CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-015/S-010

ADMINISTRATIVE DOCUMENTS

MEMORANDUM OF TELECON

DATE: September 9, 2003

APPLICATION NUMBER: NDA 21-015/S-010, Androgel® (testosterone gel) 1%

BETWEEN:

Name: Rex Horton, Manager, Regulatory Affairs
Phone: (770) 439-8545
Representing: Solvay Pharmaceuticals, Inc.

AND

Name: John C. Kim, R.Ph., J.D., Regulatory Health Project Manager
Jean Salemme, Ph.D., Chemistry Reviewer
Division of Reproductive and Urologic Drug Products, HFD-580

SUBJECT:

- To discuss the proposed patient instructions submitted in the draft labeling.

SUMMARY:

- Dr. Salemme indicated that the priming instructions in the draft physician and patient package need to be revised. Based on the dose delivery study, the pump should be primed at least three times. Therefore, the label should state that a patient should prime a new Androgel® pump canister by fully depressing the pump mechanism 3 times instead of the proposed [redacted] times in the draft labeling.

Mr. Horton agreed, and he commits to the requested change.

Actions that will be requested of the sponsor:

- The sponsor will commit to revising the Final Printed Labeling, for the patient and physician inserts, to instruct the patient to prime the pump 3 times instead of [redacted] times.

Jean Salemme, Ph.D.
Chemistry Reviewer
Division of Reproductive and Urologic Drug Products, HFD-580
DNDC II, Office of New Drug Chemistry
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/

Jean Salemme
9/25/03 09:32:45 AM

MEMORANDUM OF TELECON

DATE: August 29, 2003

APPLICATION NUMBER: NDA 21-015/S-010, Androgel® (testosterone gel) 1%

BETWEEN:

Name: Rex Horton, Manager, Regulatory Affairs
Phone: (770) 439-8545
Representing: Solvay Pharmaceuticals, Inc.

AND

Name: John C. Kim, R.Ph., J.D., Regulatory Health Project Manager
Jean Salemme, Ph.D., Chemistry Reviewer
Division of Reproductive and Urologic Drug Products, HFD-580

SUBJECT:

- To discuss the proposal to [redacted]
- To discuss and clarify the [redacted] submitted in an amendment, dated August 15, 2003, in response to an approvable letter for supplement S-010, dated August 8, 2003.

SUMMARY:

- Dr. Salemme expressed concerns that [redacted]. She informed the sponsor that they will be contacted regarding this issue after further discussions within the Division.

  Mr. Horton responded that if [redacted]

- Dr. Salemme indicated that the proposed study submitted in the recent amendment is not adequate. The sponsor already demonstrated [redacted]

  Mr. Horton responded that he will discuss this issue with the marketing and manufacturing departments.

- Dr. Salemme stated the proposed tighter limits for the isopropyl myristate content at release and during stability are acceptable. In addition, it was requested that a statement be added to the dose uniformity test on the specification to show that samples will be

taken from the top, middle, and bottom phase of the canister pump for the dose uniformity test, in accordance with the USP.

Action that is requested of the sponsor:

- The sponsor will submit an amendment with a revised specification containing tighter limits to the isopropyl myristate content and the testing protocol for the dose uniformity test.

Jean Salemme, Ph.D.
Chemistry Reviewer
Division of Reproductive and Urologic Drug Products, HFD-580
DNDC II, Office of New Drug Chemistry
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/

Jean Salemme
9/25/03 09:30:20 AM

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-015/S-010

CORRESPONDENCE

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-015\S-010

INFORMATION REQUEST LETTER

Unimed Pharmaceuticals
Attention: Suzanne LoGalbo, J.D., R.Ph.
Vice President, Regulatory Affairs
Solvay Pharmaceuticals, Inc.
901 Sawyer Road
Marietta, GA 30062

Dear Ms. LoGalbo:

Please refer to your April 9, 2003 supplemental new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for AndroGel (testosterone gel).

We are currently reviewing your submission, which provides an alternate container/closure system that consists of a multi-use pump and canister delivery system, and we have the following comments and information requests. We request a prompt written response in order to continue our evaluation of your supplemental application.

1. Please provide the name and address of the proposed alternate packaging site.

2. We note that the formulation approved for use in the approved container, [redacted] the use of an [redacted]

3. Regarding your proposed test to measure dose uniformity, we note that the proposed limits and number of samples you propose to test are not in accordance with USP dose-uniformity testing. While there is no dose-uniformity test in USP specifically for measuring the amount of a semisolid drug product dispensed from a pump, we feel that a more appropriate test for testing uniformity of dose of your product from the proposed pump dispenser is USP <601> for metered-dose delivery systems. Therefore, we recommend the dose uniformity test for your product be in accordance with USP <601> and that the number of canisters tested and the acceptance criteria chosen for the test be as follows:

   - Test one canister. At least [redacted] discharges (attenuations) collected from the canister are between [redacted] of the label claim of 1.25 g, and [redacted] attenuations are outside [redacted] of the label claim.

- If the contents of NMT [illegible] out of [illegible] discharges are outside [illegible], but within [illegible], two additional canisters are tested as above, with [illegible] attenuations from each canister. The requirements are met if NMT [illegible] out of [illegible] results are outside [illegible] and none are outside [illegible]

4. Please provide an English translation of the Pump Reproducibility study (Appendix C) and the Extractable Contents study.

5. Please describe the extractable contents test. Additionally, explain why the expected amount of 44-g and 88-g are not obtained from the [illegible]

6. Please provide an explanation of the acceptance criteria for the test "number of doses." The acceptance criteria of NLT [illegible] for the 44-g size and NLT [illegible] for the 88-g size imply that only [illegible], rather than [illegible], of the contents will be delivered.

7. The study to address the compatibility of the gel in contact with the polyethylene component of the pouch was not conducted. As such, even though you have presented three months accelerated stability data for the gel in the pouch, you have not addressed if the gel in contact with the pouch may cause additional by-products to form. Please justify why this study was not conducted.

8. We note that you reference DMF [illegible] for the description of the [illegible]. This DMF, however, addresses only the polyethylene manufacture and controls. The Supplement mentions that a [illegible] complex is used for the [illegible]. Please clarify this discrepancy. If the [illegible] material is the same material as that used in the approved packaging for Androgel, please state so. If the [illegible] material is different from that used in the approved packaging, we request the following:

   - Information pertaining to the manufacture of and quality controls for the [illegible] complex of which the [illegible] is constructed. A DMF reference with Letter of Authorization will be acceptable. [Refer to your response to the same request for information for the [illegible] for guidance as to what information is requested.]

   - A demonstration that the proposed [illegible] packaging is comparable to the packaging of the approved product as demonstrated by results from [illegible] Please refer to the FDA Guidance to Industry – Container-Closure Systems for Packaging Human Drugs and Biologics, May 1999 for further guidance.

9. For the polymer used for the piston, please determine if the polymer and the additives comply with 21 CFR for suitability for use in contact with foods. If the polymer and additives have not been previously used with foods or other drug products, then the safety of the polymer and additives will have to be established. Please note that a reference to the European Pharmacopeia is not an adequate statement as to the safety of the additives. Additionally, if the polymer and the additives do not comply with 21 CFR, then the amounts

of any polymer additive that might be present in the Androgel during the shelf-life of the product will have to be determined in order for the exposure to the additives to be accessed.

10. Please provide an explanation as to what microbiological testing has been performed in regards to the current submission.

11. We note that you propose to eliminate testing for dose uniformity, number of doses delivered, and extractable contents during stability testing. We recommend that you conduct the dose uniformity test during stability to ensure that the deliverable contents of each attenuation remain within the acceptance criteria during the shelf-life of the product.

12. Please provide a placebo sample of Androgel in the proposed new container/closure.

If you have any questions, please call Eufrecina DeGuia, Regulatory Health Project Manager, at (301) 827-4260.

Sincerely,

David T. Lin, Ph.D.
Chemistry Team Leader, for the
Division of Reproductive and Urologic Drug
Products, HFD-580
DNDC II, Office of New Drug Chemistry
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/

David T. Lin
5/21/03 10:35:39 AM
I concur.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-015/S-010

Unimed Pharmaceuticals, Inc.

Dear Dr Mondabaugh:

We have received your supplemental drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product:	AndroGel® (testosterone gel)
NDA Number:	21-015
Supplement number:	010
Review Priority Classification:	Standard
Date of supplement:	April 9, 2003
Date of receipt:	April 10, 2003

This supplemental application provides for an additional container-closure system for AndroGel®.

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 June 9, 2003 in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be August 8, 2003.

All communications concerning this supplement should be addressed as follows:

U.S. Postal Service/Courier/Overnight Mail:
Center for Drug Evaluation and Research
Division of Reproductive and Urologic Drug Products; HFD-580
Attention: Document Room 8B-45
5600 Fishers Lane
Rockville, Maryland 20857

If you have any question, please call me at (301) 827-4260.

Sincerely,

{See appended electronic signature page}

Eufrecina P. DeGuia
Regulatory Health Project Manager
Division of Reproductive and Urologic Drug 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/

Eufrecina deGuia
4/17/03 01:52:21 PM

19 Page(s) Withheld

_____ § 552(b)(4) Trade Secret / Confidential

✓ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process