CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

50-775

ADMINISTRATIVE DOCUMENTS

Summary

We, Abbott Laboratories, certify that clarithromycin bulk drug is claimed in U.S. Patent No. 4,331,803. The patent was issued on 25 May 1982 to Taisho Pharmaceuticals. Taisho Pharmaceuticals has licensed Abbott Laboratories under this patent. The patent is presently set to expire on 23 May 2005.

A second U.S. Patent for clarithromycin, crystal form I, is claimed in U.S. Patent No. 5,858,986. The patent was issued on 12 January 1999 and is presently set to expire on 24 July 2016.

A patent application for an extended-release formulation of clarithromycin is claimed in Application No. 838,900. This patent application was issued on 11 April 1997 and is presently set to expire on 11 April 2017. This patent application will be issued as a U.S. Patent later this year.

Exclusivity Checklist

NDA:	NDA 50-775 XL
Trade Name:	BIAXIN XL
Generic Name:	CLARITHROMYCIN
Applicant Name:	ABBOTT
Division:	HFD-520 / DAIDP
Project Manager:	JOSÉ R. CINTRON
Approval Date:	March 3, 2000

PART I: IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, but only for certain 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 an original NDA?	Yes	✓	No	
b. Is it an effectiveness supplement?	Yes		No	✓
c. If yes, what type? (SE1, SE2, etc.)				
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.

Explanation:

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:

Explanation:

d. Did the applicant request exclusivity?	Yes		No	✓
If the answer to (d) is "yes," how many years of exclusivity did the applicant request?				

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

2. Has a product with the same active ingredient(s), dosage form, strength, route of administration, and dosing schedule previously been approved by FDA for the same use?	Yes	✓	No	
If yes, NDA # 50-662 / NDA 50-698				
Drug Name: Clarithromycin				

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE

BLOCKS.				
3. Is this drug product or indication a DESI upgrade?	Yes		No	
IF THE ANSWER TO QUESTION 3 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS (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.	Yes		No	
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).				
Drug Product				
NDA #				
Drug Product				
NDA #				
Drug Product				
NDA #				
2. Combination product.	Yes		No	
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).				
Drug Product				
NDA #				
Drug Product				
NDA #				
Drug Product				
NDA #				
IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY				

TO THE SIGNATURE BLOCKS. IF "YES," GO TO PART III.				
PART III: THREE-YEAR EXCLUSIVITY FOR NDA'S 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.				
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. For the purposes of this section, studies comparing two products with the same ingredient(s) are considered to be bioavailability studies.				
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 BLOCKS.**				
Basis for conclusion:				
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:				
Investigation #1, Study #:				
Investigation #2, Study #:				
Investigation #3, Study #:				
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	
If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:				
Investigation #1 -- NDA Number				
Investigation #2 -- NDA Number				
Investigation #3 -- NDA Number				
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	
If you have answered "yes" for one or more investigations, identify the NDA in which a similar investigation was relied on:				
Investigation #1 -- NDA Number				
Investigation #2 -- NDA Number				
Investigation #3 -- NDA Number				
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"):				
Investigation #1				
Investigation #2				

Investigation #3				

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	Yes		No	
IND#:				
Explain:				
Investigation #2	Yes		No	
IND#:				
Explain:				
Investigation #3	Yes		No	
IND#:				
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	
IND#:				
Explain:				
Investigation #2	Yes		No	
IND#:				
Explain:				
Investigation #3	Yes		No	
IND#:				
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:				

BACK TO TOP

Signature of PM/CSO
Date: 2/28/2000

/S/

/S/
Signature of Division Director
Date: 3/2/2000

cc:
Original NDA
Division File
HFD-93 Mary Ann Holovac

BACK TO TOP

PEDIATRIC PAGE

(Complete for all original application and all efficacy supplements) -

NDA/BLA Number:	50775	**Trade Name:**	BIAXIN XL FILMTAE(CLARITHROMYCIN)500MG E
Supplement Number:		**Generic Name:**	CLARITHROMYCIN
Supplement Type:		**Dosage Form:**	CRT
Regulatory Action:	AP	**Proposed Indication:**	Acute Bacterial Exacerbation of Chronic Bronchitis (AECB) and Acute Bacterial Sinusitis

ARE THERE PEDIATRIC STUDIES IN THIS SUBMISSION?

NO, Pediatric content not necessary because of pediatric waiver

What are the INTENDED Pediatric Age Groups for this submission?

____NeoNates (0-30 Days) ____Children (25 Months-12 years)

____Infants (1-24 Months) _X_ Adolescents (13-16 Years)

Label Adequacy	Adequate for SOME pediatric age groups
Formulation Status	-
Studies Needed	-
Study Status	-

Are there any Pediatric Phase 4 Commitments in the Action Letter for the Original Submission? NO

COMMENTS:

This Page was completed based on information from a PROJECT MANAGER/CONSUMER SAFETY OFFICER, JOSE CINTRON

/S/

Signature

2/28/2000

Date

Certification Requirement for all Applications

For Approval of a Drug Product

Concerning Using Services of Debarred Persons

- DEBARMENT STATEMENT -

Any application for approval of a drug product submitted on or after June 1, 1992, must include:

> "A certification that the applicant did not and will not use in any capacity the services of any person debarred under subsections (a) or (b) (Sections 306 (a) or (b) of the Federal Food, Drug, and Cosmetic Act), in connection with this application for approval of a drug product."

Abbott Laboratories certifies that it did not and will not use in any capacity the services of any person debarred under subsections (a) or (b) [Section 306(a) or (b)], in connection with such application.

[Generic Drug Enforcement Act of 1992, Section 306(k)(1) of 21 USC 335a(k)(1)].

Greg Bosco
Product Manager, PPD Regulatory Affairs
Abbott Laboratories
Dept. 491, Bldg. AP6B-1
(847) 937-6970
100 Abbott Park Road
Abbott Park, Illinois 60064

4/30/99
Date

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	DATE OF SUBMISSION
Abbott Laboratories	March 2, 2000
TELEPHONE NO. *(Include Area Code)* (847) 937-6970	FACSIMILE (FAX) Number *(Include Area Code)* (847) 937-8002
APPLICANT ADDRESS *(Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued)*: D-491/AP6B-1SW, 100 Abbott Park Road, Abbott Park, IL 60064-6108	AUTHORIZED U.S. AGENT NAME & ADDRESS *(Number, Street, City, State, ZIP Code, telephone & FAX number)* IF APPLICABLE

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER (if previously issued) 50-775

ESTABLISHED NAME *(e.g., Proper name, USP/USAN name)*	PROPRIETARY NAME *(trade name)* IF ANY
Clarithromycin	Biaxin XL Filmtab

CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME *(If any)*	CODE NAME *(If any)*
6-O-Methylerythromycin	Abbott-56268

DOSAGE FORM:	STRENGTHS:	ROUTE OF ADMINISTRATION:
Extended-Release Tablet	500 mg	Oral

(PROPOSED) INDICATION(S) FOR USE.
Antibiotic

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 FDA Request for Information.

PROPOSED MARKETING STATUS (check one) ☑ PRESCRIPTION PRODUCT (Rx) ☐ OVER THE COUNTER PRODUCT (OTC)

NUMBER OF VOLUMES SUBMITTED 1 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.

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

NDAs - 50-662, 50-697, 50-698, 50-721

FORM FDA 356h (7/97) Created by Electronic Document Services USDHHS (301) 443-3454 EF

	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)
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	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

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 reviewed 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
Greg Bosco	Greg Bosco Sr. Product Manager	March 2, 2000

ADDRESS *(Street, City, State, and ZIP Code)*	Telephone Number
100 Abbott Park Road Abbott Park, IL 60064-6108	(847) 937-6970

Public reporting burden for this collection of information is estimated to average 40 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

DHHS, Reports Clearance Officer
Paperwork Reduction Project (0910-0338)
Hubert H. Humphrey Building, Room 531-H
200 Independence Avenue, S.W.
Washington, DC 20201

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Please DO NOT RETURN this form to this address.

FORM FDA 356h (7/97)

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Abbott Laboratories	December 7, 1999
TELEPHONE NO. *(Include Area Code)* (847) 937-6970	FACSIMILE (FAX) Number *(Include Area Code)* (847) 937-8002
APPLICANT ADDRESS *(Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued)*: D-491/AP6B-1SW, 100 Abbott Park Road, Abbott Park, IL 60064-6108	AUTHORIZED U.S. AGENT NAME & ADDRESS *(Number, Street, City, State, ZIP Code, telephone & FAX number)* IF APPLICABLE

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6-O-Methylerythromycin	Abbott-56268

DOSAGE FORM:	STRENGTHS:	ROUTE OF ADMINISTRATION:
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(PROPOSED) INDICATION(S) FOR USE:
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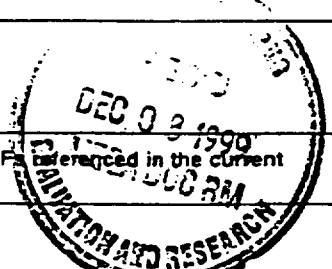

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Warning: a willfully false statement is a criminal offense, U.S. Code, title 18, section 1001.

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT	TYPED NAME AND TITLE	DATE
for	Greg Bosco Sr. Product Manager	12/7/99

ADDRESS *(Street, City, State, and ZIP Code)*	Telephone Number
100 Abbott Park Road Abbott Park, IL 60064-6108	(847) 937-6970

Public reporting burden for this collection of information is estimated to average 40 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

DHHS Reports Clearance Officer
Paperwork Reduction Project (0910-0338)
Hubert H. Humphrey Building, Room 531-H
0 Independence Avenue, S.W.
ashington, DC 20201

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.

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FORM FDA 356h (7/97)

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	DATE OF SUBMISSION
Abbott Laboratories	April 30, 1999
TELEPHONE NO. *(Include Area Code)* (847) 937-6970	FACSIMILE (FAX) Number *(Include Area Code)* (847) 937-8002
APPLICANT ADDRESS *(Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued)*: D-491/AP6B-1, 100 Abbott Park Road, Abbott Park, IL 60064-3500	AUTHORIZED U.S. AGENT NAME & ADDRESS *(Number, Street, City, State, ZIP Code, telephone & FAX number)* IF APPLICABLE

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER (If previously issued) 50-775

ESTABLISHED NAME *(e.g., Proper name, USP/USAN name)*	PROPRIETARY NAME *(trade name)* IF ANY
Clarithromycin	Biaxin XL Filmtab

CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME *(If any)*	CODE NAME *(If any)*
6-O-Methylerythromycin	Abbott-56268

DOSAGE FORM:	STRENGTHS:	ROUTE OF ADMINISTRATION:
Extended-Release Tablet	500 mg	Oral

(PROPOSED) INDICATION(S) FOR USE:
Antibiotic

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

PROPOSED MARKETING STATUS (check one) ☑ PRESCRIPTION PRODUCT (Rx) ☐ OVER THE COUNTER PRODUCT (OTC)

NUMBER OF VOLUMES SUBMITTED 97

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.

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

NDAs - 50-662, 50-697, 50-698, 50-721

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 reports 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) Financial Disclosure Information

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 reviewed 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
Greg Bosco	Greg Bosco Product Manager	4/30/99

ADDRESS *(Street, City, State, and ZIP Code)*	Telephone Number
100 Abbott Park Road Abbott Park, IL 60064-3500	(847) 937-6970

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DHHS, Reports Clearance Officer
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200 Independence Avenue, S.W.
Washington, DC 20201

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FORM FDA 356h (7/97)

CONSULTATION REQUEST/RESPONSE
Office of Post-Marketing Drug Risk Assessment
(OPDRA; HFD-400)

DATE SENT: October 29, 1999	DUE DATE: N/A	OPDRA CONSULT #: 99-038

TO (Division): Gary Chikami, M.D.
Director, Division of Anti-Infective Drug Products
(HFD-520)

PRODUCT NAME: Biaxin XL™ Filmtab (Clarithromycin Extended-release Tablets) NDA#: 50-775	MANUFACTURER: Abbott Laboratories

CASE REPORT NUMBER(S): N/A

SUMMARY:

In response to the request by the Division of Anti-Infective Drug Products, OPDRA conducted a review of the potential name confusion between the proposed proprietary name, Biaxin XL™, and other approved proprietary/generic names. This review includes a study conducted within OPDRA with emphasis on the evaluation of the potential medication errors in handwriting and verbal communication of this proposed proprietary name.

OPDRA RECOMMENDATION:

OPDRA has no objections to the use of the proprietary name, Biaxin XL™. See review.

/S/ 11/1/99

Jerry Phillips
Associate Director for Medication Error Prevention
Office of Post-Marketing Drug Risk Assessment
Phone: (301) 827-3246
Fax: (301) 827-5189

/S/ 11/2/99

Peter Honig, M.D.
Deputy Director
Office of Post-Marketing Drug Risk Assessment
Center for Drug Evaluation and Research
Food and Drug Administration

Office of Post-Marketing Drug Risk Assessment
HFD-400; Rm 15B-03
Center for Drug Evaluation and Research

Proprietary Name Review

DATE OF REVIEW: **October 29, 1999**

NDA#: **50-775**

NAME OF DRUG: **Biaxin XL™ Filmtab; 500 mg**
(Clarithromycin Extended-release Tablets)

NDA HOLDER: **Abbott Laboratories**

I. INTRODUCTION

This consult is in response to a request sent on August 2, 1999, from the Division of Anti-Infective Drug Products to review a proposed proprietary drug name, Biaxin XL, regarding potential name confusion with other proprietary/generic drug names. In addition, the container labels and carton labeling were reviewed for possible interventions in minimizing medication errors.

The proposed proprietary name, Biaxin XL, was previously reviewed by the Labeling and Nomenclature Committee (LNC) in September 1999 and was found to be acceptable.

PRODUCT INFORMATION

Biaxin is available as clarithromycin immediate-release tablets and granules for oral suspension. Abbott Laboratories are seeking an approval for clarithromycin extended release tablet, Biaxin XL. Clarithromycin is a semi-synthetic macrolide antibiotic. It is indicated for the treatment of mild to moderate infections caused by susceptible strains of the designated microorganisms such as *Haemophilus parainfluenzae, Staphylococcus aureus, Haemophilus influenza, Moraxella catarrhalis,* and *Streptococcus pneumoniae.* Clarithromycin is rapidly absorbed from the gastrointestinal tract after oral administration. In fasting human subjects, peak serum concentrations were attained within 2 hours after oral dosing. Elimination half-life was 3 to 4 hours with 250 mg administered every 12 hours and 5 to 7 hours for 500 mg administered 8 to 12 hours. The renal clearance of clarithromycin is relatively independent of the dose size and approximates the normal glomerular filtration rate. Clarithromycin is principally excreted via the liver and kidney. Clarithromycin may be administered without dosage adjustment to patients with hepatic impairment and normal renal function. However, in the presence of severe renal impairment with or without coexisting hepatic impairment, decreased dosage or prolonged dosing intervals may be appropriate. It is recommended

that Biaxin XL be taken with food. The usual dose is two 500 mg tablets once daily. Biaxin XL Filmtab is supplied in 500 mg strength.

II. RISK ASSESSMENT

In order to predict the potential medication errors and to determine the degree of confusion of this proposed proprietary name, Biaxin XL, with other drug names, the medication error staff of OPDRA searched American Drug Index (42nd Edition), Drug Facts and Comparisons (1998 Edition), PDR (53rd Edition, 1999), Drug Product Reference File (DPRF), and EES (Established Evaluation System) for possible sound-alike or look-alike names to approved and unapproved drug products. A focus group discussion was conducted to review all of the findings from the searches. In addition, OPDRA conducted a study of written and verbal analysis of the proposed proprietary name employing health practitioners within OPDRA to evaluate potential errors in handwriting and verbal communication of the name. This exercise was conducted to simulate an actual practice setting.

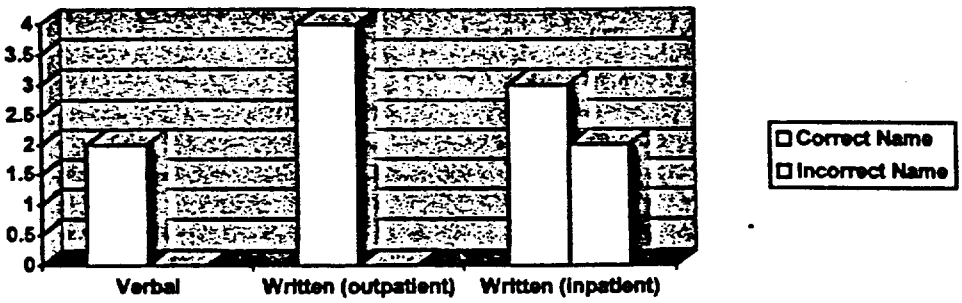
A. Study conducted within OPDRA

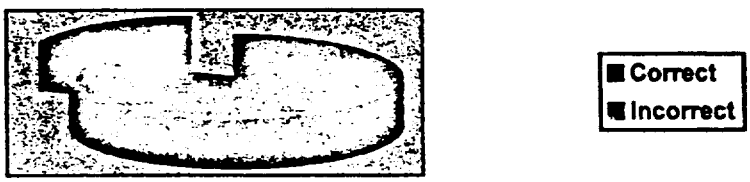
1) Methodology

This study involved 18 health professionals comprised of pharmacists, physicians, and nurses within OPDRA to determine the degree of confusion between Biaxin XL and other drug names due to the similarity in handwriting and verbal pronunciation of the name. Random samples of the written orders, either inpatient or outpatient, were delivered to the participating health professionals via e-mail. In addition, verbal orders for Biaxin XL via voice mail were sent to the participating health professionals for their review. After receiving the prescription orders, the participants sent their interpretations of the prescriptions vial e-mail to the medication error staff. After receiving the interpretations, the correct spelling of the proposed proprietary name was sent to the health professionals with a request for handwriting samples of the names. The medication error staff then reviewed the samples of the handwritten names.

2) Results

We received responses from eleven participants, nine of which interpreted the proposed proprietary name correctly. Two interpretations for verbal orders, four for outpatient written orders, and five for inpatient written orders were received. The results are as follows:





Incorrect names include: Bioxin XL & Biaxin

3) Discussion

The results of the verbal and written analysis study demonstrate that nine out of eleven participants interpreted the proposed proprietary name correctly. Majority of the participants did not have difficulty interpreting the proposed tradename except for one participant who confused the extended-release Biaxin XL for Biaxin. The confusion could have been attributed to the fact that Biaxin is currently available and Biaxin XL is not a familiar drug to health professionals. However, if Biaxin XL is approved, education to differentiate the two formulations should be provided to healthcare professionals in order to minimize medication errors.

B. Focus Group Findings

1) Biaxin XL is an extended–release product with a once daily dosing regimen. The abbreviation, XL, is a known term for extended-release formulation (i.e. Lodine XL, Toprol XL, Glucotrol XL, Minipress XL, Ditropan XL, and Procardia XL), and the XL products typically have once daily dosing schedules. Furthermore, searches in available texts, databases, and the handwriting samples did not produce any significant new information to render Biaxin XL objectionable.

2) Having an overlapping strength (500 mg) for two drug products with same active ingredient and different pharmacokinetics is a known associated risk factor in dispensing and/or prescribing errors. Biaxin and Biaxin XL fit this profile.

3) The abbreviation, "XL", has been the cause of several medication errors with

Procardia. The liquid-filled nifedipine capsules have been administered sublingually because the modifier, "XL", was verbally misunderstood for "SL" (sublingual) off-labeled use. OPDRA does not consider this a risk factor for Biaxin XL.

III. LABELING, PACKAGING, AND SAFETY RELATED ISSUES

In the review of the packaging and the labeling of Biaxin XL, OPDRA has attempted to focus on safety issues relating to possible medication errors. Many of the items discussed in this consult involve issues normally reviewed by the chemist and the medical officer.

OPDRA has reviewed the current labeling and has identified several areas of possible improvement, which might minimize potential user error.

A. CONTAINER LABEL

Abbott laboratories is the manufacturer for both immediate release Biaxin and Biaxin XL, and therefore, the proposed labels for Biaxin XL are very similar to Biaxin labels except for the color differentiation among the different strengths. In addition, both Biaxin and Biaxin XL are available in 500 mg strength. In order to differentiate the two dosage forms with identical strength, OPDRA recommends that the labels for these products appear distinctly different. We believe that the "XL" modifier could be a different color than the proprietary name, "Biaxin".

B. BLISTER PACK LABEL

"Dose 1, Dose 2, Dose 3... Dose 7" on the back of the blister pack should be replaced with "Day 1, Day 2, Day 3... Day 7" to clarify that only one dose (two tablets) should be taken per day.

C. CARTON LABELING

See comments under CONTAINER LABEL.

IV. RECOMMENDATIONS

A. OPDRA has no objections to the use of the proprietary name, Biaxin XL.

B. OPDRA recommends the above labeling revisions which might lead to safer use of the product.

OPDRA would appreciate feedback of the final outcome of this consult (e.g. copy of the revised label/labeling/packaging). We would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Lauren Lee, Pharm.D. at (301)827-3243.

/S/ 4/1/99

Lauren Lee, Pharm.D.
Safety Evaluator
Office of Post-Marketing Drug Risk Assessment

Concur:

/S/ 4/1/99

Jerry Phillips, RPh
Associate Director for Medication Error Prevention
Office of Post-Marketing Drug Risk Assessment

CC:

Office Files
HFD-520: Jose Cintron, Consumer Safety Officer, Division of Anti-Infective Drug Products
HFD-400: Jerry Phillips, Associate Director, OPDRA
HFD-400: Peter Honig, Deputy Director, OPDRA
HFD-2 : Mac Lumpkin, Acting Director, OPDRA

Financial Disclosure by Clinical Investigators

Abbott Laboratories is submitting the following information under the provisions of 21 CFR 54.4. Provided in this section is a Form FDA 3454 Certification: Financial Interests and Arrangements of Clinical Investigators and a Form FDA 3455 Disclosure: Financial Interests and Arrangements of Clinical Investigators covering the following clinical studies: M97-734, M97-814, M97-667 and M97-756.

This section is organized in the following manner:

- Form FDA 3454
  - List of names of clinical investigators, for each study, meeting the requirements of 21 CFR 54.2(a), (b) and (f).
  - List of names of clinical investigators, for each study, that are employees of Abbott Laboratories.
  - List of names of clinical investigators (Studies M97-667 and M97-756) where the sponsor was not able to obtain the information required under 21 CFR 54.2(b) from the investigators. The procedures taken to obtain this information, showing due diligence on the part of the sponsor, are provided.

- Form FDA 3455
  - Details of the individual's disclosable financial arrangements and interests, along with a description of steps taken to minimize the potential bias of clinical study results is provided for one investigator.

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 attached lists	

☐ (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
Roland T. Catherall	Vice President, Regulatory Affairs
FIRM/ORGANIZATION: Abbott Laboratories, Pharmaceutical Products Division	
SIGNATURE: Roland T. Catherall	DATE: 4/29/99

Paperwork Reduction Act Statement

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

Study No. M97-734

Certification: Financial Interests and Arrangements of Clinical Investigators

Principal Investigator
Robert F. O'Dea*
Murray Keene
Norman Weinstein

APPEARS THIS WAY
ON ORIGINAL

* Principal Investigator is listed only to identify the site. The principal investigator is an employee of the Sponsor.

Study No. M97-734
Clinical Investigators who are Employees of the Sponsor

Principal Investigator
Robert F. O'Dea
Paolo Baroldi
Scott Brun
John Cavanaugh
Thao Doan
Susana deDennis
Dionisio Yorro
Linda Balen
Marietta Centko
Daniel Selness

APPEARS THIS WAY
ON ORIGINAL

Note: **Principal Investigator is bolded.**

Study No. M97-814
Certification: Financial Interests and Arrangements of Clinical Investigators

Principal Investigator
Robert F. O'Dea*
Murray Keene
Norman Weinstein

APPEARS THIS WAY
ON ORIGINAL

* Principal Investigator is listed only to identify the site. The principal investigator is an employee of the Sponsor.

Study No. M97-814
Clinical Investigators who are Employees of the Sponsor

Principal Investigator
Robert F. O'Dea
Paolo Baroldi
Scott Brun
John Cavanaugh
Thao Doan
Susana deDennis
Dionisio Yorro
Linda Balen
Marietta Centko
Daniel Selness

Note: **Principal Investigator is bolded.**

Study No. M98-976

Certification: Financial Interests and Arrangements of Clinical Investigators

Principal Investigator
H. Wayne Hutman
Ernesto Fuentes
DarLene Stevens

APPEARS THIS WAY
ON ORIGINAL

APPEARS THIS WAY
ON ORIGINAL

Note: **Principal Investigator is bolded**

Study No. M97-667
Certification: Financial Interests and Arrangements of Clinical Investigators

Principal Investigators		
Lawrence K. Alwine		
Jane Hidalgo		
Frances Seoane		
Mark Blatter		
Judy Costantini	Janet Breslin	Tobey A. Kresel
Judith P. Giga	Amy Gosling	Dolly Maben
Edward C. Ketyer	Scott Tyson	Amy L. McGarrity
Sarah E. Kohl	Celeste Welkons	Carol Miller
Raymond O'Toole	Sharon Wolkin	Kimberly M. Pezzone
Joel Safier	Kochikar Gopalkrishna Pai	Lynn Regina
Katherine L. Walczak	Harvey M. Rubin	Keith S. Reisinger
Judy Zabkar	Todd Wolynn	Tracy Shenk
Barbara Braman	Lee Haniford	
John Dixon		
Scott Dorfner		
Bruce Douglas		
David Blessing	Rhonda L. Durant	Karen A. Riesinger
Dan Crawford	Tim Janzen	Michael Tso
Nancy Dougherty	Walter Norton	
James L Fidelholtz		
Douglas Behrman	Sue Fidelholtz	Marsha Zartman
Allison Fidelholtz	Angela Vaughan	
Ronald Gilman		
Alvan E. Fisher	Lynne A. Haughey	Charles Bruce Sherman
Stephen Gugenheim *		
Richard S. Cohen		
James B. Harris		
James Herron		
A. Ali Imam		
Frank Canavan	Amit Patel	Encarna Zamanian
Judy Kallman	Mahfooz Peshimam	

Note: Principal Investigator is bolded

*** = Principal Investigator is listed only to identify site. The sponsor was not able to obtain the information required under 21 CFR 54.2(b) from this investigator. This investigator can be found on the Due Diligence list for this Study.**

Study No. M97-667
Certification: Financial Interests and Arrangements of Clinical Investigators

Principal Investigators		
Arnold Lentnek Lucrecia Bennett Thomas Sheftel		
James McCarty Neydi S. Ellis Janice Harms		
Steven Miller James Dunlay		
John Murray * John Holsinger		
John E. Pappas Gary Margolies Debra Schilder		
Marshall Sack Murat Argun David Carter Richard DeBehnke	George Handley Jerry Hood William Lockette	Bruce Page Dana Sprute Dennis Welch
Guy A. Settipane		
Umedchandra K. Shah * Kiran D. Mehta Nayan R. Shah		
William N. Smith Charles H. DeBusk Luis C. Pannocchia		
Richard I. Sperling Michael D. Achey Evan R. Kaiser	Yelena Levin George J. Pereira	Susan Thomas
Paul V. Williams Leonard C. Altman Jonathan W. Becker Clifton T. Furukawa Michelle R. Hinatsu	Michael S. Kennedy Mary V. Lasley Dominick A. Minotti	Gail G. Shapiro Brian A. Smart Frank S. Virant

Note: Principal Investigator is bolded

*** = Principal Investigator is listed only to identify site. The sponsor was not able to obtain the information required under 21 CFR 54.2(b) from this investigator. This investigator can be found on the Due Diligence list for this Study.**

M97-667

Due Diligence Procedures

The procedures taken to obtain the information required under 21 CFR 54.2(b) from the investigators, showing due diligence on the part of the sponsor, are as follows.

1. Individual letters were sent to each investigator which included financial disclosure request forms. Forms were provided for the principal investigator and all subinvestigators as defined in 21 CFR 54.2(d). A letter of receipt was included in each package and the investigator was required to sign and fax back to the sponsor.

2. The investigators were required to fill out the financial disclosure request forms and return them to the sponsor by a specified date.

3. Each investigator who did not return the financial disclosure request forms by the specified date were individually contacted on a follow-up basis by phone.

4. A final date of 4/15/99 was established for the return of the financial disclosure request forms in order for Abbott to verify the information. Any investigator still outstanding was placed on the following Due Diligence Listing.

Study No. M97-667
Due Diligence Listing

Principal Investigators		
Marie-Claude Audet		
Danielle Bélanger		
Alain Martel		
Marie-Helene Tremblay		
Larry Barnes		
Gail L. Shutt		
Mark T. Weeks		
Mark Blatter *		
Amy Ackman	Abhaykumar G. KemKar	Janet Ries
Debra Amelio	Robert G. Lesnock	Vicki Seel
Christine M. Badke	Susan Logut	Virginia Shannon
Cyndi Getty	Becky Loutsion	Tandy Shaw
Clare Grzejka	Kim McIntosh	Marilyn Stanko
Harry L. Haus	Valerie Mead	Laurie A. Jimirro Wehner
Charles Hsu	Donna Quakinbush	
Robert Blattner		
Alan Ackerman	John Ebens	Donald Rademacher
Russell B. Branum	Nancy Elder	Keith Thompson
Mark Bernsten	Neal Fellers	David Tryggestad
Ethan Cary	Dale Kliner	Daniel Zenk
Robert Cash	J. Chandler Major	
Robert Cohen		
Kevin L. Schaffer		
Edward Diamond		
Guy M. Dugan	Robert W. Hart	John E. Pantano
Don A. Harden	Jeffrey P. Huml	
John Dixon *		
Charles C. Snow		
Lois A. Nesbit		
Scott Dorfner *		
Stanley A. Markunas		
James I. Fidelholtz *		
Howard Bernie	Holly Giglio	Connie Swing

Note: Principal Investigator is bolded

*** = Principal Investigator is listed only to identify site. The sponsor was successful in obtaining the information required under 21 CFR 54.2(b) from this investigator. This investigator can be found on the Certification list for this Study.**

Study No. M97-667
Due Diligence Listing

Principal Investigators		
Louis Ganier		
Brenda J. Adams	Martin Gabica	Kristine Mors
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Ronald Gilman *		
David L. Fried		
Dean Gray		
Todd Child	Steve Miller	Richard Nielsen
Stephen Gugenheim		
Daniel R. Fear		
Philip Halverson		
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James B. Harris *		
A. D'Angelo	R. Hruskovich	D. Krichbaum
Stephen Hawes		
Patricia Dunlap	Teresa Price	
Hunter Hoover	Vickie Zimmer	
Jeffrey Hopland		
Arnold Hopland		
Gregory W. Coppola		
A. Ali Imam *		
Jane. Houtz		
Jeffrey Muller		
Jonathan Matz		
David B. K. Golden		
Ana Marie Pasatiempo		
Dennis McCluskey		
Kendrick Bashor	Angela DeJulius	Marilyn Perkowski
Brian Cain	Robert Parsons	Patricia Summers
Edward McNellis		
Jeffrey Deal	Raymond Kaplan	Stuart Owens
Jeffrey Fenwick	Russell Kitch	C. Willy Schwenzfeier
Steven Miller *		
Peter A. Holt	Lisa Piastrelli	
Mala B. Mehta	Thomas M. Zizic	

Note: Principal Investigator is bolded

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Study No. M97-667
Due Diligence Listing

Principal Investigators		
John Murray		
Kelley Allen	Laura Fisher	Elizabeth Mejia-Millan
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Tonya Durham	Elizabeth Jones	Barry Schumer
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Sharon Hausman-Cohen	Charles Felger	David Joseph
Nathan Schultz		
Donna Brosler	Valerie Friedman	Jennifer Thompson
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David Denmead	Rosario Roverso	
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Frank Garamy	Kathy Henke	Sherry Huneytcutt
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William N. Smith *		
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B J. Ellington		
Joseph W. Sokolowski, Jr.		
Vincent Acampora	Nicholas Basso	Andrew Levin
Donald Auerbach	Kathleen Goldstein	Irwin Spirn

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Study No. M97-667
Due Diligence Listing

Principal Investigators		
Eric S.Solomon		
Robert Bashinsky	Kenneth Harman	Andrew McCown
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Jeffrey A. Wald		
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Paul V. Williams*		
Timothy G. Wighton		

APPEARS THIS WAY
ON ORIGINAL

Note: Principal Investigator is bolded

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Study No. M97-756
Certification: Financial Interests and Arrangements of Clinical Investigators

Principal Investigators		
Jay Adler		
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Joseph Arno		
William Ashworth *		
Gerri Henderson	Philemon R. Merrill, Jr	Cynthia Slot
Robert Jelaco	Carolyn Powell	
Thomas Bell *		
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Tim Hegel		
George Bensch		
William Chapman	Jerry Rapert	Samantha Walker
Kathy Hancock	Sandra Vallery	
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David I. Bernstein	Karen Joan Murphy	Brenda A. Wentstru
I. Leonard Bernstein		
Gary Bowman		
Deborah Allen-Brown	Diana Doll	Margaret Lowery
Chris Bowman	Irene Hanson	Nooshig Luz Salvador
Mark Bowman	Charles Ireland	Timothy Voirin
Jon Christofersen	Alma Latham	Nancy Webb
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Shari Brazinsky		
Timothy Bruya		
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Toni E. Huff	Michelle Sherwood	
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David Waterson		
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David W. Drennen		

Note: **Principal Investigator is bolded**

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Study No. M97-756
Certification: Financial Interests and Arrangements of Clinical Investigators

Principal Investigators		
William Randall Cox		
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Daniel David*		
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Eileen Robinson		
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Mike Fitch		
Debbra M. Gale		
H. Bruce Goodwin, III		
Meera Dewan *		
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Chester Fisher		
Karen Bradish		
Allison Foster		
John Fox		
Caroline Gellrick		
Lewis A. Fraterelli	Bernadette Pacheco	
Mark Nicholls	Glen O. Stocking, III	
John Given		
Cynthia Monnette		
Vina Gohill		
Darlene Clark	J. Scott Morrow	Kelly K. O'Sullivan-Stobbe
Robert Eichel	Alan Mostov	Erick G. Velez
Nancy Goldworm	Judith M. Stephan	

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Study No. M97-756
Certification: Financial Interests and Arrangements of Clinical Investigators

Principal Investigators		
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Wayne Harper * Philip Ashburn Charles Barish Donald Campbell Bulent Ender	Benjamin Ferdon Jonathan Flescher Ella Grach-Derensteyn Arvind Jariwala	Stuart Levin Daniel Mollin Teresa Rosebrough Treva Tyson
Thomas Hartley Lisa Huber	Twyla Magaw	Mary Petroff
Stephen Hawes		
Vernon Hershberger Margaret M. McCormick		
Robert Howard		
A. Ali Imam Frank Canavan Judy K. Kallman	Amit I. Patel Mahfooz Peshimam	Encarna Zamanian
Gary Incaudo * Barbara Holt	Carol Riley	L. Gretchen Wooding
Michael Jackson Virginia H. Jackson		
David James		
William Jannetti Isabelita V. Chua Jonathan David Rosalinda G. Loza	Hipolito Mariano Mercedes B. Samson	Maribelle Sunga Catalina S. D. Villanueva
Spencer Jones * Laura Huck		
Karen Kahn Jaleh Lansing	Robin Mishler	Marty O'Quin

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Principal Investigators		
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Mark Bernsten	Nancy Elder	Donald Rademacher
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Ethan Cary	Meshelle. Kolanz	Brian Schmalhors
Robert Cash	Charles Lehman	Keith Thompson
Scott Corliss	J. Chandler Major	David Tryggestad
Thomas Deen	Lisa Moreno	Daniel Zenk
John Ebens	William Oligmueller	
H. Jerome Koser		
Francis J. Averill	Sandra Galligan	Sara Ann McGilvary
Pamela Darley	Betty L. Howsare	Lynne Merriam
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Jing Liu		
Lyndon Mansfield		
Concepcion M. Aguirre	Gonzalo A. Diaz	Catherine P. Mendoza
Henry Milgrom		
Jerry Miller		
Andrew P. Brockmyre	Mark C. Jenkins	Linda R. Qualls
Joyce Caldwell	Page McClanahan	James Schrenker
Joel D. Gonce	James L. McCoy	Edward M. Stirman
Vaughan D. Hall	Susan Norton	Stephaine Tipton
Alfred L. Harkleroad, II	Thelma Orton	Kathy Urbin
Katie Haughs	Peter B. Platzer	
Timothy Moriarty		
Donald Cvitkovich	Victor Ortega	Ann Weiller
William Dent	Lewallen Sheffer	

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Study No. M97-756
Certification: Financial Interests and Arrangements of Clinical Investigators

Principal Investigators		
Zev Munk *		
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Linda D. Burton		
Lillian Hartland		
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Mahfooz Peshimam		
Frank Canavan	Amit I. Patel	
Judy K. Kallman	Encarna Zamanian	
Albert J. Razzetti		
Kim Marsden		
Keith S. Reisinger		
Mark M. Blatter	Dolly .Maben	Charles Stotler
Dawn Horner	**John C. Onderko**	
Mario Rosenberg *		
Corazon A. Flores		
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Mark Rosenthal		
Marshall Sack		
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Pradeep Bekal	David Frimer	Krishnamurthi Ramprasad
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Jeffrey B. Bloomer	Kim Richard Jurell	Ronald Schneider
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Christine Colman		
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Deepak Santram *		
Robert Schmidt		
L. Bernice Springer		

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Study No. M97-756
Certification: Financial Interests and Arrangements of Clinical Investigators

Principal Investigators		
Eric Schenkel		
Deborah Conover	Melody Hughes	
Susan Hahn	Shirin Jadidi	
J. David Schmitz *		
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Jeffrey Schul		
Lisa Chaplin		
Sharon Pratt		
Graham Scott		
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Nathan Segall		
Umedchandra Shah *		
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Alan Sheff		
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Gregg Roby		
Paul Siami *		
Kim Billings	Mark W. Graves	Richard W. Kincaid
Karen T. Brake	Darla R. Grossmann	Brenda Streiter
Mark F. Conway	Sudheer Gurram	Andrew C. Thieneman
Roger L. Crouse	James E. Gutmann	
Gary Erdy	Charles G. Hiam	
Sudeep Singh *		
Mikhail A. Alper	Linnea Faeth	Saad Hijazi
Irma Yolanda Castro	Sonia Garcia	
Milton Soiferman		
Barbara Menin		
Donald Spink		
John Sutherland		
Kristine Bamber	Joanne LaRocca	Julie Smith
Ted Bonebrake	Katherine Lee	Courtney Strubel
Cindy Gomis	Douglas McLaws	Pamela S. Trenkamp
James D. Hoehns	Marcia O'Brien	
Joseph Kinskey	Traci Skierka	

Note: Principal Investigator is bolded

* = **Principal Investigator is listed only to identify site. The sponsor was not able to obtain the information required under 21 CFR 54.2(b) from this investigator. This investigator can be found on the Due Diligence list for this Study.**

Study No. M97-756

Certification: Financial Interests and Arrangements of Clinical Investigators

Principal Investigators		
David Swieskowski *		
Judith Blackburn	Susan Kennedy	Avis Burr Pieper
JoEllen Heims	Kevin Moore	Kathy Shriner
Donald Taylor		
Martin Throne		
Sally H. Gillen		
Elizabeth Wilkins		
Frank Tiffany		
Stuart Topkis *		
Cheryl Collins		
Kenneth Warren		
Martha Marie Chandler	Lucinda Stevens	
Laura Melissa McMinn	Kristi Denyse Williams	
Steven Weinstein		
Judy Charm	Cynthia Guest	Sarina McClelland
Charles. White Sr.		
Wendy W. Britt	Martha Johnson	Mary Sarason
Suzanne M. Connor	Cristie Dawn Jones	Lucinda Stevens
Joe H. Davis	Tonya Matheny	Charles White, Jr.
Walter Fletcher.	Billie Mayberry	
Reggie Henderson	Laura Melissa McMinn	

Note: **Principal Investigator is bolded**

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

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

DISCLOSURE: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

The following information concerning Abdul Aziz, M.D. (*Name of clinical investigator*), who participated as a clinical investigator in the submitted study M97-734 and M97-814 (*Name of clinical study*), is submitted in accordance with 21 CFR part 54. The named individual has participated in financial arrangements or holds financial interests that are required to be disclosed as follows:

Please mark the applicable checkboxes.

☐ any financial arrangement entered into between the sponsor of the covered study and the clinical investigator involved in the conduct of the covered study, whereby the value of the compensation to the clinical investigator for conducting the study could be influenced by the outcome of the study;

☐ any significant payments of other sorts made on or after February 2, 1999 from the sponsor of the covered study such as a grant to fund ongoing research, compensation in the form of equipment, retainer for ongoing consultation, or honoraria;

☐ any proprietary interest in the product tested in the covered study held by the clinical investigator;

☒ any significant equity interest as defined in 21 CFR 54.2(b), held by the clinical investi- gator in the sponsor of the covered study.

Details of the individual's disclosable financial arrangements and interests are attached, along with a description of steps taken to minimize the potential bias of clinical study results by any of the disclosed arrangements or interests.

NAME	TITLE
Roland T. Catherall	Vice President, Regulatory Affairs
FIRM/ORGANIZATION	
Abbott Laboratories, Pharmaceutical Products Division	
SIGNATURE Roland T. Catherall	DATE 4/09/99

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

Study No. M97-734 & M97-814
Disclosure: Financial Interests and Arrangements of Clinical Investigators

Principal Investigator
Robert F. O'Dea **Abdul Aziz**

As provided in Form FDA 3455, the above mentioned sub-investigator, Abdul Aziz, holds financial interests that are required to be disclosed. Details of Dr. Aziz's disclosable financial arrangements and interests are summarized below, along with a description of the steps taken to minimize the potential bias of clinical study results.

Summary

Dr. Aziz had an equity interest in Abbott Laboratories (Abbott stock) that exceeds [redacted] during the time he participated in these studies. His activities in these studies amounted to participation in subject screening physicals, subject entrance physicals and subject exit physicals. Studies M97-734 and M97-814 were both Phase I studies designed to assess the steady-state bioavailability of clarithromycin extended-release tablets and the effect of food on the steady-state bioavailability of clarithromycin extended-release tablets, respectively. The purpose of each of the studies was to evaluate pharmacokinetic parameters, therefore, Dr. Aziz's participation did not bias the clinical study results.

Note: Principal Investigator is listed only to identify the site. The principal investigator is an employee of the Sponsor.

MEMORANDUM

Date: August 19, 1999

To: Dr. David A. Lepay, Director, DSI/HFD-340
Dr. Matthew Thomas, CIB Reviewer/HFD-344

From: Dr. Gary K. Chikami, Director, Review Division/HFD520 /S/

Subject: Request for Clinical Inspections for NDA 50-775

In support of the above mentioned NDA/Supplement for Biaxin XL Filmtab (clarithromycin) Extended Released Tablets, the sponsor Abbott Laboratories has submitted the results of the following pivotal protocols for the indications identified below:

Indication	Pivotal Protocol #	Investigator's Name/Address
1.Maxilary Sinusitis	Protocol M97-667	William N. Smith, M.D. New Tazewell Family Practice Center, PC 309 Broad Street New Tazewell, TN 37825
2. Acute Exacerbation Chronic Bronchitis (AECB)	Protocol M97-756	Merra Dewan, M.D./Khandalavala, M.D. 1912 Elm Suite 26 Omaha, NE 68144
3. AECB	Protocol M97-756	William Jannetti, M.D. HANA Research Med. Center, Inc. 8615 Knott Avenue Suite 8 Buena Park, CA 80602

The following site is the "For Cause" site to be inspected:

[redacted]

Justification: Sites with large number of patients and DSI has received previous complaints of non-compliance.

We have discussed this application with Dr. Thomas and as a result identified the above protocols/sites for inspection.

NDA 50-775 DSI

We have requested more than four sites for inspection domestic because of the following reasons: Sites with large number of patients

We request that the inspections are performed and the Inspection Summary Results are provided by inspection summary goal date. We intend to make a regulatory decision on this application by March 3, 2000.

Should you require any additional information please contact: Mr. Jose R. Cintron at 301-827-2125.

Concurrence:

Medical Team Leader: Dr. Mercedes Albuerne /S/ 8/23/99

Medical Reviewer: Dr. Nasim Moledina /S/ 8/23/99

Distribution: IND/NDA 50-775
HFD-520/Division File
HFD-520/Project Manager/JCintron
HFD-520/MO/NMoledina
HFD-520/TLMO/MAlbuerne
HFD-344/CIB/MThomas

U.S. Food and Drug Administration
Center for Drug Evaluation and Research

MEMORANDUM

Date: **June 30, 1999**

From: Team Leader, Division of Anti-Infective Drug Products, HFD-520

Subject: NDA 50-775 (Clarithromycin Extended Release Tablets)

To: Project Manager, Jose Cintron, HFD-520

The desk copy (vol. 1 of 97) of the subject NDA was reviewed and found to contain no toxicology data for review. Clarithromycin has several approved NDAs at present and new supporting toxicity data is not needed for the approval of the extended release tablet. Based upon the safety information available to the Pharmacology-Toxicology Team, I recommend approval of this NDA.

/S/

Robert E. Osterberg, Ph.D. √

ABBOTT

Pharmaceutical Products Division

Abbott Laboratories
100 Abbott Park Road
D-491, AP6B-1SW
Abbott Park, Illinois 60064-6108

April 30, 1999

Mellon Bank
Three Mellon Bank Center
27th Floor (FDA 360909)
Pittsburgh, PA 15259-0001

Subject: USER FEE I.D. NUMBER 3713

Dear Sir or Madam:

Enclosed is a check in the amount of [redacted] to cover the user fee payment for the following application:

Product Name:	Biaxin XL Filmtab
Generic Name:	Clarithromycin Extended Release Tablets
Indication for use:	Antibiotic
Type of Submission:	Original NDA for new dosage form. Clinical data included.
NDA Number:	NO50775
Name of Sponsor:	Abbott Laboratories
Address:	D491, Building AP6B/1SW PPD Regulatory Affairs 100 Abbott Park Road Abbott Park, Illinois 60064-3500
Contact Person:	Peter Noblin
Telephone Number:	847-937-5091

We would appreciate receiving a receipt for this payment; for your convenience, I have enclosed a self-addressed, stamped envelope.

Sincerely,

Peter Noblin
Associate Director, Regulatory Affairs

Enclosures: Abbott Check Number - [redacted], User Fee Cover Sheet,
Self-Addressed, Stamped Envelope

cc: Peter Noblin, D491, AP6B/1
Jeanne Fox, D491, AP6B/1
Greg Bosco, D491, AP6B/1
Paula Bourland, D404, AP9A/1
Sandra Harder, D387, AP6C/1
Kathy Christianson, D344, AP6D/1