CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

204399Orig1s000

STATISTICAL REVIEW(S)

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Translational Sciences
Office of Biostatistics

MEMORANDUM OF STATISTICAL REVIEW

NDA#:	204399/N0000
Drug Name:	Testosterone Gel 1% (VOGELXO)
Indication(s):	Replacement Therapy in Male Hypogonadism
Applicant:	Upsher-Smith Laboratories, Inc.
Date(s):	Submission Date: 10/18/2012
	PDUFA Due Date: 08/18/2013
Review Priority:	Standard
Biometrics Division:	Division of Biometrics 3
Statistical Reviewer:	Xin Fang, Ph.D., Statistical Reviewer
Concurring Reviewers:	Mahboob Sobhan, Ph.D., Statistical Team Leader
Medical Division:	Division of Bone, Reproductive and Urologic Drug Products
Clinical Team:	Martin E. Kaufman, D.P.M., M.B.A., Clinical Reviewer
	Donald McNellis, MD., Clinical Team Leader
Project Manager:	Jeannie M Roule

Keywords: Bioequivalent, NDA Review, Clinical Studies

BACKGROUND

The sponsor, Upsher-Smith Laboratories Inc, submitted a 505(b)(2) application for testosterone gel 1% in the treatment of hypogonadal men. The efficacy and safety data of this drug were cross-referenced to Testim 1% testosterone gel (NDA 021454) owned by Auxilium Pharmaceuticals Inc.

Testosterone 1% gel was developed under IND 76,654. In a meeting on November 8, 2007, the Division communicated to the sponsor that two studies will be required: one to study the effect of washing on testosterone bioavailability, and the other to study the person-to-person transferability of this drug.

The Division also suggested that if the hand washing studies show no significant differences in the residual between the test and a reference listed drug after washing, then showering studies would not be required. In addition, the division agreed with the sponsor to use Testim 1% testosterone gel as the reference drug.

The sponsor provided the following five completed pharmacokinetic and pharmacodynamic studies in support of this application:

- Pilot bioequivalent study P06-001
- Pivotal bioequivalent study P06-011
- Comparative cumulative skin irritation and sensitization study P08-001
- Hand washing study P10-002
- Transferability study P10-003

CONCLUSION

Since none of the submitted studies had new efficacy data, no statistical review was necessary.

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/s/

XIN FANG
07/15/2013

MAHBOOB SOBHAN
07/17/2013

STATISTICS FILING CHECKLIST FOR A NEW NDA

NDA Number: 204-399/0000 **Applicant:** Upsher-Smith Laboratories, Inc. **Stamp Date:** 10/18/2012

Drug Name: Testosterone Gel 1% **NDA Type:** Original/Standard **Indication:** Replacement Therapy in Male Hypogonadism

On **initial** overview of the NDA application for RTF:

	Content Parameter	Yes	No	NA	Comment
1A	Paper Submission: Index is sufficient to locate necessary reports, tables, data, etc.			X	
1B	Electronic Submission: Indexing and reference links within the electronic submission are sufficient to permit navigation through the submission, including access to reports, tables, data, etc.	X			
2	ISS, ISE, and complete study reports are available (including original protocols, subsequent amendments, etc.)	X			505(b)(2), no ISE
3	Safety and efficacy were investigated for gender, racial, and geriatric subgroups investigated.			X	
4	Data sets in EDR are accessible and conform to applicable guidances (e.g., existence of define.pdf file for data sets).	X			

IS THE STATISTICAL SECTION OF THE APPLICATION FILEABLE? ___YES_____

Content Parameter (possible review concerns for 74-day letter)	Yes	No	NA	Comment
Designs utilized are appropriate for the indications requested.			X	
Endpoints and methods of analysis are specified in the protocols/statistical analysis plans.			X	
Interim analyses (if present) were pre-specified in the protocol and appropriate adjustments in significance level made. DSMB meeting minutes and data are available.			X	
Appropriate references for novel statistical methodology (if present) are included.			X	
Safety data organized to permit analyses across clinical trials in the NDA/BLA.	X			
Investigation of effect of dropouts on statistical analyses as described by applicant appears adequate.			X	

Information requests for the Applicant: None at this time.

The Applicant submitted five pharmacokinetic/pharmacodynamic studies: two bioequivalence studies, one skin irritation study, one hand washing study, and one transfer study. No statistical review is needed because no new efficacy data was submitted.

Xin Fang, Ph.D. 12/07/2012

Reviewing Statistician Date

Sonia Castillo, Ph.D. 12/07/2012

Acting Team Leader Date

File name: 5_Statistics Filing Checklist for a New NDA_204399

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/s/

XIN FANG
12/13/2012

SONIA CASTILLO
12/13/2012