NDA 20-241

Lamictal® Tablets 25 mg, 50mg, 100mg, 150mg, 200mg, 250mg

Request for Marketing Exclusivity

Pursuant to Sections 505(c)(3)(D)(iv) and 505(j)(4)(D)(iv) of the Federal Food, Drug, and Cosmetic Act and 21CFR 314.108(b)(5), Glaxo Wellcome Inc. requests three years of exclusivity from the date of approval of Lamictal® 25 mg, 50mg, 100mg, 150mg, 200mg, and 250mg as monotherapy for the treatment of partial seizures in adults with epilepsy.

We hereby certify as to the following:

Item 8, Section 8.15 of this application contains a list of published studies or publicly available reports of clinical investigations known to Glaxo Wellcome through a literature search that are relevant to the use of Lamictal as monotherapy for the treatment of partial seizures in adults with epilepsy. Glaxo Wellcome has thoroughly searched the literature and to the best of our knowledge, the list is complete and accurate and, in our opinion, such published studies or publicly available reports do not provide a sufficient basis for the approval of Lamictal for such use.

Thus, Glaxo Wellcome Inc. is entitled to exclusivity as this application contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and sponsored by Glaxo Wellcome Inc. The following investigations are "essential to the approval of the application" in that there are no other data available that could support FDA approval of the application:

Study US 30/31 A Multicenter, Double-Blind, Active-Control Evaluation of the Efficacy and Safety of Lamotrigine Monotherapy in Patients with Partial Seizures

The clinical investigation is defined as "new" as it has not been relied on by the FDA to demonstrate substantial evidence of effectiveness of a previously approved drug product for any indication or of safety for a new patient population and do not duplicate the results of another investigation that was relied on by FDA to demonstrate the effectiveness or safety in a new patient population of a previously approved drug application.

These investigations were "conducted or sponsored by Glaxo Wellcome" in that Glaxo Wellcome Inc. was the sponsor of the investigational new drug application under which the investigations essential to approval of the application were conducted.

Elizabeth A. McConnell

Elizabeth A. McConnell, Pharm.D.
Project Director, Regulatory Affairs

2/11/97
Date

APPEARS THIS WAY
ON ORIGINAL

NDA 20-764

Lamictal® Chewable DispersibleTablets 5 mg, 25 mg, 100mg

Request for Marketing Exclusivity

Pursuant to Sections 505(c)(3)(D)(iv) and 505(j)(4)(D)(iv) of the Federal Food, Drug, and Cosmetic Act and 21CFR 314.108(b)(5), Glaxo Wellcome Inc. requests three years of exclusivity from the date of approval of Lamictal® Chewable Dispersible Tablets 5 mg, 25 mg, and 100mg as monotherapy for the treatment of partial seizures in adults with epilepsy.

We hereby certify as to the following:

Item 8, Section 8.15 of this application contains a list of published studies or publicly available reports of clinical investigations known to Glaxo Wellcome through a literature search that are relevant to the use of Lamictal as monotherapy for the treatment of partial seizures in adults with epilepsy. Glaxo Wellcome has thoroughly searched the literature and to the best of our knowledge, the list is complete and accurate and, in our opinion, such published studies or publicly available reports do not provide a sufficient basis for the approval of Lamictal for such use.

Thus, Glaxo Wellcome Inc. is entitled to exclusivity as this application contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and sponsored by Glaxo Wellcome Inc. The following investigations are "essential to the approval of the application" in that there are no other data available that could support FDA approval of the application:

Study US 30/31	A Multicenter, Double-Blind, Active-Control Evaluation of the Efficacy and Safety of Lamotrigine Monotherapy in Patients with Partial Seizures

The clinical investigation is defined as "new" as it has not been relied on by the FDA to demonstrate substantial evidence of effectiveness of a previously approved drug product for any indication or of safety for a new patient population and do not duplicate the results of another investigation that was relied on by FDA to demonstrate the effectiveness or safety in a new patient population of a previously approved drug application.

These investigations were "conducted or sponsored by Glaxo Wellcome" in that Glaxo Wellcome Inc. was the sponsor of the investigational new drug application under which the investigations essential to approval of the application were conducted.

Elizabeth McConnell

Elizabeth A. McConnell, Pharm.D.
Project Director, Regulatory Affairs

9/3/98
Date

APPEARS THIS WAY
ON ORIGINAL

PEDIATRIC PAGE

(Complete for all original application and all efficacy supplements)

NDA/BLA Number:	20241	Trade Name:	LAMICTAL (LAMOTRIGINE) TABLETS
Supplement Number:	3	Generic Name:	LAMOTRIGINE
Supplement Type:	SE1	Dosage Form:	TAB
Regulatory Action:	AP	Proposed Indication:	Conversion to monotherapy in adults with partial seizures who are receiving treatment with a single-enzyme inducing anti-epileptic drug (EIAED).

IS THERE PEDIATRIC CONTENT IN THIS SUBMISSION? NO

What are the INTENDED Pediatric Age Groups for this submission?

____NeoNates (0-30 Days)____Children (25 Months-12 years)
____Infants (1-24 Months) ____Adolescents (13-16 Years)

Label Status -
Formulation Status -
Studies Needed -
Study Status -

APPEARS THIS WAY
ON ORIGINAL

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, JACKIE WARE

/S/
Signature

1/4/99
Date

APPEARS THIS WAY
ON ORIGINAL

PEDIATRIC PAGE

(Complete for all original application and all efficacy supplements)

NDA/BLA Number:	20764	Trade Name:	LAMICTAL CD CHEWABLE DISPERSIBLE TABLETS
Supplement Number:	1	Generic Name:	LAMOTRIGINE
Supplement Type:	SE1	Dosage Form:	TAB
Regulatory Action:	AP	Proposed Indication:	Conversion to monotherapy in adults with partial seizures who are receiving treatment with a single-enzyme inducing anti-epileptic drug (EIAED).

IS THERE PEDIATRIC CONTENT IN THIS SUBMISSION? NO

What are the INTENDED Pediatric Age Groups for this submission?

____NeoNates (0-30 Days)____Children (25 Months-12 years)
____Infants (1-24 Months) ____Adolescents (13-16 Years)

Label Status -
Formulation Status -
Studies Needed -
Study Status -

APPEARS THIS WAY
ON ORIGINAL

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. JACKIE WARE

/S/
Signature

1/4/99
Date

APPEARS THIS WAY
ON ORIGINAL

NDA 20-241

LAMICTAL® (lamotrigine tablets)

Supplemental New Drug Application for:
Monotherapy for Partial Seizures in Adults

DEBARMENT CERTIFICATION

Glaxo Wellcome hereby certifies that to the best of its knowledge and belief, it did not and will not use in any capacity the services of any person debarred under section 306(a) or (b) of the Generic Drug Enforcement Act of 1992 in connection with this application.

18 FEB 97

Charles E. Mueller
Head, International Compliance Services
World Wide Compliance

Date

.....

The list of Glaxo Wellcome Principal Investigators for the above titled submission has been compared with the 19Jun96 Food and Drug Administration Debarment List and the 21Nov95 Disqualified, Restricted, and Given Assurances lists.

Jeanne Kistler

18 Feb 97

Jeanne Kistler
Compliance Services Coordinator
World Wide Compliance

Date

GlaxoWellcome

June 3, 1997

Robert S. Young, M.D., Special Investigator
Division of Scientific Investigations
Center for Drug Evaluation and Research
Food and Drug Administration
HFD-344, Room 125
7520 Standish Place
Rockville, MD 20855

Re: NDA 20-241; LAMICTAL® (lamotrigine) Tablets
General Correspondence

Dear Dr. Young:

Reference is made to our telephone conversation on May 28, 1997 in which you requested information concerning Supplement 003 (Adult Monotherapy) to the aforementioned NDA submitted February 24, 1997. Specifically, you requested a list of investigators as well as patient enrollment per site for Protocol 30/31, "A Multicenter, Double-Blind, Active Control Comparison of the Efficacy and Safety of Lamotrigine Monotherapy in Patients with Partial Seizures."

Appended is the information you requested. The list is separated by protocol; however, because the protocols were identical, the data were combined and a single analysis was conducted.

We trust that this information will aid in your efforts to coordinate site audits. If you have any additional questions, please to not hesitate to contact me at 919-483-6466.

Sincerely,

Elizabeth McConnell

Elizabeth A. McConnell, Pharm.D.
Project Director
Regulatory Affairs

cc: Jackie Ware, Pharm.D., Regulatory Management Officer, HFD-120

Glaxo Wellcome Inc.
Five Moore Drive
PO Box 13398
Research Triangle Park
North Carolina 27709

Telephone
919 248 2100

LIST OF INVESTIGATORS AND PATIENT ENROLLMENT – LAMICTAL, ADULT EPILEPSY, MONOTHERAPY INDICATION, PROTOCOL(S) 30/31

PROTOCOL 30

Name/Address	Study/ Center	Number of Pts per Center
Stephen Collins, M.D. University Hosp. of Cleveland Dept. of Neurology 11100 Euclid Avenue Lakeside 3200 Cleveland, OH 44106	US 30–01	06
J. Christine Dean, M.D. Epilepsy Institute of North Carolina 3726 Vest Mill Road Winston–Salem, NC 27103	US 30–02	03
Edward Faught, M.D. (Gilliam) University of Alabama at Birmingham 1719 6th Avenue South, C1B312 Birmingham, AL 35294	US 30–03	12
Frank Gilliam, M.D. (Faught) University of Alabama at Birmingham 1719 6th Avenue South, Rm. 312 Birmingham, AL 35294	US 30–03	
Robert Leroy, M.D. Neurological Clinic of Texas 7777 Forest Lane Suite B–410 Dallas, TX 75230	US 30–04	05
Chi–Wan Lai, M.D. University of Kansas Medical Center Dept. of Neurology, Room 1033C 3901 Rainbow Boulevard Kansas City, KS 66160–7314	US 30–05	04
Kenneth D. Laxer, M.D. Northern California Comprehensive Epilepsy Program The Medical Center at UCSF 400 Parnassus Avenue, Room A–889 San Francisco, CA 94143–0138	US 30–06	02
William Garnett, Pharm.D. (Pellock) Division of Child Neurology Medical College of Virginia Dept. of Neurology MCV Box 980211 Richmond, VA 23298–0211	US 30–07	02

PROTOCOL 30 (continued)

Name/Address	Study/ Center	Number of Pts per Center
John M. Pellock, M.D. (Garnett) Division of Child Neurology Medical College of Virginia Dept. of Neurology Randolph Minor Hall, Room 702 307 College St. Richmond, VA 23298	US 30–07	
R. Eugene Ramsay, M.D. International Center for Epilepsy 1150 Northwest 14th St., Suite 410 Miami, FL 33136	US 30–08	04
James Cereghino, M.D. (Salinsky) Oregon Health Sciences University Epilespy Center, CDW3 School of Medicine 3181 S.W. Sam Jackson Park Road Portland, OR 97201–3098	US 30–10	01
Martin Salinsky, M.D. (Cereghino) Oregon Health Sciences University Epilespy Center, CDW3 School of Medicine 3181 S.W. Sam Jackson Park Road Portland, OR 97201–3098	US 30–10	
John C. Jones, M.D. (Spencer) University of Wisconsin Hosp. Epilepsy Treatment Center H4/612 Dept. of Neurology H4/612–6180 600 Highland Avenue Madison, WI 53792–6180	US 30–12	01
Nancy Spencer, M.D. (Jones) University of Wisconsin Hosp. Epilepsy Treatment Center 600 Highland Avenue Madison, WI 53792	US 30–12	
D. Frank Fleming, M.D. Eastern Carolina Neurological Assocs. 2501 Stantonsburg Rd. Greenville, NC 27834	US 30–13	01
William B. Svoboda, M.D. St. Francis Regional Medical Center Comprehensive Epilepsy Center 929 N. St. Francis Wichita, KS 67214	US 30–14	03

PROTOCOL 30 (continued)

Name/Address	Study/ Center	Number of Pts per Center
Blanca Vazquez, M.D. Dept. of Neurology Hosp. for Joint Diseases 301 East 17th St. New York, NY 10003	US 30–15	16
Neil Schaul, M.D. Long Island Jewish Medical Center 270–05 76th Avenue New Hyde Park, NY 11042	US 30–20	02
Ahmad Beydoun, M.D. University of Michigan Hosp Dept. of Neurology University Hosp. 1B300/0036 1500 E. Medical Center Drive Ann Arbor, MI 48109–0036	US 30–21	02
Jerry Tomasovic, M.D. Texas Neurosciences Institute 4410 Medical Drive, Suite 400 San Antonio, TX 78229	US 30–24	01
Mary Derbenwick, M.D. Atlantic Institute of Clinical Research 350 N. Clyde Morris Blvd. Daytona Beach, FL 32114	US 30–25	01

PROTOCOL 31

Name/Address	Study/ Center	Number of Pts per Center
Richard Brower, M.D. Dept. of Neurology Southwestern Medical Center University of Texas 5323 Harry Hines Boulevard Dallas, TX 75235–9036	US 31–04	02
Mercedes Jacobson, M.D. (Malcowicz) Mid–Atlantic Regional Epilepsy Center Medical College of PA 3300 Henry Avenue Philadelphia, PA 19129	US 31–06	
Denise E. Malkowicz, M.D. (Jacobson) Mid–Atlantic Regional Epilepsy Center Medical College of PA 3300 Henry Avenue Philadelphia, PA 19129	US 31–06	03
Fumisuke Matsuo, M.D. (Matsuo/Foley) University of Utah Medical Ctr. Dept. of Neurology, Rm 3A339 50 North Medical Drive Salt Lake City, UT 84132	US 31–07	03
Georgia D. Montouris, M.D. Epi–Care Center 930 Madison Avenue, Suite 700 Memphis, TN 38103	US 31–09	09
Patricia Penovich, M. D. The MN Epilepsy Group, P.A. 310 N. Smith Avenue, Suite 300 St. Paul, MN 55102	US 31–10	01
William E. Rosenfeld, M.D. The Comprehensive Epilepsy Care Center for Children and Adults St. Lukes North Medical Building 222 South Woods Mill Road Suite 610 Chesterfield, MO 63017	US 31–11	05
Kevin Ruggles, M.D. Dept. of Neurology Marshfield Clinic 1000 N. Oak Avenue Marshfield, WI 54449–1830	US 31–13	05
J. Chris Sackellares, M.D. University of Florida Dept. of Neurology Shands Teaching Hosp. at the University of Florida Gainesville, FL 32608	US 31–14	14

PROTOCOL 31 (continued)

Name/Address	Study/ Center	Number of Pts per Center
Steven Schachter, M.D. Comprehensive Epilepsy Center Beth Israel Hosp. – Kirstein 225 330 Brookline Avenue Boston, MA 02215	US 31–15	08
Robert T. Simkins, D.O. The Methodist Hosp. Main Station 423 6565 Fannin Houston, TX 77030	US 31–16	04
James Valeriano, M.D. Allegheny General 420 E. North Avenue Suite 206 Pittsburgh, PA 15212	US 31–17	09
Kevan VanLandingham, M.D. Neurology Dept. Duke University Medical Center 202F Bell Bldg., Trent Drive Durham, NC 27710	US 31–18	03
Alan Wilensky, M.D. Harborview Medical Center Regional Epilepsy Center ZA50 325 9th Avenue Seattle, WA 98104	US 31–19	01
Martha Morrell, M.D. Stanford University Medical Center Comprehensive Epilepsy Center Dept. of Neurology Room H–3160 Stanford, CA 94305–5235	US 31–20	03
Cynthia Harden, M.D. Assistant Professor of Neurology and Clinical Neurophysiology Comprehensive Epilepsy Center Room K–615 New York Hosp.–Cornell Medical Center 525 E. 68th St. New York, NY 10021	US 31–21	01
Selwyn–Lloyd McPherson, M.D. Selson Clinics 2725 Abington Court, Suite 200 Akron, OH 44333	US 31–22	01
Gregory Chang, M.D. Dept. of Neurology Room 5641 LAC–USC Medical Center 1200 N. State St. Los Angeles, CA 90033–1084	US 31–23	16

PROTOCOL 31 (continued)

Name/Address	Study/ Center	Number of Pts per Center
Victor Biton, M.D. Arkansas Epilepsy Program #1 Lile Drive Little Rock, AK 72205	US 31–24	01
Alexandre Todorov, M.D. Neurology Practice, PC 1325 McFarland Boulevard, Suite 201 Northport, AL 35476	US 31–26	01

GlaxoWellcome

October 20, 1998

DESK COPY

Paul D. Leber, M.D., Director
Division of Neuropharmacological Drug Products
Center for Drug Evaluation and Research
Office of Drug Evaluation I
Food and Drug Administration
HFD-120, Woodmont II, Room 4037
1451 Rockville Pike
Rockville, MD 20852

Re: NDA 20-241/S-003; LAMICTAL® (lamotrigine) Tablets
NDA 20-764/S-001; LAMICTAL® CD (lamotrigine) Chewable Dispersible Tablets
Amendment to Pending Application
Response to Approvable Letter: Labeling

Dear Dr. Leber:

Reference is made to the Agency's October 16, 1998 APPROVABLE letter for these applications. We hereby amend our application with revised proposed labeling in response to the Agency's APPROVABLE letter.

As noted in the Agency's approvable letter and proposed labeling, Glaxo Wellcome concurs with the majority of the Agency's suggestions regarding changes to the INDICATIONS and DOSAGE AND ADMINISTRATION sections. Clarification of these sections are proposed which do not alter the intended message proposed by the Agency.

Specifically, we are proposing the following for the INDICATIONS section, which also appears verbatim in the DOSAGE AND ADMINISTRATION section. We propose that it appear as regular type without underlining in the INDICATIONS section and as bolded type in the DOSAGE AND ADMINISTRATION section:

LAMICTAL is indicated for conversion to monotherapy in adults with partial seizures who are receiving treatment with a single EIAED.

Safety and effectiveness of LAMICTAL have not been established 1) as initial monotherapy, 2) for conversion to monotherapy from non–enzyme-inducing

Glaxo Wellcome Inc.
Five Moore Drive
PO Box 13398
Research Triangle Park
North Carolina 27709

Telephone
919 483 2100

AEDs (e.g., valproate), or 3) for simultaneous conversion to monotherapy from two or more concomitant AEDs (see DOSAGE AND ADMINISTRATION).

We believe that this proposal conveys the limitations on the use of LAMICTAL monotherapy while maintaining consistency with other parts of the INDICATIONS section as discussed in 21 CFR 201.57(c)(3)(i)(iv). For consistency with other sections of the package insert, the term "not indicated for" has been changed to "the safety and effectiveness of LAMICTAL have not been established". In particular, we note that the currently approved labeling dose not specifically state that LAMICTAL is not indicated for pediatric epilepsies outside of Lennox-Gastaut syndrome; rather, it states that the safety and effectiveness of LAMICTAL in pediatric patients other than those with Lennox-Gastaut syndrome have not been established.

We also propose modifying the statement regarding conversion to monotherapy from multiple AEDs to clarify that there are no specific guidelines that can be offered for the simultaneous withdrawal of multiple AEDs to achieve LAMICTAL monotherapy. However, there are adequate discontinuation strategies described in the current labeling for the withdrawal of AEDs in patients being maintained on adjunctive therapy with LAMICTAL. Once withdrawal to a single AED in addition to LAMICTAL is achieved, the label as proposed will provide guidance regarding conversion to LAMICTAL monotherapy, with appropriate limitations.

Enclosed with this submission is the following labeling:

1. Annotated version of the proposed package insert from the Agency's October 16, 1998 approvable letter with our suggested revisions **(Attachment 1)**.

2. Revised proposed package insert for LAMICTAL Tablets and LAMICTAL Chewable Dispersible Tablets (without annotations) **(Attachment 2)**.

This amendment is being submitted to NDA 20-241/S-003 and incorporated by reference to NDA 20-764/S-001.

Desk copies are being provided to Russell Katz, M.D., Deputy Director and Jacqueline Ware, Pharm.D., Regulatory Management Officer, under separate cover.

We look forward to working with the Agency to finalize the approval of these applications and will be available to discuss our proposals at your convenience.

If you have any questions regarding this submission, please do nc 'nesitate to call me at 919-483-6466.

Sincerely,

Elizabeth McConnell

Elizabeth A. McConnell, Pharm.D.
Project Director
Regulatory Affairs

Cc: Russell Katz, M.D., Deputy Director, HFD-120
Jacqueline Ware, Pharm.D., Regulatory Management Officer, HFD-120

APPEARS THIS WAY
ON ORIGINAL

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 last page.

FOR FDA USE ONLY

APPLICATION NUMBER

APPLICANT INFORMATION

NAME OF APPLICANT
Glaxo Wellcome Inc.

DATE OF SUBMISSION
October 20, 1998

TELEPHONE NO. (Include Area Code)
(919) 483-2100

FACSIMILE (FAX) Number *(Include Area Code)*
(919) 483-5063

APPLICANT ADDRESS *(Number, Street, City, State, Country, ZIP Code or Mail Code and U.S. License number if previously issued)*:
Five Moore Drive
Research Triangle Park, NC 27709

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) 20-241

ESTABLISHED NAME *(e.g., Proper name, USP/USAN name)*
Lamotrigine

PROPRIETARY NAME *(trade name)* IF ANY
Lamictal® Tablets

CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME *(If any)*
3,5-diamino-6-(2,3-dichlorophenyl)-*as*-triazine

CODE NAME (If any)
BW430C

DOSAGE FORM:
Tablets

STRENGTHS:
25mg, 100mg, 150mg, 200mg

ROUTE OF ADMINISTRATION:
Oral

(PROPOSED) INDICATION(S) FOR USE
Adjunctive treatment of partial seizures in adults with epilepsy

APPLICATION INFORMATION

APPLICATION TYPE (check one)
[X] 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
[X] 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
Response To Approvable Letter - Labeling

PROPOSED MARKETING STATUS (check one)
[X] PRESCRIPTION PRODUCT (Rx)
[ ] OVER THE COUNTER PRODUCT (OTC)

NUMBER OF VOLUMES SUBMITTED 1

THIS APPLICATION IS
[X] 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)

This application contains the following items: *(Check all that apply)*	
	1. Index
X	2. Labeling (check one) [x] 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 (21 CFR 314.50 (d) (2), 21 CFR 601.2)
	6. Human pharmacokinetics and bioavailability section (21 CFR 314.50 (d) (3) , 21 CFR 601.2)
	7. Clinical Microbiology (21 CFR 314.50 (d) (4))
	8. Clinical data section (21 CFR 314.50 (d) (5))
	9. Safety update report (21 CFR 314.50 (d) (5) (vi) (b) , 21 CFR 601.2)
	10. Statistical section (21 CFR 314.50 (d) (6) , 21 CFR 601.2)
	11. Case report tabulations (21 CFR 314.50 (f) (1) , 21 CFR 601.2)
	12. Case reports forms (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 314.5 (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 biologic 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
Elizabeth McConnell	**Elizabeth A. McConnell, Pharm.D.** **Project Director, Regulatory Affairs**	**October 20, 1998**

ADDRESS (*Street, City, State, and ZIP Code*)	Telephone Number
Five Moore Drive **Research Triangle Park, NC 27709**	**(919) 483-6466**

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

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.

Please DO NOT RETURN this form to this address.

FORM FDA 356h (4/97)