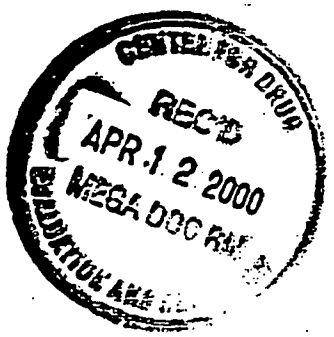
Correspondence from Applicant
04-11-00

[redacted]

[redacted]

DRAPHARMA, INC.

215 956-2200 Tel
215 443-9531 Fax



April 11, 2000

Ms. Kalyani Bhatt
Center for Drug Evaluation & Research
Food and Drug Administration
Document Control Room
9201 Corporate Boulevard
Rockville, MD 20850

NEW CORRESPONDENCE

NC

RE: NDA 50-781
Tradename: Minocycline PTS
Desk Copy of Volume 1.4

Dear Ms. Bhatt:

Reference is made to our telephone conference call on April 7, 2000 during which you requested an additional volume 1.4 of our NDA for Dr. Riley.

Enclosed is his desk copy.

If you have any questions regarding this submission, please contact me at (215) 956-2207.

Sincerely,

[redacted]

Markus F. Herzig
Executive Director of Regulatory Affairs

Form FDA1571
Submitted in triplicate

ORIGINAL

Correspondence from Applicant

04-11-00

RAPHARMA, INC.
www.orapharma.com

732 Louis Drive
Warminster, PA 18974

215-956-2200 Tel
215-443-9531 Fax

April 11, 2000

NDA ORIG AMENDMENT

Jonathan K. Wilkin, MD
Director, Division of Dermatological and Dental Drug Products (HFD-540)
Center for Drug Evaluation & Research
Food and Drug Administration
Document Control Room
9201 Corporate Boulevard
Rockville, MD 20850

BC

RE: NDA 50-781
Minocycline PTS
Amendment: CMC – Method Validation

Dear Dr. Wilkin:

Reference is made to a telephone conference call on April 7, 2000 between Ms. K. Bhatt, Dr. M. Gautam-Basak and Dr. Riley from your Division and the undersigned regarding CMC issues in the above referenced NDA.

Enclosed is an errata sheet clarifying some minor compilation errors that were found when preparing the revised methods validation volume. This submission will replace volume 1.6 in the original NDA, and this new volume is identified as volume 2.1. The submission contains one archival and three review copies as required by the guidelines.

If you have any questions regarding this submission, please contact me at (215) 956-2207.

Sincerely,

Markus F. Herzig
Executive Director of Regulatory Affairs

ORIGINAL

Form FDA1571

Correspondence from Applicant

04-0400

215/956-2200 Tel
215/443-9531 Fax

4/5/00

1, 2000

NDA ORIG AMENDMENT

Jonathan K. Wilkin, MD
Director, Division of Dermatological and Dental Drug Products (HFD-540)
Center for Drug Evaluation & Research
Food and Drug Administration
Document Control Room
9201 Corporate Boulevard
Rockville, MD 20850

NEW C

NC

RE: NDA 50-781
Amendment: ~~FDA~~ Requested Information

Dear Dr. Wilkin:

Reference is made to a telephone conversation between Ms. K. Bhatt in your Division and undersigned during which Ms. Bhatt requested the attached pages for the above referenced NDA.

One page contains our request for the waiver to conduct pediatric studies and the second page identifies the location of the GCP statements in our clinical reports.

u have any questions, I can be reached at (215) 956-2207.

Sincerely,

Markus F. Herzig
Executive Director, Regulatory Affairs

MFH:stk

Attachments

ORIGINAL

Form FDA 356h
Submitted in Duplicate

Correspondence from Applicant
03-13-00

PHARMA, INC.
www.orapharma.com

732 Louis Drive
Warminster, PA 18974
215 956-2200 Tel
215 443-9531 Fax

MAR 14 2000

NDA ORIG AMENDMENT

March 13, 2000

Jonathan K. Wilkin. MD
Director, Division of Dermatological and Dental Drug Products (HFD-540)
Center for Drug Evaluation & Research
Food and Drug Administration
Document Control Room
9201 Corporate Blvd.
Rockville, MD 20850

B2

RE: **NDA 50-781** (formerly submitted as NDA 21-206)
TRADEMARK ™(Minocycline PTS), 1 mg
NDA Amendment - Reviewer's Aid

Dear Dr. Wilkin:

With reference to the Pre-NDA meeting held June 7, 1999, OraPharma, Inc. agreed that following submission of the NDA, they would provide as reviewer aids the electronic text documents (in MS Office Word 97 format) from the primary portions of the NDA (except for CMC). OraPharma also clarified electronic submission requirements for Section 11 (CRTs), Section 12 (CRFs) and select listings from Section 8 (Clinical Data) on January 13, 2000 with Dr. Randy Levin and Ken Edmunds by teleconference. At that time, Dr. Levin stated that electronic items submitted for use by FDA reviewers should be ready for archive, and should meet guideline requirements as a partial submission as PDF files with appropriate bookmarking.

In review, OraPharma has submitted electronic Sections 11, 12 and listings from Section 8 as part of the original NDA on February 16, 2000. An amendment was submitted to the NDA on February 29, 2000 modifying electronic data from Section 11 and Section 8 listings. OraPharma now provides, as a convenience to the reviewer, the text files from the main portions of the NDA in both PDF and Word formats. The enclosed CD contains two file folders for NDA 50-781, one contains PDF files that follows the electronic submission guidance for NDAs and the other contains Word files. Review and archive copies are submitted.

Please be aware that OraPharma does not intend this NDA to be reviewed as an electronic submission because not all files necessary for review have been provided.

ORIGINAL

The PDF files provided are bookmarked internally, and are hyperlinked from the *amendtoc.pdf* file to the respective indexes and documents. No links exist to external appendices, references. datasets and many reports since they have not been provided as part of this reviewer's aid. No links are present in the Word files. A copy of this cover letter and the Form FDA 356h are also provided on the CD.

The electronic files are virus free (McAfee ViruScan 4.0.3, March 8, 2000).

If you have any further questions about these materials, please do not hesitate to contact me at 215-956-2207.

Sincerely,

Markus Herzig

Markus F. Herzig
Executive Director, Regulatory Affairs

Correspondence from Applicant
02-29-00

'HARMA, INC.

732, [illegible] Drive
Warminster, PA 18974
215 956-2200 Tel
215 443-9531 Fax

MAR 0 1 2000

February 29, 2000

Jonathan K. Wilkin, MD
Director, Division of Dermatological and Dental Drug Products (HFD-540)
Center for Drug Evaluation & Research
Food and Drug Administration
Document Control Room
9201 Corporate Blvd.
Rockville, MD 20850

NDA ORIG AMENDMENT

RE: **NDA 50-781** (formerly submitted as NDA ——)
TRADEMARK ™(Minocycline PTS), 1 mg
NDA Amendment

Dear Dr. Wilkin:

In accordance with CFR 314.60, OraPharma, Inc. hereby amends NDA 50-781 (formerly submitted as NDA ——) for minocycline PTS. 1mg. Reference is made to the cover letter in the original NDA where after receiving a fax from your Division on February 7, 2000 regarding preferences for electronic data submission, OraPharma has revised the electronic items accordingly. An archive and review copy is submitted.

Please note that no changes have been made to the electronic data submitted in the original NDA for Section 12 – CRFs; no new CD is submitted for that section. The CD submitted in Volume 1.122 of the original NDA for CRFs should be used for review.

In contrast, electronic data on CD for Section 11 (CD located in Vol. 1.122) and Section 8 (CDs located in Vol. 1.20 and copied in Vol. 1.100) from the original NDA submission should be considered obsolete and not reviewed. Five new CDs containing revised Section 8 and Section 11 data are provided in this NDA amendment. To review, Section 8 electronic data consists of selected tables and listings from pivotal trials OPI-103A and OPI-103B. ISE and ISS. Section 11 CRT's contains SAS transport files of study datasets. A summary table listing the names of the files on the CDs is attached.

Files are virus free (McAfee VirusScan v4.0.3, engine 4.0.35a, Dec. 8. 1999).

ORIGINAL

Please note the following about the electronic data now submitted:

1. Section 8 – Clinical

The electronic files associated with this section are located in the N———clinstat/ subdirectory. The tables and data listings within this directory have not undergone any type of content-change compared to what was sent in the original February 16, 2000 submission. The only changes made to the files, as well as the TOC files located in N———clinstat/, are the following:

- Bookmarks have been added to the PDF files to assist reviewers as they navigate through this information.
- The CLINDEX index has been updated to allow reviewers to search on numbers as well as text.

2. Section 11 - CRT

The electronic files associated with this section are located in the N———crt/ subdirectory. The files in this directory, and all its subdirectories, were updated to reflect the changes requested by FDA in the fax correspondence sent to OraPharma on February 7, 2000 from Ms. Kalyani Bhatt. Our initial response to this fax was sent to you on February 24, 2000 as Serial Submission No. 120 to IND ——'. In particular, please note:

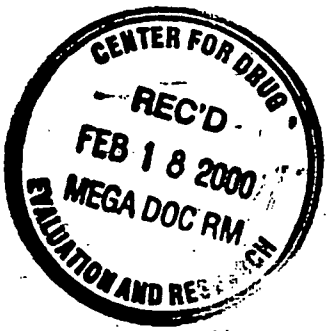
- SAS export files, a version of DEFINE.PDF and a version of the BLANKCRF.PDF have been prepared for each study and analysis and are located in the appropriate N———/crt/datasets/ subdirectory.
- In the February 7, 2000 fax from Ms. Bhatt, a request was made to (1) include instructions on converting the SAS export files and (2) include a SAS contents for each of the export files. The SAS contents (roughly 250 pages) are included with this letter, and both the export conversion instructions as well as the SAS contents are available electronically within each of the DEFINE.PDF files. All SAS export files were created using the Guidance-suggested SAS macro which can be obtained from the SAS web site at http://www.sas.com/software/industry/pht/fda/macro.html.

The CDs produced for this NDA amendment were burned with NDA number —— prior to OraPharma's notification on February 28, 2000 of the NDA number change to 50-781. If the Division believes it is necessary to submit new CDs with the NDA number changed to 50-781, please inform me immediately. If you have any further questions regarding this submission, please contact me at (215) 956-2207.

Sincerely,

Markus F. Herzig
Executive Director, Regulatory Affairs

ORAPHARMA, INC.
www.orapharma.com



732 Louis Drive
Warminster, PA 18974
215/956-2200 Tel
215/443-9531 Fax

February 17, 2000

Ms. K. Bhatt,
Project Manager,
Division of Dermatological and Dental Drug Products - HFD-540
Center for Drug Evaluation & Research
Food and Drug Administration
9201 Corporate Blvd.
Rockville, MD 20850

NEW CORRESP
NC

RE: NDA —— TRADEMARK ™(Minocycline PTS), 1 mg
DESK COPIES of Volume 1.1
Missing Page 63 of Volume 1.1

Dear Ms. Bhatt:

OraPharma, Inc. has submitted the above referenced NDA for Minocycline PTS, 1 mg. Please find enclosed five DESK COPIES of the Application Summary Volume 1.1 for:

Dr. Johathan Wilkin, Division Director
Dr. John Kelsey, Dental Team Leader,
Dr. Wilson DeCamp, Chemistry Team Leader,
Dr. Abigail Jacobs, Pharmacology Team Leader
Ms. K. Bhatt, Project Manager,

In addition, it has come to our attention that page 63 of Volume 1.1, may have been inadvertently omitted from the archival and reviewer's copies of NDA —— Enclosed are 10 copies of this page for insertion into the archival and reviewer's copies of Volume 1.1 if needed.

This page has already been inserted in the DESK COPIES enclosed.

If you have any further questions about these materials, please do not hesitate to contact me at 215-956-2207.

Sincerely,

Markus Herzig

Markus F. Herzig
Executive Director, Regulatory Affairs

ORIGINAL

ORAPHARMA, INC.
www.orapharma.com

732 Louis Drive
Warminster, PA 18974

215/956-2200 Tel
215/443-9531 Fax

February 16, 2000

Food and Drug Administration
Center for Drug Evaluation & Research
Central Document Control Room
12229 Wilkins Avenue
Rockville, MD 20852

RE: **NDA** ——
TRADEMARK ™(Minocycline PTS), 1 mg
Original New Drug Application

Attention: Jonathan K. Wilkin, MD
Director, Division of Dermatological and Dental Drug Products (HFD-540)

Dear Dr. Wilkin:

Pursuant to Section 505 (b) of the Federal Food, Drug and Cosmetic Act and 21 CFR 314.50, OraPharma, Inc. herewith submits our original New Drug Application, Form FDA 356h and supporting documents for Trademark (Minocycline PTS) 1 mg. Trademark is a tetracycline derivative incorporated into a sustained release dosage form consisting of poly(glycolide-co-dl-lactide) for subgingival administration.

Please note that the above-referenced number has been pre-assigned to this application which was the subject of an IND meeting on November 17, 1997 and a pre-NDA meeting with Agency personnel on June 7, 1999.

Please also note that OraPharma, Inc. has received a small business waiver regarding the user fee, and the letter granting our request is enclosed in item 18.

Trademark (Minocycline PTS) 1 mg was developed clinically in the United Stated. U.S. studies have been conducted originally under Lederle Laboratories Investigational New Drug Application, Number —— which resides in HFD-540, FDA's Division of Dermatologic and Dental Drug Products. Subsequently, this IND was transferred to OraPharma, Inc. who conducted the Phase 3 clinical trials. All information contained in IND —— is hereby incorporated into this application by cross-reference.

Reference is made to telephone conversations and teleconferences with Dr. Randy Levin and Ken Edmunds from the FDA in which agreements were reached to submit the CRTs and data listings in electronic format according to the FDA guidelines.

For completeness of this submission, the electronic files for Section 11 are submitted in the format originally planned. However, after having received guidance from your Division on February 7, 2000 via telefax, we are revising this section accordingly. The revised Section 11 will be submitted as an amendment to this NDA within 30 days. We believe that the submission of this amendment should not be a filability concern for this NDA.

Reference is also made to the June 7, 1999 pre-NDA meeting during which Dr. See, Pharmacology-Toxicology Reviewer requested OraPharma, Inc. or Wyeth-Ayerst to submit the pharmacology and toxicology data (information) from previous oral and intravenous minocycline NDAs as desk copies. Under separate cover, four (4) volumes of non-clinical information OraPharma, Inc. received from Wyeth-Ayerst have been sent to the Reviewer. Volume one to three contain information for NDA 50-315 and Volume 4 contains information for NDA 50-444 as well as subsequent annual reports which included animal (non-clinical) information.

OraPharma, Inc. formally requests marketing exclusivity for minocycline PTS as provided for in CFR 314.108 because new clinical investigations were performed.

We trust that you will find the enclosed document well organized, complete, and easy to review. Therefore, review and evaluation at your earliest convenience would be greatly appreciated. Please contact the undersigned of this office at (215) 956-2207 if you have any questions or comments regarding the enclosed application.

Please note that OraPharma, Inc. considers this application and all correspondence related thereto as confidential, proprietary, trade secret information and hereby claims protection from disclosure under the applicable sections of 18 U.S.C. and Title 21 of the Code of Federal Regulations.

Sincerely,

Markus F. Herzig
Executive Director, Regulatory Affairs

MFH:stk

Attachments

Form FDA 356h

Archival Copy	Volumes: 1.1 - 1.122
Chemistry Review Copy	Volumes: 1.1 - 1.7
Pharmacology Review Copy	Volumes: 1.1, 1.8, - 1.110
Biopharmaceutics Review Copy	Volumes: 1.1, 1.11 - 1.16
Micorbiology Review Copy	Volumes: 1.1, 1.17-1.19
Medical Review Copy	Volumes: 1,1, 1.20 - 1.99, 1.122
Biostatistics Review Copy	Volumes: 1.1, 1.100 - 1.121

Desk Copies of Application Summary, Volume 1.1:
- Dr. Johathan Wilkin, Division Director, HFD - 540
- Dr. John Kelsey, Dental Team Leader, HFD - 540
- Dr. Wilson DeCamp, Chemistry Team Leader, HFD-540
- Dr. Abigail Jacobs, Pharmacology Team Leader, HFD-540
- Ms. K. Bhatt, Project Manager, HFD - 540

Division of Dermatologic and Dental Drug Products
Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane, HFD-540
Rockville, MD 20857

FACSIMILE TRANSMISSION RECORD

DATE: 2-16-01 Pages (including cover) 15

TO: Markus Herzig

COMPANY: Orapharma, INC.

ADDRESS: 732 Louis Drive, Warminster, Pa. 18974

FAX PHONE#: 215 443-9531 Our Fax # (301) 827-2075

Voice # (301) 827-2020

MESSAGE:

Markus,

Attach is your Approval letter Label, Carton + Packaging

NOTE: We are providing the attached information via telephone facsimile for your convenience. This material should be viewed as unofficial correspondence. Please feel free to contact me if you have any questions regarding the contents of this transmission.

FROM: Kalyani Bhatt

TITLE: Project Manager

TELEPHONE: 301-827-2020

MESSAGE CONFIRMATION

02/16/01 17:52

NO.	MODE	BOX	GROUP
928	TX		

DATE/TIME	TIME	DISTANT STATION ID	PAGES	RESULT	ERROR PAGES	S.CODE
02/16 17:48	04'00"	912154439531	015/015	OK		0000

Division of Dermatologic and Dental Drug Products
Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane, HFD-540
Rockville, MD 20857

FACSIMILE TRANSMISSION RECORD

DATE: 2-16-01 **Pages (including cover)** 15

TO: Markus Herzig

COMPANY: Orapharma, Inc.

ADDRESS: 732 Louis Drive, Warminster, Pa. 18974

FAX PHONE#: 215 443-9531 **Our Fax # (301) 827-2075**

Voice # (301) 827-2020

MESSAGE:

Markus,

Attach is your Approval letter, Label, Carton + Packaging

NOTE:

OraPharma, Inc.
732 Louis Drive
Warminster, PA 18974
215-956-2200
Facsimile: 215-443-9531

ORAPHARMA INC.

FAX COVER SHEET

To:	Ms. Kalyani Bhatt, Project Manager	**From:**	Markus Herzig
Company:	Division of Dermatologic / Dental Drug Products	**Date:**	2/16/2001
Fax No.:	301-827-2091	**No. of pages w/cover:**	2
RE:	Response to 1:35 PM Telephone Conversation Tradename Arestin™		

[X] *Urgent* [ ] *Reply ASAP* [ ] *Please comment* [ ] *Please review* [ ] *For your information*

Dear Ms. Bhatt:

Attached is a copy of the Tradename commitments.

Sincerely,

Markus Herzig

Markus F. Herzig

OraPharma, Inc.
732 Louis Drive
Warminster, PA 18974
215-956-2200
Facsimile: 215-443-9531

ORAPHARMA INC.

FAX COVER SHEET

To:	Ms. Kalyani Bhatt, Project Manager	**From:**	Markus Herzig
Company:	Division of Dermatologic / Dental Drug Products	**Date:**	2/16/2001
Fax No.:	301-827-2091	**No. of pages w/cover:**	1
RE:	Tradename Arestin™ Additional Commitment		

[X] *Urgent* [ ] *Reply ASAP* [ ] *Please comment* [ ] *Please review* [ ] *For your information*

Dear Ms. Bhatt:

OraPharma, Inc. commits to submit 15 day expedited reports for any name confusion between our Arestin and the previous Arestin product.

Sincerely,

Markus F. Herzig

OraPharma, Inc.
732 Louis Drive
Warminster, PA 18974
215-956-2200
Facsimile: 215-443-9531

ORAPHARMA INC.

FAX COVER SHEET

To:	Ms. Kalyani Bhatt, Project Manager	**From:**	Markus Herzig
Company:	Division of Dermatologic / Dental Drug Products	**Date:**	2/16/2001
Fax No.:	301-827-2091	**No. of pages w/cover:**	1
RE:	Package Insert		

[X] *Urgent* [ ] *Reply ASAP* [ ] *Please comment* [ ] *Please review* [ ] *For your information*

Dear Ms. Bhatt:

Reference is made to a telephone conversation earlier today between Dr. Kelsey and Ms. Bhatt and Mr. Herzig for OraPharma, Inc. in which Dr. Kelsey requested to have the last sentence before table 4 in the "Adverse Reactions" section deleted.

Mr. Herzig concurred to have that sentence removed from the package insert.

Sincerely,

Markus F. Herzig

OraPharma, Inc.
732 Louis Drive
Warminster, PA 18974
215-956-2200
Facsimile: 215-443-9531

ORAPHARMA INC.

FAX COVER SHEET

To:	Ms. Kalyani Bhatt, Project Manager	**From:**	Markus Herzig
Company:	Division of Dermatologic / Dental Drug Products	**Date:**	2/16/2001
Fax No.:	301-827-2091	**No. of pages w/cover:**	
RE:	Response to Telephone Conversation		

[X] *Urgent* [ ] *Reply ASAP* [ ] *Please comment* [ ] *Please review* [ ] *For your information*

Dear Ms. Bhatt:

Reference is made to your telephone call today requesting a response for the inclusion of measuring the absence of e-coli in the bioburden testing of our product. We have responded to the request by the Microbiologist and are measuring the absence of e-coli in our bioburden testing.

I informed you that we have included this test in the methodology and confirm the inclusion of the specification in the supplement which we will submit post FDA action. The test demonstrates the absence of e-coli in the product.

Sincerely,

Markus F. Herzig

OraPharma, Inc.
732 Louis Drive
Warminster, PA 18974
215-956-2200
Facsimile: 215-443-9531

ORAPHARMA INC.

FAX COVER SHEET

To:	Ms. Kalyani Bhatt, Project Manager	**From:**	Markus Herzig
Company:	Division of Dermatologic / Dental Drug Products	**Date:**	2/9/2001
Fax No.:	301-827-2091	**No. of pages w/cover:**	1
RE:	Acceptance of Arestin Draft Label		

[X] *Urgent* [ ] *Reply ASAP* [ ] *Please comment* [ ] *Please review* [ ] *For your information*

Dear Ms. Bhatt:

OraPharma, Inc. would like to inform you that we accept the 2nd draft label from the FDA faxed to OraPharma, Inc. on December 5, 2000.

Two minor corrections would need to be made to that draft. The word "CONTRA-INDICATIONS" is misspelled in the draft copy as "CONTRADICTIONS" and in Table 4 the pocket depth reduction listed as –1.32mm should read — mm in the Study OPI-103B, SRP and ARESTIN column.

With these two corrections OraPharma, Inc. accepts the draft label as provided.

Sincerely,

Markus F. Herzig

OraPharma, Inc.
732 Louis Drive
Warminster, PA 18974
215-956-2200
Facsimile: 215-443-9531

ORAPHARMA INC.

FAX COVER SHEET

To:	Ms. Kalyani Bhatt, Project Manager	**From:**	Markus Herzig
Company:	FDA	**Date:**	1/29/2001
Fax No.:	301-827-2075	**No. of pages w/cover:**	1
RE:	NDA-50-781		
CC:	Drs. De Camp, Gautam-Basak		

[X] *Urgent* [ ] *Reply ASAP* [ ] *Please comment* [ ] *Please review* [ ] *For your information*

Dear Ms. Bhatt:

OraPharma, Inc., in conjunction with outside contractors, has developed specifications for the particle size of bulk microspheres and has submitted these specifications in our submission dated January 25, 2001. We would like to have the laboratory who conducts this testing and has validated the method officially added to the NDA.

Is it permissible to do this at this time in the review process or does the FDA wish to have this information submitted post the action-letter timeframe?

Additionally, an outside laboratory, which OraPharma, Inc. contracted, has developed and validated an improved bioburden test and again, we would like to have your decision on whether or not we should submit this information now as an amendment or later as a supplement.

Please let me have your decisions as soon as possible if you would like to have this information included in this NDA as an amendment.

Please don't hesitate to call me at 215-956-2207 if you have any questions regarding this telefax.

Sincerely,

Markus F. Herzig

OraPharma, Inc.
732 Louis Drive
Warminster, PA 18974
215-956-2200
Facsimile: 215-443-9531

ORAPHARMA INC.

FAX COVER SHEET

To:	Ms. Kalyani Bhatt, Project Manager	**From:**	Markus Herzig
Company:	Division of Dermatologic / Dental Drug Products	**Date:**	1/24/01
Fax No.:	301-827-2091	**No. of pages w/cover:**	15
RE:	Particle Size Specification for Bulk Microspheres		

[X] *Urgent* [ ] *Reply ASAP* [ ] *Please comment* [ ] *Please review* [ ] *For your information*

Dear Ms. Bhatt:

Attached are the particle size specifications for the Bulk Microspheres as requested by Dr. De Camp in our teleconference of January 23, 2001. This information will be included in January 26th submission under a separate tab.

Sincerely,

Markus F. Herzig

ORAPHARMA, INC.
www.orapharma.com

732 Louis Drive
Warminster, PA 18974

215/956-2200 Tel
215/443-9531 Fax

January 24, 2001

Jonathan K. Wilkin, MD
Director, Division of Dermatological and Dental Drug Products (HFD-540)
Center for Drug Evaluation & Research
Food and Drug Administration
Document Control Room
9201 Corporate Boulevard
Rockville, MD 20850

RE: NDA 50-781
Arestin (minocycline hcl) microspheres, 1mg
Amendment: Particle Size Specification for Bulk Microspheres

Dear Dr. Wilkin:

Reference is made to a telephone conference between Drs. De Camp and Gautam-Basak and Ms. K. Bhatt from your Division and the undersigned on January 23, 2001. During the conversation Dr. De Camp requested that OraPharma, Inc. provide an acceptance criteria for a particle size specification for the Bulk Microspheres based on the data submitted in a table provided to Ms. Pagano in the Philadelphia district office on December 12, 2000. Also requested was a copy of the method used to obtain the data for said table (appendix 1). Dr. De Camp requested to submit a revised specification for bulk microspheres (STM 110), including the particle size specification.

Dr. De Camp asked to have this information faxed as quickly as possible. He further stated that we should provide as much of the information as possible requested in the November 28 and December 22, 2000 telefax by no later than January 29, 2001. He informed me that we should indicate under the specific question that this information is not yet available.

Attached to this letter as Appendix 2 is OraPharma specifications and test Method number 119 (STM 119). This STM contains the particle size acceptance criteria and corresponding test method that we propose for minocycline PTS microspheres (bulk microspheres). The specification was generated on the basis of particle size data from the NDA stability and clinical lots and also from commercial scale lots. The test method differs from that used for obtaining the data communicated to Ms. Pagano on December 12, 2000 in that the suspension medicine was changed from ——— to ——— The latter is less viscous

and reduces the tendency for formulation of air bubbles which interfere with the test method.

The OraPharma bulk microspheres specifications and test method (STM 110) and the particle size specification test method (STM 119) will be combined in the future. However, for expediency to provide the particle size test method it is provided as a separate method.

Available answers to the November 28 and December 22, 2000 telefaxes will be submitted by, January 26, 2001. As requested by Dr. Gautam-Basak I will fax the cover letter for that amendment to you.

Further, in order to have the information provided in this telefax incorporated into the NDA, I will enclose it as a separate tab in the January 26, 2001 amendment.

If you have any questions regarding this submission, please contact me at (215) 956-2207.

Sincerely,

Markus F. Herzig
Executive Director, Regulatory Affairs and Quality Assurance

Form FDA 356h
Submitted in duplicate

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

APPLICATION TO MARKET A NEW DRUG, BIOLOGIC, OR AN ANTIBIOTIC DRUG FOR HUMAN USE

(Title 21, Code of Federal Regulations, 314 & 601)

Form Approved: OMB No. 0910-0338
Expiration Date: April 30, 2000
See OMB Statement on page 2.

FOR FDA USE ONLY
APPLICATION NUMBER

APPLICANT INFORMATION

NAME OF APPLICANT OraPharma, Inc.	DATE OF SUBMISSION January 24, 2001
TELEPHONE NO. *(Include Area Code)* 215-956-2200	FACSIMILE (FAX) Number (Include Area Code) 215-443-9531
APPLICANT ADDRESS *(Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued)*: 732 Louis Drive Warminster, PA 18974	AUTHORIZED U.S. AGENT NAME & ADDRESS (Number, Street, City, State, ZIP Code, telephone & FAX number) IF APPLICABLE Markus F. Herzig 732 Louis Drive Warminster, PA 18974

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER OR BIOLOGICS LICENSE APPLICATION NUMBER (If previously issued) 50-781

ESTABLISHED NAME (e.g., Proper name, USP/USAN name) Minocycline PTS (Minocycline Periodontal Therapeutic System)	PROPRIETARY NAME (trade name) IF ANY ARESTIN™
CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (If any) 7 - dimethylamine - 6 - demethyl - 6 - deoxytetracycline hydrochloride	CODE NAME (If any) --

DOSAGE FORM: topical	STRENGTHS: 1 mg	ROUTE OF ADMINISTRATION: Subgingival

(PROPOSED) INDICATION(S) FOR USE: Adjunctive therapy to scaling and root planing procedures in patients with adult periodontitis

APPLICATION INFORMATION

APPLICATION TYPE *(check one)*
☒ NEW DRUG APPLICATION (21 CFR 314.50) ☐ ABBREVIATED APPLICATION (ANDA, AADA, 21 CFR 314.94)
☐ BIOLOGICS LICENSE APPLICATION (21 CFR part 601)

IF AN NDA, IDENTIFY THE APPROPRIATE TYPE ☒ 505 (b) (1) ☐ 505 (b) (2) ☐ 607

IF AN ANDA, OR AADA, IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION
Name of Drug — Holder of Approved Application

TYPE OF SUBMISSION *(check one)*
☐ ORIGINAL APPLICATION ☒ AMENDMENT TO A PENDING APPLICATION ☐ RESUBMISSION
☐ PRESUBMISSION ☐ ANNUAL REPORT ☐ ESTABLISHMENT DESCRIPTION SUPPLEMENT ☐ SUPAC SUPPLEMENT
☐ EFFICACY SUPPLEMENT ☐ LABELING SUPPLEMENT ☐ CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT ☐ OTHER

REASON FOR SUBMISSION Requested Information

PROPOSED MARKETING STATUS *(check one)*	☒ PRESCRIPTION PRODUCT (Rx)	☐ OVER THE COUNTER PRODUCT (OTC)
NUMBER OF VOLUMES SUBMITTED _____	THIS APPLICATION IS ☒ PAPER	☐ PAPER AND ELECTRONIC ☐ ELECTRONIC

ESTABLISHMENT INFORMATION

Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary) Include name, address, contact, telephone number, registration number (CFN), DMF number, and manufacturing steps and/or type of testing (e.g. Final dosage form, Stability testing) conducted at the site. Please indicate whether the site is ready for inspection or, if not, when it will be ready.

NA

Cross References (list related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs referenced in the current application)

NA