PACKAGING COORDINATORS, INC.

December 3, 1999

Food and Drug Administration
Chief Drug Master File Staff
12229 Wilkins Avenue
Rockville, MD 20852

To Whom It May Concern:

PCI is engaged in the packaging and labeling of pharmaceutical products as a contracting services firm. PCI is registered with the Food and Drug Administration as follows:

Drug Master File (DMF) Number:	[redacted]
Registration of FDA Annual Drug Establishment Number:	2530802
Last satisfactory FDA inspection:	9/16-17/1999
Labeler Code Assignment Number:	032618
The location of the facility is as follows:	Packaging Coordinators, Inc. 3001 Red Lion Road Philadelphia, PA 19114
PCI authorized official:	Mary Foster, Pharm D, Vice President Corporate Quality Assurance/Regulatory Affairs
Phone:	(215) 612-1526

PCI certifies that the methods, facilities and controls used for the packaging of the drug product are in conformance with all applicable requirements of the Food Drug and Cosmetic Act and specifically the Code of Federal Regulations, *Title 21 Parts 210 and 211* for *Current Good Manufacturing Practices* and with all applicable local, state regulations. PCI hereby authorizes FDA to incorporate by reference, aforementioned DMF, for OraPharma Inc., 732 Louis Drive, Warminster, PA 18974.

Pharmaceutical Product Name: Minocycline Periodontal Therapeutic System.

Packaging Operation: Primary and secondary packout.

Under Section 306 (k) (2) and (b) (1) Packaging Coordinators, Inc. hereby certifies that we have not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food Drug and Cosmetic Act in connection with this application.

It is understood that the information in DMF Number 11520 shall be treated as confidential.

Mary Foster — Signature of PCI authorized official

12-3-99 — Date

cc: Paul Alvater, President of Contract Services, PCI
J. Welch, Sales, PCI

WITHHOLD 4 PAGE (S)

[redacted] Review of Financial Information

2. Slots J, Rams TE. 1990. Antibiotics in periodontal therapy: advantages and disadvantages. J Clin Periodontol 17: 479-493.

Financial Disclosure:

The Sponsor has provided the required certification (Form FDA 3454) regarding financial interests and arrangements of clinical investigators. The Sponsor has certified that the value of compensation to the investigator was not influenced by the outcome of the study. One investigator has received a $1000/ month consulting retainer since Februray 1997. Four other investigators had stock or stock options in OraPharma valued at over $100,000 each, based on the stock price at the time of this review. The Biostatistics reviewer was asked to re-evaluate those sites to determine if there was anything unusual about the reported results and to assess the impact of those sites on the overall studies. In one instance, San Antonio (Study 103A), the mean baseline pocket depth for the active arm was the highest among all sites in the study and the mean baseline pocket depth for the S/RP arm was the lowest among all sites. Since we know that the deeper the pocket at baseline, the better the response is expected to be, the situation described would likely favor the active arm. In fact, the delta between the active and S/RP arms at that site was the second highest among all sites in that study. If that site is dropped from the analysis, the p-value for the comparison goes from .047 to .237. This site did enroll a large number subjects, so dropping it would be expected to have some effect on the p-value, but it seems unlikely that the change would be so dramatic based on the number of subjects alone. Based on the unusual nature of the data and the fact that the investigator received substantial compensation, the Division has asked the Division of Scientific Investigations (DSI) to audit the site prior to making a final decision about the approvability of this NDA.

Pediatric Waiver:

Adult periodontitis, as its name indicates, affects only adults, so no studies in children are indicated.

Recommendation:

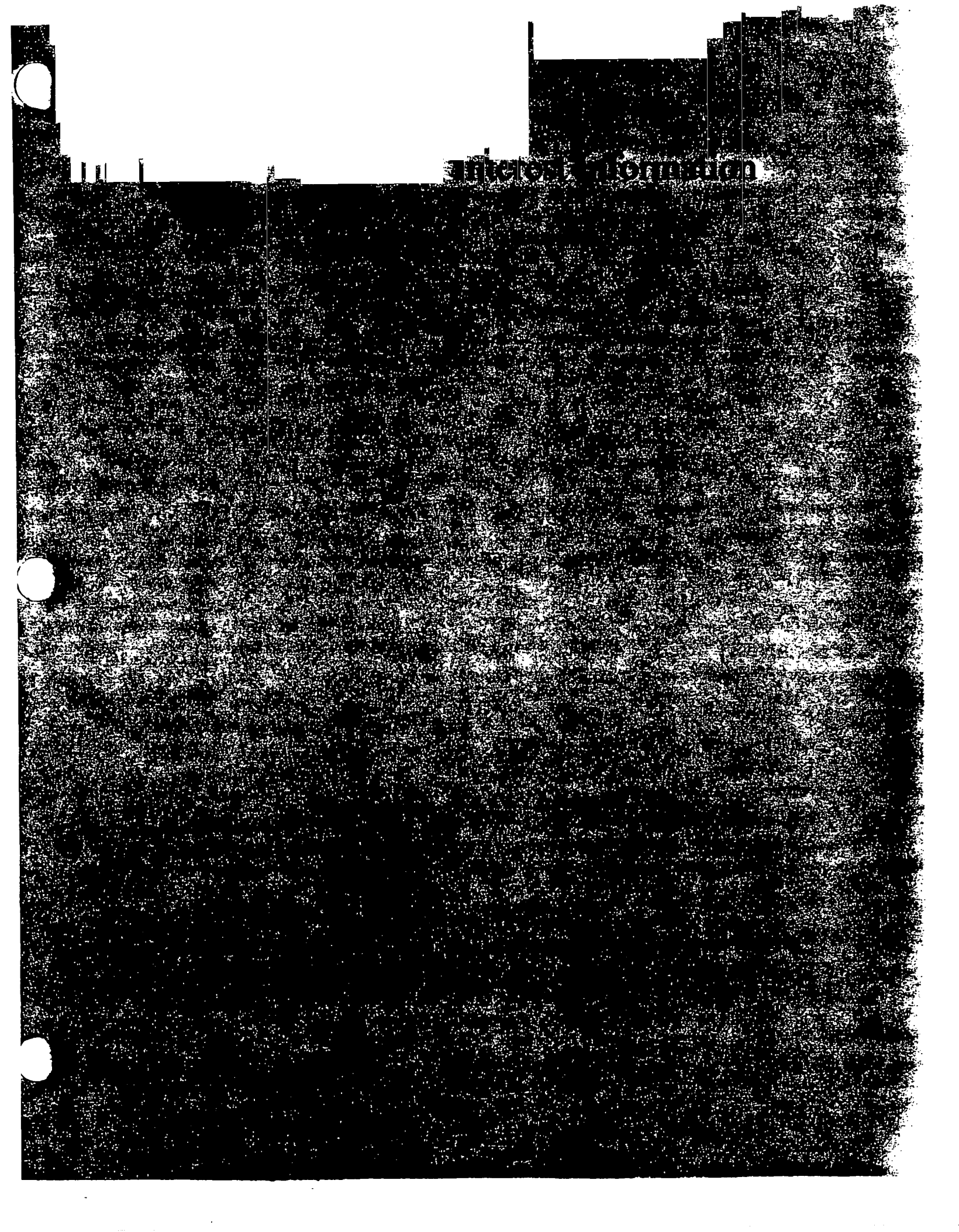
NDA 50-781 for ARESTIN™ (minocycline hydrochloride), Microspheres, 1 mg is approvable with the labeling changes recommended above, contingent upon the DSI audit of the San Antonio site not resulting in the disqualification of the data from that site.

/S/ D.D.S 12-18-00

Clarence C. Gilkes, D.D.S.

for DFS 12/18/00

Original to NDA 50-781



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:**	November 16, 2000
Fax No.:	301-827-2075	**No. of pages w/cover:**	5
RE:	NDA-50-781		

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

Ms. Bhatt:

Attached is the corrected form FDA 3454.

If you need any additional information, please don't hesitate to contact me.

Sincerely,

Markus F. Herzig
Executive Director Regulatory Affairs

ORAPHARMA, INC.

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

November 16, 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 Boulevard
Rockville, MD 20850

RE: NDA 50-781
Minocycline PTS
Amendment: Requested Financial Interest Information

Dear Dr. Wilkin:

Enclosed is the corrected form FDA 3454 as requested by Ms. Bhatt.

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

Sincerely,

Markus F. Herzig

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

Form FDA 356h
Submitted in duplicate

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration

Form Approved: OMB No. 0910-0396
Expiration Date: 3/31/02

CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

With respect to all covered clinical studies (or specific clinical studies listed below (if appropriate)) submitted in support of this application, I certify to one of the statements below as appropriate. I understand that this certification is made in compliance with 21 CFR part 54 and that for the purposes of this statement, a clinical investigator includes the spouse and each dependent child of the investigator as defined in 21 CFR 54.2(d).

Please mark the applicable checkbox.

☒ (1) As the sponsor of the submitted studies, I certify that I have not entered into any financial arrangement with the listed clinical investigators (enter names of clinical investigators below or attach list of names to this form) whereby the value of compensation to the investigator could be affected by the outcome of the study as defined in 21 CFR 54.2(a). I also certify that each listed clinical investigator required to disclose to the sponsor whether the investigator had a proprietary interest in this product or a significant equity in the sponsor as defined in 21 CFR 54.2(b) did not disclose any such interests. I further certify that no listed investigator was the recipient of significant payments of other sorts as defined in 21 CFR 54.2(f).

Clinical Investigators		
	See Attachments 3 and 4	

☐ (2) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that based on information obtained from the sponsor or from participating clinical investigators, the listed clinical investigators (attach list of names to this form) did not participate in any financial arrangement with the sponsor of a covered study whereby the value of compensation to the investigator for conducting the study could be affected by the outcome of the study (as defined in 21 CFR 54.2(a)); had no proprietary interest in this product or significant equity interest in the sponsor of the covered study (as defined in 21 CFR 54.2(b)); and was not the recipient of significant payments of other sorts (as defined in 21 CFR 54.2(f)).

☐ (3) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that I have acted with due diligence to obtain from the listed clinical investigators (attach list of names) or from the sponsor the information required under 54.4 and it was not possible to do so. The reason why this information could not be obtained is attached.

NAME	TITLE
James A. Ratigan	Chief Financial Officer
FIRM/ORGANIZATION: OraPharma, Inc.	
SIGNATURE: James A Ratigan	DATE: 1-24-00

Paperwork Reduction Act Statement

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Public reporting burden for this collection of information is estimated to average 1 hour per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to the address to the right:

Department of Health and Human Services
Food and Drug Administration
5600 Fishers Lane, Room 14C-03
Rockville, MD 20857

FORM FDA 3454 (2/00)

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

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

FOR FDA USE ONLY
APPLICATION NUMBER

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

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

APPLICANT INFORMATION

NAME OF APPLICANT	DATE OF SUBMISSION
OraPharma, Inc.	November 16, 2000
TELEPHONE NO. *(Include Area Code)*	FACSIMILE (FAX) Number (Include Area Code)
215-956-2200	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)	PROPRIETARY NAME (trade name) IF ANY
Minocycline PTS (Minocycline Periodontal Therapeutic System)	ARESTIN™

CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (If any)	CODE NAME (If any)
7 - dimethylamine - 6 - demethyl - 6 - deoxytetracycline hydrochloride	—

DOSAGE FORM:	STRENGTHS:	ROUTE OF ADMINISTRATION:
topical	1 mg	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) ☐ 507

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 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

This application contains the following items: *(Check all that apply)*

☐	1. Index	
☐	2. Labeling *(check one)*	☒ Draft Labeling ☐ Final Printed Labeling
☐	3. Summary (21 CFR 314.50(c))	
☐	4. Chemistry section	
☐	A. Chemistry, manufacturing, and controls information (e.g. 21 CFR 314.50(d) (1), 21 CFR 601.2)	
☐	B. Samples (21 CFR 314.50 (e) (1), 21 CFR 601.2 (a)) (Submit only upon FDA's request)	
☐	C. Methods validation package (e.g. 21 CFR 314.50 (e) (2) (i), 21 CFR 601.2)	
☐	5. Nonclinical pharmacology and toxicology section (e.g. 21 CFR 314.50 (d) (2), 21 CFR 601.2)	
☐	6. Human pharmacokinetics and bioavailability section (e.g. 21 CFR 314.50 (d) (3), 21 CFR 601.2)	
☐	7. Clinical Microbiology (e.g. 21 CFR 314.50 (d) (4))	
☐	8. Clinical data section (e.g. 21 CFR 314.50 (d) (5), 21 CFR 601.2)	
☐	9. Safety update report (e.g. 21 CFR 314.50 (d) (5) (vi) (b), 21 CFR 601.2)	
☐	10. Statistical section (e.g. 21 CFR 314.50 (d) (6), 21 CFR 601.2)	
☐	11. Case report tabulations (e.g. 21 CFR 314.50 (f) (1), 21 CFR 601.2)	
☐	12. Case report forms (e.g. 21 CFR 314.50 (f) (2), 21 CFR 601.2)	
☐	13. Patent information on any patent which claims the drug (21 U.S.C. 355 (b) or (c))	
☐	14. A patent certification with respect to any patent which claims the drug (21 U.S.C. 355 (b) (2) or (j) (2) (A)	
☐	15. Establishment description (21 CFR Part 600, if applicable)	
☐	16. Debarment certification (FD&C Act 306 (k) (1))	
☐	17. Field copy certification (21 CFR 314.50(k) (3))	
☐	18. User Fee Cover Sheet (Form FDA 3397)	
☒	19. OTHER (Specify)	Certification: Financial Interest and Arrangements of Clinical Investigators

CERTIFICATION

I agree to update this application with new safety information about the product that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. If this application is approved, I agree to comply with all applicable laws and regulations that apply to approved applications, including, but not limited to the following:

1. Good manufacturing practice regulations in 21 CFR 210 and 211, 606, and/or 820.
2. Biological establishment standards in 21 CFR Part 600.
3. Labeling regulations in 21 CFR 201, 606, 610, 660 and/or 809.
4. In the case of a prescription drug or biological product, prescription drug advertising regulations in 21 CFR 202.
5. Regulations on making changes in application in 21 CFR 314.70, 314.71, 314.72, 314.97, 314.99, and 601.12.
6. Regulations on Reports in 21 CFR 314.80, 314.81, 600.80 and 600.81.
7. Local, state and Federal environmental impact laws.

If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act, I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.

The data and information in this submission have been review and, to the best of my knowledge are certified to be true and accurate.

Warning: a willfully false statement is a criminal offense, U.S. Code, title 18, section 1001.

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT	TYPED NAME AND TITLE	DATE
Markus F. Herzig	Markus F. Herzig, Executive Director Regulatory Affairs and Quality Assurance	November 16, 2000

ADDRESS *(Street, City, State, and ZIP Code)*	TELEPHONE NUMBER
732 Louis Drive Warminster, PA 18974	215-956-2200

Please DO NOT RETURN this form to this address.

§54 FINANCIAL DISCLOSURE BY CLINICAL INVESTIGATORS

The following information in this section:

1. A signed form FDA 3454 by OraPharma, Inc. Chief Financial Officer.
2. A disclosure of Financial Interests of Principal and Subinvestigators who participated in the Phase 3 Pivotal Trials.
3. A list of all Principal and Subinvestigators who participated in the Pivotal Studies.
4. A signed Financial Certificate form for each Principal Investigator.

Attachment 1

Public Health Service
Food and Drug Administration

Form Approved: OMB No. 0910-0396
Expiration Date: 3/31/02

CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

With respect to all covered clinical studies (or specific clinical studies listed below (if appropriate)) submitted in support of this application, I certify to one of the statements below as appropriate. I understand that this certification is made in compliance with 21 CFR part 54 and that for the purposes of this statement, a clinical investigator includes the spouse and each dependent child of the investigator as defined in 21 CFR 54.2(d).

Please mark the applicable checkbox.

☐ (1) As the sponsor of the submitted studies, I certify that I have not entered into any financial arrangement with the listed clinical investigators (enter names of clinical investigators below or attach list of names to this form) whereby the value of compensation to the investigator could be affected by the outcome of the study as defined in 21 CFR 54.2(a). I also certify that each listed clinical investigator required to disclose to the sponsor whether the investigator had a proprietary interest in this product or a significant equity in the sponsor as defined in 21 CFR 54.2(b) did not disclose any such interests. I further certify that no listed investigator was the recipient of significant payments of other sorts as defined in 21 CFR 54.2(f).

Clinical Investigators		
	See Attachments 3 and 4	

☐ (2) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that based on information obtained from the sponsor or from participating clinical investigators, the listed clinical investigators (attach list of names to this form) did not participate in any financial arrangement with the sponsor of a covered study whereby the value of compensation to the investigator for conducting the study could be affected by the outcome of the study (as defined in 21 CFR 54.2(a)); had no proprietary interest in this product or significant equity interest in the sponsor of the covered study (as defined in 21 CFR 54.2(b)); and was not the recipient of significant payments of other sorts (as defined in 21 CFR 54.2(f)).

☐ (3) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that I have acted with due diligence to obtain from the listed clinical investigators (attach list of names) or from the sponsor the information required under 54.4 and it was not possible to do so. The reason why this information could not be obtained is attached.

NAME	TITLE
James A. Ratigan	Chief Financial Officer
FIRM/ORGANIZATION	
OraPharma, Inc.	
SIGNATURE	**DATE**
James A Ratigan	1-24-00

Paperwork Reduction Act Statement

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Public reporting burden for this collection of information is estimated to average 1 hour per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to the address to the right:

Department of Health and Human Services
Food and Drug Administration
5600 Fishers Lane, Room 14C-03
Rockville, MD 20857

Attachment 2

	Total number of shares and stock options held	Fully Diluted % Ownership Interest

Prinicpal Investigators

Thomas E. Van Dyke, DDS, PhD
Department of Periodontology
Goldman School of dental Medicine
Boston University
100 E. Newton Street, Suite 207
Boston, MA 02118-2392

David L. Cochran, DDS
Department of Periodontology
Health Scince Center at San Antonio
Univeristy of Texas
7703 Floyd Drive
San Antonio, TX 78284-7894

Sub-Investigators

Attachment 3

Financial Disclosure by Clinical Investigators

List of all principal- and sub-investigators: Investigators with financial interests in OraPharma, Inc. appear **bolded.**

Principal Investigators	Sub-Investigators
Connie L. Drisko, DDS Department of Periodontics, Endodontics and Dental Hygiene School of Dentistry University of Louisville 501 South Preston, Room 236 Louisville, KY 40292	[redacted]
Robert J. Genco, DDS, PhD Department of Oral Biology School of Dental Medicine State University of New York at Buffalo 120 Foster Hall 3435 Main Street Buffalo, NY 14214-3092	[redacted]
William Killroy, DDS, MS &John W. Rapley, DDS, MS (Co-principal PI) Department of Periodontology School of Dentistry University of Missouri at Kansas City 650 East 25th Street Kansas City, MO 64108	[redacted]
Ira B. Lamster, DDS, MMSc Department of Periodontology School of Dental and Oral Surgery Columbia University 630 West 168th Street, PH-7E-110 New York, NY 10032	[redacted]

David W. Paquette, DDS, MPH, DMSc
Department of Periodontology
School of Dentistry
University of North Carolina at Chapel Hill
Brauer Hall, CB#7450
Chapel Hill, NC 27599-7450

[redacted]

Thomas E. VanDyke, DDS, PhD
Department of Periodontology
Goldman School of Dental Medicine
Boston University
100 E. Newton Street, Suite 207
Boston, MA 02118-2392

[redacted]

Jack G. Caton, DDS, MS
Department of Periodontology
Eastman Dental Center
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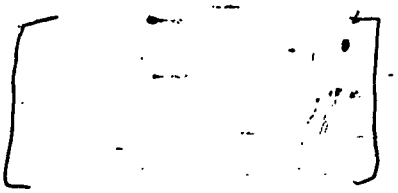
625 Elmwood Avenue
Rochester, NY 14620

[redacted]

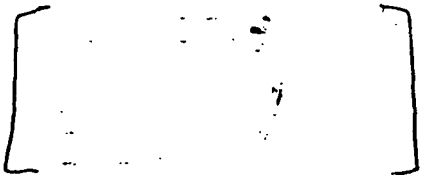
David L. Cochran, DDS
Department of Periodontology
Health Science Center at San Antonio
University of Texas
7703 Floyd Drive
San Antonio, TX 78284-7894

[redacted]

Joseph P. Fiorellini, DMD, DMSc
Department of Periodontology
Harvard School of Dental Medicine
188 Longwood Avenue
Boston, MA 02115



Richard J. Oringer, DDS, DMSc
Department of Periodontics
School of Dental Medicine
State University of New York at Stony Brook
B-530 Health Science Center
Stony Brook, NY 11794-8703



Georgia K. Johnson, DDS, MS
University of Iowa
Dental Science Building, S452
Iowa City, IA 52242

N. Ingvar Magnusson, DDS
Department of Oral Biology
University of Florida
1600 SW Archer Road
Gainesville, FL 32610

Sigmund Socransky, DMD
Department of Periodontology
Forsyth Dental Center
140 The Fenway
Boston, MA 02115

Larry L. Wolff, DDS, PhD
Division of Periodontology
School of Dentistry
University of Minnesota
17-164 Moos Tower
515 Delaware Street, SE
Minneapolis, MN 55455

[redacted]

G. Rutger Persson, DDS
Department of Periodontics
School of Dentistry
University of Washington
Box 357444
D-522 Health Science Building
Seattle, WA 98195-7444

[redacted]

Donald F. Adams, DDS, MS
Department of Periodontology
School of Dentistry
Oregon Health Science University
611 Southwest Campus Drive
Portland, OR 97201

[redacted]

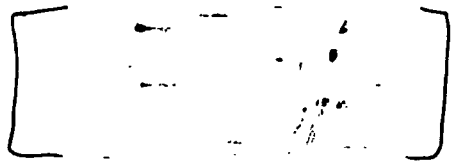
Gary C. Armitage, DDS, MS
Division of Periodontology
School of Dentistry, Dept. of Stomatology
University of California, San Francisco
521 Parnassus Avenue, Box 0650
San Francisco, CA 94143

[redacted]

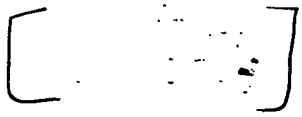
William V. Giannobile, DDS, DMSc
Department of Periodontics
School of Dentistry
University of Michigan
1011 North University Avenue
Ann Arbor, MI 48109-1075

[redacted]

Richard A. Reinhardt, DDS, PhD
College of Dentistry
University of Nebraska Medical Center
40th and Holdrege
Lincoln, NE 68583-0757



John W. Dean III, DDS, PhD
Department of Periodontology
School of Dental Medicine
University of Connecticut Health Center
263 Framington Avenue
Framington, CT 06030-1710



John C. Gunsolley, DDS, MS
Department of Periodontology
University of Maryland Dental School
666 West Baltimore Street
Baltimore, MD 21201

Thomas C. Hart, DDS, PhD
Department of Dentistry
Bowman Gray School of Medicine
Wake Forest University
Medical Center Boulevard
Salem, NC 27175

Bernard D. Shapiro, DDS
65 Garden Street
Wethersfield, CT 06109

Attachment 4

Clinical Investigator Financial Certification

This information below is provided in accordance with 21 CFR Part 54 in regard to the following clinical study.

OraPharma, Inc.
Pharmaceutical Company

Minocycline Periodontal Therapeutic System
Investigating Product

Multicenter Phase III Trial of Minocycline Periodontal Therapeutic System (Minocycline PTS): Adjunctive Use in Patients with Adult Periodontitis (OPI-103A & B)
Title of Study/Protocol #

Dr. Gary Armitage
Investigator

Yes ☐ No ☑	Do you, your spouse or dependent children have a financial arrangement with **OraPharma, Inc.**, whereby the value of compensation to you, your spouse or dependent children could be influenced by the outcome of the study? This includes compensation that could be grater for a favorable clinical result, compensation in the form of an equity interest in **OraPharma, Inc.** or compensation tied to sales of the product tested in the above study such as a royalty interest. If yes, the nature of the financial arrangement is as follows:
Yes ☐ No ☑	Do you, your spouse or dependent children have a proprietary interest in **Minocycline Periodontal Therapeutic Systems (Minocycline MPTS)** such as patent rights or rights under a patent, trademark, copyright or licensing agreement? If yes, the nature of the proprietary interest is as follows:
Yes ☐ No ☑	Do you, your spouse or dependent children, or any of you combined have a significant equity interest in **OraPharma, Inc.** such as an ownership interest, stock options or any other financial interest whose value cannot be readily determined through reference to public prices, or any equity in **OraPharma, Inc.** (if it is a publicly traded organization) exceeding $50,000, or any combination of these? If yes, the amount and nature of the equity interest is as follows:
Yes ☐ No ☑	Have you, your spouse or dependent children, or any of you combined received payments from **OraPharma, Inc.** such as an ownership interest, stock options or any other financial interest whose value cannot be readily determined through reference to public prices, or any equity interest in **OraPharma, Inc.** (if it is a publicly traded organization) exceeding $50,000, or any combination of these? If yes, the amount and nature of the equity interest is as follows:
Yes ☐ No ☑	Have you, your spouse or dependent children, or any of you combined received payments from **OraPharma, Inc.** in excess of $25,000, exclusive of the costs of conducting the clinical studies, such as honoraria, a grant or grants to fund ongoing research, compensation in the form of equipment, or retainers for ongoing consultation? If yes, the amount and nature of the payment is as follows:

To the best of my knowledge, the information provided above is correct and complete. I understand that I am obligated to amend this statement and notify **OraPharma, Inc.** promptly if there is any change in this information during the conduct of the clinical studies listed above or during one year after the studies have been completed.

Signature of Investigator	Sept. 5, 1999 Date

Clinical Investigator Financial Certification

This information below is provided in accordance with 21 CFR Part 54 in regard to the following clinical study.

OraPharma, Inc.
Pharmaceutical Company

Minocycline Periodontal Therapeutic System
Investigating Product

Multicenter Phase III Trial of Minocycline Periodontal Therapeutic System (Minocycline PTS): Adjunctive Use in Patients with Adult Periodontitis (OPI-103A & B)
Title of Study/Protocol #

Dr. Jack Caton
Investigator

Yes ☐ No ☒	Do you, your spouse or dependent children have a financial arrangement with **OraPharma, Inc.**, whereby the value of compensation to you, your spouse or dependent children could be influenced by the outcome of the study? This includes compensation that could be grater for a favorable clinical result, compensation in the form of an equity interest in **OraPharma, Inc.** or compensation tied to sales of the product tested in the above study such as a royalty interest. If yes, the nature of the financial arrangement is as follows:
Yes ☐ No ☒	Do you, your spouse or dependent children have a proprietary interest in **Minocycline Periodontal Therapeutic Systems (Minocycline MPTS)** such as patent rights or rights under a patent, trademark, copyright or licensing agreement? If yes, the nature of the proprietary interest is as follows:
Yes ☐ No ☒	Do you, your spouse or dependent children, or any of you combined have a significant equity interest in **OraPharma, Inc.** such as an ownership interest, stock options or any other financial interest whose value cannot be readily determined through reference to public prices, or any equity in **OraPharma, Inc.** (if it is a publicly traded organization) exceeding $50,000, or any combination of these? If yes, the amount and nature of the equity interest is as follows:
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To the best of my knowledge, the information provided above is correct and complete. I understand that I am obligated to amend this statement and notify **OraPharma, Inc.** promptly if there is any change in this information during the conduct of the clinical studies listed above or during one year after the studies have been completed.

Jack L. Caton Signature of Investigator	9/3/99 Date

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Dr. David Cochran
Investigator

Yes ☐ No ☒	Do you, your spouse or dependent children have a financial arrangement with **OraPharma, Inc.**, whereby the value of compensation to you, your spouse or dependent children could be influenced by the outcome of the study? This includes compensation that could be grater for a favorable clinical result, compensation in the form of an equity interest in **OraPharma, Inc.** or compensation tied to sales of the product tested in the above study such as a royalty interest. If yes, the nature of the financial arrangement is as follows:
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Signature of Investigator	10/8/99 Date

Clinical Investigator Financial Certification

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Dr. Joseph Fiorellini
Investigator

Yes ☐ No ☑	Do you, your spouse or dependent children have a financial arrangement with **OraPharma, Inc.**, whereby the value of compensation to you, your spouse or dependent children could be influenced by the outcome of the study? This includes compensation that could be grater for a favorable clinical result, compensation in the form of an equity interest in **OraPharma, Inc.** or compensation tied to sales of the product tested in the above study such as a royalty interest. If yes, the nature of the financial arrangement is as follows:
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PTF Signature of Investigator	9/3/99 Date

Clinical Investigator Financial Certification

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Dr. William Giannobile
Investigator

Yes ☐ No ☑	Do you, your spouse or dependent children have a financial arrangement with **OraPharma, Inc.**, whereby the value of compensation to you, your spouse or dependent children could be influenced by the outcome of the study? This includes compensation that could be grater for a favorable clinical result, compensation in the form of an equity interest in **OraPharma, Inc.** or compensation tied to sales of the product tested in the above study such as a royalty interest. If yes, the nature of the financial arrangement is as follows:
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Signature of Investigator	9/2/99 Date

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Dr. Georgia Johnson
Investigator

Yes ☐ No ☒	Do you, your spouse or dependent children have a financial arrangement with **OraPharma, Inc.**, whereby the value of compensation to you, your spouse or dependent children could be influenced by the outcome of the study? This includes compensation that could be grater for a favorable clinical result, compensation in the form of an equity interest in **OraPharma, Inc.** or compensation tied to sales of the product tested in the above study such as a royalty interest. If yes, the nature of the financial arrangement is as follows:
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Signature of Investigator	Date
	9-5-99