroneously lists Batch X045 as the clinical material used in the study, please state clearly that the study report is in

error.

Please confirm receipt of this email and respond as soon as possible.

Regards,
Jeannie

Jeannie Roule
Regulatory Project Manager
Division of Reproductive and Urologic Products
Center for Drug Evaluation and Research
Food and Drug Administration
Phone: (301) 796-2130 (main)
Direct Line: (301) 796-3993
Fax: (301) 796-9897
Email: jeannie.roule@fda.hhs.gov

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

/s/

JEANNIE M ROULE
08/04/2011

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 202763 **INFORMATION REQUEST**

Teva Pharmaceuticals USA
Attention: Robert S. Vincent
Director, Regulatory Affairs
400 Chestnut Ridge Road
Woodcliff Lake, NJ 07677

Dear Mr. Vincent:

Please refer to your New Drug Application (NDA) dated January 13, 2011, received January 14, 2011, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for testosterone gel 1%.

Reference is also made to the clinical and analytical inspections that were performed between June 6 and 21, 2011, by the Division of Bioequivalence and GLP Compliance (DBGC) at (b) (4) for your Study 70343, entitled, *"Randomized, Open-Label, Two-Way Crossover, Bioequivalence Study of Testosterone 1% Topical Gel Formulation and Androgel (Reference) Following a 100 mg Dose in Hypogonadal Male Volunteers."* Following the inspections, Form FDA-483 was issued to (b) (4) on June 21, 2011.

Reference is also made to a July 11, 2011, response by (b) (4) t to Observations 1 through 4 cited on the Form FDA-483.

We have completed our review of the (b) (4) response and have the following comments and requests for additional information:

Regarding (b) (4) response to Observation 1, documentation was not provided to confirm the retraining of "Technician 1." In addition, the response did not include source documentation for Table A, shown on pages 3 and 4. Thus, it is not clear how the reanalysis results shown in Table A were generated. In addition, we note that 8 of the 26 samples were reanalyzed by the same "Technician 1" that conducted the original analysis. Based on these deficiencies, we conclude that the (b) (4) response to Observation 1 does not adequately address the concern cited in the Form FDA-483.

Based on our continued concerns related to the Form FDA-483 observations, we request that you submit a revised study report for Study 70343, to include new bioequivalence (BE) analysis results using data generated from re-integrated chromatograms, but excluding data generated from 6 subjects in question (Subjects 60, 61, 62, 92, 93, and

94). You should also submit supporting documentation to explain how the chromatograms were re-integrated consistently (e.g., using a standard operating procedure [SOP]).

If you have any questions, call Jeannie Roule, Regulatory Project Manager at (301) 796-3993.

Sincerely,

{See appended electronic signature page}

Jennifer Mercier
Chief, Project Management Staff
Division of Reproductive and Urologic Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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

/s/

JENNIFER L MERCIER
08/02/2011

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: July 28, 2011

TO: NDA 202763

THROUGH: Jeannie Roule

SUBJECT: Letter of Authorization (LOA) from (b) (4) regarding an inspection report from the FDA

APPLICATION NUMBER: NDA 202763 (testosterone gel)

A LOA was requested so that the FDA could discuss with the Applicant (Teva Pharmaceuticals) the inspection report and 483 forms that were generated from an audit of Project 70343.

1 Page has been Withheld in Full as b4 (CCI/TS) immediately following this page

---

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

/s/

JEANNIE M ROULE
07/28/2011
LOA from (b) (4)

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 202763

INFORMATION REQUEST

Teva Pharmaceuticals USA
Attention: Robert S. Vincent
Director, Regulatory Affairs
400 Chestnut Ridge Road
Woodcliff Lake, NJ 07677

Dear Mr. Vincent:

Please refer to your New Drug Application (NDA) dated January 13, 2011, received January 14, 2011, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for testosterone gel 1%.

We are reviewing your submission and have the following comments and information requests. After you have received this letter, please contact us promptly, so that we can schedule a teleconference and discuss these issues in more detail.

- The proposed specification for isopropyl palmitate, [redacted] (b) (4) is too wide. The acceptance criteria for this component should be set based on the amount of isopropyl palmitate found in the drug product used at the time of the clinical trials. Since isopropyl palmitate is critical [redacted] (b) (4), the acceptance criteria for this component is expected to be set as for an active ingredient [redacted] (b) (4) of target) unless justification is provided. The average content of isopropyl palmitate for the drug product Batch X028 used in the bioequivalence (BE) study (Study 70343) was [redacted] (b) (4) w/w.

- Provide formulation information and release and stability data on Batch X045 that was used in the skin irritation and sensitization study (Study 10936025), if available, and for any other batches which were used in clinical studies.

- [redacted] (b) (4)

If you have any questions, call Jeannie Roule, Regulatory Project Manager at (301) 796-3993.

Sincerely,

{See appended electronic signature page}
Jennifer Mercier
Chief, Project Management Staff
Division of Reproductive and Urologic Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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

/s/

JENNIFER L MERCIER
05/26/2011

Memorandum (ONDQA Meeting Minutes)

Date: May 12, 2011
Participants: Zhengfang Ge, Ph.D., Reviewer
Donna Christner, Ph.D. CMC lead
Moo-Jhong Rhee, Ph.D., Branch Chief
Subject: Content variation (b) (4) isopropyl palmitate, in the drug products

Background:

The proposed drug products in this NDA are testosterone gel 1% supplied in sachets (2.5g and 5g) (b) (4). The proposed formulation of the products in (b) (4) package presentations containing the same amount of isopropyl palmitate (b) (4) (b) (4) (b) (4) as shown in the following Table:

Qualitative/Quantitative Composition

Ingredients	Function	Amount (gm) / 2.5 gm sachet	Amount (gm) / 5 gm sachet	(b) (4)	Amount (gm) / 1.25 gm Activation	Amount (% w/w)
Testosterone, USP	Active	0.025	0.05		0.0125	1.00
Dehydrated Alcohol, USP	(b) (4)	(b) (4)	(b) (4)		(b) (4)	(b) (4)
Carbomer Homopolymer Type C (b) (4)						
Isopropyl Palmitate, NF	(b) (4)					
Sodium Hydroxide, NF	(b) (4)					
Purified Water, USP						
Total:	-	**2.5**	**5.0**		**1.25**	**100**

(b) (4)

Quantity of isopropyl palmitate at the time of batch release

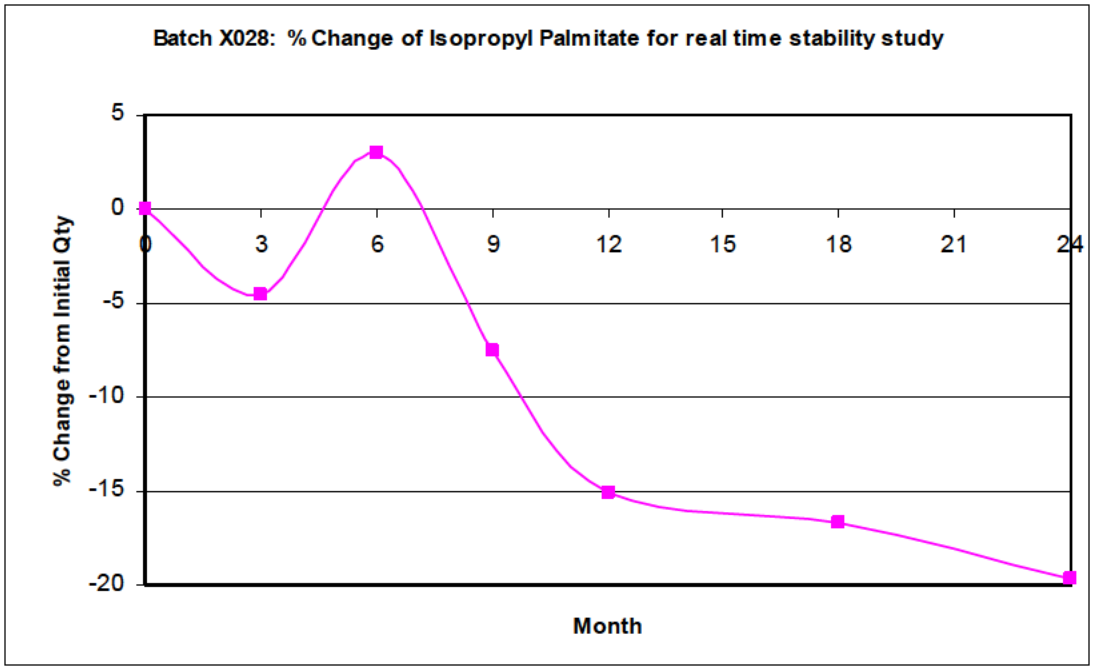
(b) (4)

The BE study was conducted using Batch X028 (5g sachets manufactured in February, 2008) during March, 2008 to November, 2008. Stability data for this batch shown that isopropyl palmitate decreased from (b) (4) after 24 months

storage under 25ºC/60%RH as shown below. Therefore, it is also questionable whether aged products in sachets are bioequivalent with the products used in the BE study. Since the average content of isopropyl palmitate during the BE study is (b) (4) the acceptance limits of the isopropyl palmitate for the drug product specification should be set within (b) (4)

Stability data of isopropyl palmitate for batch X028 (b) (4)

(b) (4)



Conclusion:

Based on in-depth discussion within CMC review team, it was decided to have a t-con with the sponsor to address this issue with the following requests:

1. Since the average content of isopropyl palmitate for the drug product batch X028 is (b) (4) during the BE study, your acceptance criteria for this component in the drug product specification should be set in the range of (b) (4) with a target at (b) (4).
2. (b) (4)

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

/s/

ZHENGFANG GE
05/13/2011

MOO JHONG RHEE
05/13/2011
Chief, Branch IV

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: April 8, 2011

TO: NDA 202763

THROUGH: Jeannie Roule

SUBJECT: IR request from ClinPharm

APPLICATION NUMBER: NDA 202763 (testosterone gel)

The Clinical Pharmacology reviewer requested that I send the attached Information Request to the Applicant.

Please see attached email correspondences for all of the details.

Roule, Jeannie

From: Robert Vincent [Rob.Vincent@tevausa.com]
Sent: Friday, April 08, 2011 12:00 PM
To: Roule, Jeannie
Cc: Philip Erickson; Jill Pastore; Aglaye Metellus
Subject: RE: NDA 202763 Testosterone Gel 1%

Dear Jeannie,

I confirm receipt of the below e-mail and am communicating this as appropriate within the Teva organization.

Regards,

Rob

From: Roule, Jeannie [mailto:Jeannie.Roule@fda.hhs.gov]
Sent: Friday, April 08, 2011 11:26 AM
To: Robert Vincent
Subject: NDA 202763 Testosterone Gel 1%

Dear Robert,

The Clinical Pharmacology reviewer has the following request for information:

Incurred sample reanalysis (ISR) is recommended to evaluate the accuracy of the incurred samples analyzed.

We note that ISR was only conducted in the Bioequivalence Study 70343 for 20 out of 4135 samples (i.e., approximately 0.5%) analyzed. The number of samples for ISR should equal to at least 5% of the total sample size. We request that you either submit additional ISR results or conduct additional ISR to ensure the reliability of the study data.

Please acknowledge receipt of this email and respond at your earliest convenience.

Regards,
Jeannie

From: Robert Vincent [mailto:Robert.Vincent@tevausa.com]
Sent: Wednesday, February 23, 2011 7:49 AM
To: Roule, Jeannie
Cc: Aglaye Metellus; Jill Pastore; Stephen Dobkowski
Subject: NDA 202763 Testosterone Gel 1%

RE: (b) (4) **202763**

Dear Jeannie,

On January , Teva Pharmaceuticals USA submitted an NDA containing a Paragraph IV certification for **Testosterone Gel 1%**. The purpose of this email is to request acceptance of our utilization of Federal Express tracking documentation as evidence of receipt of Notice of Certification by the NDA holder and patent assignees in lieu of USPS return receipt, in accord with 21 CFR 314.52(e).

Please let me know if this request is found acceptable.

Sincerely,

Robert S. Vincent
Director, Regulatory Affairs
TEVA Pharmaceuticals USA

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

/s/

JEANNIE M ROULE
04/13/2011

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 202763

FILING COMMUNICATION

Teva Pharmaceuticals USA
Attention: Robert S. Vincent
Director, Regulatory Affairs
400 Chestnut Ridge Road
Woodcliff Lake, NJ 07677

Dear Mr. Vincent:

Please refer to your New Drug Application (NDA) dated January 13, 2011, received January 14, 2011, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for testosterone gel 1%.

We also refer to your submission dated January 26, 2011.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, in accordance with 21 CFR 314.101(a), this application is considered filed 60 days after the date we received your application. The review classification for this application is **Standard**. Therefore, the user fee goal date is November 14, 2011.

We are reviewing your application according to the processes described in the Guidance for Review Staff and Industry: Good Review Management Principles and Practices for PDUFA Products. Therefore, we have established internal review timelines as described in the guidance, which includes the timeframes for FDA internal milestone meetings (e.g., filing, planning, midcycle, team and wrap-up meetings). Please be aware that the timelines described in the guidance are flexible and subject to change based on workload and other potential review issues (e.g., submission of amendments). We will inform you of any necessary information requests or status updates following the milestone meetings or at other times, as needed, during the process. If major deficiencies are not identified during the review, we plan to communicate proposed labeling and, if necessary, any postmarketing commitment requests by October 17, 2011.

During our filing review of your supplemental application, we identified the following potential review issues:

1. The bioequivalence study was conducted using the arms/shoulders only as the application site for all 100 mg of testosterone. The current approved labeling for AndroGel 1% calls for application of 100 mg of testosterone to both arms/shoulders as well as both sides of

the abdomen. Comment on whether this difference has any impact on the final determination of bioequivalence to the reference listed drug (RLD).

2. In the transfer study, you compared your testosterone gel to the RLD. We prefer that the primary analysis for this study be the comparison of PK parameters (Cmax and AUC) obtained from female partners at baseline to PK parameters obtained after the rubbing procedure with men who used your product, not a comparison of transferability between your product and the RLD. In order that we may conduct this analysis, submit the 24 hour baseline of total testosterone measured on Day -1 (with and without T-shirt) and compare the baseline and post-rubbing procedure PK parameters (C_{max} and AUC) for your product. This information should include the calculated percent difference between the baseline and the post-rubbing procedure PK parameters (C_{max} and AUC) for each individual.

3. In the hand-washing study, the measurement of residual testosterone on the subjects' hands prior to hand-washing, after applying the drug product to the application site, was not conducted. Therefore, it is not possible to calculate the percentage of the testosterone removed by the hand washing procedure (a "wash-off percentage"). Lacking a "wash-off percentage," explain how this study provides sufficient evidence to conclude that the product is largely removed from the hands by washing.

4. We note that there was no application site washing study conducted. We believe that a study evaluating the effect of washing on removing residual testosterone from the application site is necessary in addition to the hand-washing study. We believe that the application site washing study, conducted at 2 hours after application of the product, is needed to support labeling language indicating that washing the application site will limit the potential for interpersonal transfer. You may propose to conduct this study under the terms of a post-marketing requirement.

5. The lack of a formal trade name may engender a potential for medication errors. For example, there may be other testosterone transdermal products named "testosterone 1%" with different application sites compared to your product, and these could be erroneously dispensed in place of your product. Comment on the potential medication errors that may result from the lack of a tradename.

We also request that you submit the following information:

Pharmacology/Toxicology:

6. To meet the nonclinical requirements for an NDA under a 505(b)(2) application, submit scientific justification for your reliance on AndroGel's nonclinical data. In addition, submit published literature references to support the nonclinical sections of the labeling (Sections 8 and 13).

Chemistry Manufacturing and Controls:

7. Provide additional stability data by June 13, 2011.

We are providing the above comments to give you preliminary notice of potential review issues. Our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our review. Issues may be added, deleted, expanded upon, or modified as we review the application.

If you have not already done so, you must submit the content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. The content of labeling must be in the Prescribing Information (physician labeling rule) format. Please respond only to the above requests for additional information. While we anticipate that any response submitted in a timely manner will be reviewed during this review cycle, such review decisions will be made on a case-by-case basis at the time of receipt of the submission.

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We acknowledge receipt of your request for a full waiver of pediatric studies for this application. Once we have reviewed your request, we will notify you if the full waiver request is denied and a pediatric drug development plan is required.

If you have any questions, call Jeannie Roule, Regulatory Health Project Manager, at (301) 796-3993.

Sincerely,

{See appended electronic signature page}

George Benson, M.D.
Deputy Director
Division of Reproductive and Urologic Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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

/s/

GEORGE S BENSON
03/28/2011

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

TO *(Office/Division)*: Controlled Substance Staff
Corinne Moody

FROM (*Name, Office/Division, and Phone Number of Requestor)*:
Jeannie Roule, Regulatory Project Manager
Division of Reproductive and Urologic Products
(301) 796-3993

DATE	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
February 1, 2011		202763	edr	January 14, 2011

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
testosteroen gel 1%	Standard	Androgen	August 14, 2011

NAME OF FIRM: Teva Pharmaceuticals

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE / ADDITION
- ☐ MEETING PLANNED BY
- ☐ PRE-NDA MEETING
- ☐ END-OF-PHASE 2a MEETING
- ☐ END-OF-PHASE 2 MEETING
- ☐ RESUBMISSION
- ☐ SAFETY / EFFICACY
- ☐ PAPER NDA
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- ☐ OTHER *(SPECIFY BELOW)*:

II. BIOMETRICS

- ☐ PRIORITY P NDA REVIEW
- ☐ END-OF-PHASE 2 MEETING
- ☐ CONTROLLED STUDIES
- ☐ PROTOCOL REVIEW
- ☐ OTHER (SPECIFY BELOW):
- ☐ CHEMISTRY REVIEW
- ☐ PHARMACOLOGY
- ☐ BIOPHARMACEUTICS
- ☐ OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILTY STUDIES
- ☐ PHASE 4 STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL - BIOPHARMACEUTICS
- ☐ IN-VIVO WAIVER REQUEST

IV. DRUG SAFETY

- ☐ PHASE 4 SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- ☐ DRUG USE, e.g., POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- ☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
- ☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
- ☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

- ☐ CLINICAL
- ☐ NONCLINICAL

COMMENTS / SPECIAL INSTRUCTIONS: All of the documents for this NDA are available via edr. testosterone products are considered a Class III controlled substance.
Your input and comments are greatly appreciated

SIGNATURE OF REQUESTOR
Jeannie Roule

METHOD OF DELIVERY (Check one)
☐ DFS ☐ EMAIL ☐ MAIL ☐ HAND

PRINTED NAME AND SIGNATURE OF RECEIVER

PRINTED NAME AND SIGNATURE OF DELIVERER

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

/s/

JEANNIE M ROULE
02/01/2011

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADM NISTRATION

REQUEST FOR DDMAC LABELING REVIEW CONSULTATION

Please send immediately following the Filing/Planning meeting

TO:

CDER-DDMAC-RPM

FROM: (Name/Title, Office/Division/Phone number of requestor)

Jeannie Roule, Regulatory Project Manager
Division of Reproductive and Urologic Products
(301) 796-3993

REQUEST DATE	IND NO.	NDA/BLA NO.	TYPE OF DOCUMENTS (PLEASE CHECK OFF BELOW)
February 1, 2011		202763	electronic

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE (Generally 1 week before the wrap-up meeting)
Tstosterone gel 1%	Standard	Androgen	September 5, 2011

NAME OF FIRM: Teva Pharmaceuticals

PDUFA Date: November 14, 2011

TYPE OF LABEL TO REVIEW

TYPE OF LABELING:
(Check all that apply)
✓PACKAGE INSERT (PI)
☐ PATIENT PACKAGE INSERT (PPI)
✓ CARTON/CONTAINER LABELING
✓MEDICATION GUIDE
☐ INSTRUCTIONS FOR USE(IFU)

TYPE OF APPLICATION/SUBMISSION
✓ORIGINAL NDA/BLA
☐ IND
☐ EFFICACY SUPPLEMENT
☐ SAFETY SUPPLEMENT
☐ LABELING SUPPLEMENT
☐ PLR CONVERSION

REASON FOR LABELING CONSULT
✓INITIAL PROPOSED LABELING
☐ LABELING REVISION

EDR link to submission: \\FDSWA150\NONECTD\N202763\N_000\2011-01-13

Please Note: There is no need to send labeling at this time. DDMAC reviews substantially complete labeling, which has already been marked up by the CDER Review Team. After the disciplines have completed their sections of the labeling, a full review team labeling meeting can be held to go over all of the revisions. Within a week after this meeting, "substantially complete" labeling should be sent to DDMAC. Once the substantially complete labeling is received, DDMAC will complete its review within 14 calendar days.

COMMENTS/SPECIAL INSTRUCTIONS:

Mid-Cycle Meeting: [Insert Date] June 13, 2011

Labeling Meetings: [Insert Dates] Label planning: June 20. Others to be scheduled

Wrap-Up Meeting: [Insert Date] Sometime in mid-September

SIGNATURE OF REQUESTER Jeannie Roule	
SIGNATURE OF RECEIVER	METHOD OF DELIVERY (Check one) ☐ eMAIL ☐ HAND

Reference ID: 2899073

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

/s/

JEANNIE M ROULE
02/01/2011

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADM NISTRATION

REQUEST FOR CONSULTATION

TO *(Division/Office)*:
Mail: OSE

FROM: Jeannie Roule, Regulatory Project Manager
Division of Reproductive and Urologic Products
(301) 796-3993

DATE	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
February 1, 2011		202763	electronic	January 14, 2011

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
Testosterone gel 1%	Standard	Androgen	September 1, 2011

NAME OF FIRM: Teva Pharmaceuticals

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE/ADDITION
- ☐ MEETING PLANNED BY
- ☐ PRE--NDA MEETING
- ☐ END OF PHASE II MEETING
- ☐ RESUBMISSION
- ☐ SAFETY/EFFICACY
- ☐ PAPER NDA
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ✓ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- ☐ OTHER *(SPECIFY BELOW)*:

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
☐ TYPE A OR B NDA REVIEW ☐ END OF PHASE II MEETING ☐ CONTROLLED STUDIES ☐ PROTOCOL REVIEW ☐ OTHER (SPECIFY BELOW):	☐ CHEMISTRY REVIEW ☐ PHARMACOLOGY ☐ BIOPHARMACEUTICS ☐ OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILTY STUDIES
- ☐ PHASE IV STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL-BIOPHARMACEUTICS
- ☐ IN-VIVO WAIVER REQUEST

IV. DRUG EXPERIENCE

- ☐ PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- ☐ DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- ☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
- ☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
- ☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

- ☐ CLINICAL
- ☐ PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS:

Edr link: **\\FDSWA150\NONECTD\N202763\N_000\2011-01-13**

Please have DRISK review the REMS and Medguide
Please have DMEPA review the PI, carton and container.

SIGNATURE OF REQUESTER Jeannie Roule	METHOD OF DELIVERY (Check one) ☐ MAIL ☐ HAND
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

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

/s/

JEANNIE M ROULE
02/01/2011

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 202763

NDA ACKNOWLEDGMENT

Teva Pharmaceuticals USA
Attention: Robert S. Vincent
Director, Regulatory Affairs
400 Chestnut Ridge Road
Woodcliff Lake, NJ 07677

Dear Mr. Vincent:

We have received your New Drug Application (NDA) submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

Name of Drug Product: testosterone gel 1%

Date of Application: January 13, 2011

Date of Receipt: January 14, 2011

Our Reference Number: NDA 202763

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on March 15, 2011, in accordance with 21 CFR 314.101(a).

If you have not already done so, promptly submit the content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Failure to submit the content of labeling in SPL format may result in a refusal-to-file action under 21 CFR 314.101(d)(3). The content of labeling must conform to the content and format requirements of revised 21 CFR 201.56-57.

The NDA number provided above should be cited at the top of the first page of all submissions to this application. Send all submissions, electronic or paper, including those sent by overnight mail or courier, to the following address:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Reproductive and Urologic Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

All regulatory documents submitted in paper should be three-hole punched on the left side of the page and bound. The left margin should be at least three-fourths of an inch to assure text is not obscured in the fastened area. Standard paper size (8-1/2 by 11 inches) should be used; however, it may occasionally be necessary to use individual pages larger than standard paper size. Non-standard, large pages should be folded and mounted to allow the page to be opened for review without disassembling the jacket and refolded without damage when the volume is shelved. Shipping unbound documents may result in the loss of portions of the submission or an unnecessary delay in processing which could have an adverse impact on the review of the submission. For additional information, please see http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/ucm073080.htm.

If you have any questions, call Jeannie Roule, Regulatory Health Project Manager at (301) 796-3993.

Sincerely,

{See appended electronic signature page}

Jennifer Mercier
Chief, Project Management Staff
Division of Reproductive and Urologic Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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

/s/

JENNIFER L MERCIER
01/25/2011