CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:NDA 50761

CORRESPONDENCE

NFD 520/TROSTLE

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 50-761

MAY 14 1998

SmithKline Beecham Pharmaceuticals
Attention: Sharon W. Shapowal, R.Ph.
One Franklin Plaza, P.O. Box 7929
Philadelphia, PA 19101-7929

Dear Ms. Shapowal:

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

Name of Drug Product: Amoxil ® (amoxicillin) Chewable Tablets

Therapeutic Classification: Standard

Date of Application: April 15, 1998

Date of Receipt: April 16, 1998

Our Reference Number: 50-761

Unless we notify you within 60 days of our receipt date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on June 16, 1998, in accordance with 21 CFR 314.101(a).

If you have any questions, please contact Mr. Stephen T. Trostle, Regulatory Health Project Manager, at (301) 827-2125.

Please cite the NDA number listed above at the top of the first page of any communications concerning this application.

Sincerely yours,

5/14/98

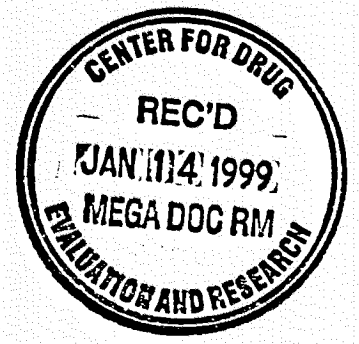
James D. Bona, R.Ph., M.P.H.
Chief, Project Management Staff
Division of Anti-Infective Drug Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

SmithKline Beecham
Pharmaceuticals

TBC
ORIGINAL

January 13, 1999

NDA 50-761
Amoxil® (amoxicillin) Chewable Tablets
Pediatric q12h dosing



Gary Chikami, M.D., Director
Center for Drug Evaluation and Research
Division of Anti-Infective Drug Products (HFD-520)
Food and Drug Administration
9201 Corporate Boulevard
Rockville, MD 20850

Amendment to Pending NDA – 18 Month Stability Report on bottles with pin-holes in the induction seal
– 18 Month Stability Report on single unit, non-child resistant aluminum foil blister packs

Dear Dr. Chikami:

Reference is made to the New Drug Application for Amoxil® (amoxicillin) Chewable Tablets Pediatric q12h dosing, submitted on April 15, 1998, and filed under Section 505(b) of the Act on July 18, 1998, in accordance with 21 CFR 314.101(a).

At this time and in accordance with an agreement made between representatives of SmithKline Beecham and FDA (reference meeting of January 14, 1997, including Drs. Katague and Chen and Mr. Kitz and Ms. Maglennon), we are amending the application to provide an 18 month stability update.

Further reference is made to telephone conversations between Ms. Maglennon [SB] and Dr. Yu [FDA] on December 17/18, 1998, wherein it was agreed that 18 month stability data for bottles with pin-holes in the induction seal would be supplied by January 15, 1999 and that 18 month stability data for bottles without pin-holes in the induction seal [i.e. commercial pack] would be supplied by end of February, 1999.

Further, as explained in the aforementioned conversation, the proposed commercial bottle pack [without pin-holes in the induction seal] was placed on stability later than the original pack [with pin-holes in the induction seal], therefore, the samples are still currently on store and end of February, 1999 is the earliest possible timing for FDA receipt of this data. However, SB would like to point out that the 18 month data for the bottle with pin-holes in the induction seal [provided herein as Attachment 1] is acceptable and our 12 month stability update submitted September 8, 1998 clearly demonstrated superiority of the bottle pack without pin-holes over the bottle pack with pin-holes.

Therefore, the proposed commercial bottle pack bottle [without pin-holes in the induction seal] should easily comply with an 18 month (or longer) shelf life.

Thank you for your kind consideration of the enclosed information. This amendment is being submitted in duplicate. If you have any questions or requests regarding this submission, please do not hesitate to contact me at (610) 917-6457.

Sincerely,

Sharon M. Maglennon
Assistant Director
Regulatory Affairs – North America

cc: Desk Copy – S. Trostle (HFD-520)
S. Shapowal (FP1005)
A. Yu (Chemistry Reviewer)

000002

BC

ORIG AMENDMENT

ORIGINAL

SB

SmithKline Beecham

Pharmaceuticals

Regulatory Affairs - U.S.
Anti-Infectives and Biological Therapeutic Areas

September 1998

NDA 50-761
Amoxil ® (amoxicillin) Chewable Tablets
Pediatric q12h dosing

Gary Chikami, M.D., Director
Center for Drug Evaluation and Research
Division of Anti-Infective Drug Products (HFD-520)
Food and Drug Administration
9201 Corporate Boulevard
Rockville, Maryland 20850

Amendment to a Pending NDA: **– revised debarment certification**
– 12 month stability report

Dear Dr. Chikami:

Reference is made to the New Drug Application for *Amoxil* (amoxicillin) Chewable Tablets Pediatric q12h dosing, submitted on April 15, 1998, and filed under section 505(b) of the Act on July 18, 1998, in accordance with 21 CFR 314.101(a). At this time, we are amending the NDA for *Amoxil* Chewable Tablets, q12h, to provide the following information:

Revised Debarment Certification

As requested by Mr. José Cintron on June 4, 1998, and as submitted the same day by facsimile by Dr. Robert Pietrusko, a revised debarment certification is herein supplied to the file.

Twelve Month Stability Report

- Twelve month stability update, per the agreement made between representatives of the FDA and SmithKline Beecham (reference the meeting of January 14, 1997, involving Drs. Katague and Chen, and Mr. Kitz and Ms. Maglennon). For convenience of review, this report is in the form of a total update of Section 7 of the Drug Product section of NDA 50-761 (ref. Volume 1.003, pages 000192 - 000332), and begins on page 000007 of this submission.
- Based on this additional data, our proposal for commercial packaging is revised: We request approval for marketing in the bottles described in the application which incorporate induction seals without pin holes (referred to in the original NDA and the attached report as the "alternate package"). (See conclusions in Sections 8.2 and 9.0 of the Twelve Month Stability Report.)
- An alternate "fast" assay analytical method is provided, now being used for generation of dissolution profiles. (See Section 10.0 of the Twelve Month Stability Report.)

Thank you for your kind consideration of the enclosed information. This amendment is being submitted in duplicate. If you have any questions or requests regarding this submission, please do not hesitate to contact me at (215) 751-3468.

Sincerely,

Sharon W. Shapowal

Sharon W. Shapowal, R.Ph.
Associate Director
U.S. Regulatory Affairs

Desk Copy: Mr. S. Trostle (HFD-520)

SmithKline Beecham
Pharmaceuticals

DESK COPY
J. Cintron

Regulatory Affairs - U.S.
Anti-Infectives and Biological Therapeutic Areas

Amendment to a Pending NDA
NDA 50-761
Amoxil® (amoxicillin) Chewable Tablets
Pediatric q12h dosing

March 31, 1999

Janice Soreth, M.D., Acting Director
Center for Drug Evaluation and Research
Division of Anti-Infective Drug Products (HFD-520)
Food and Drug Administration
9201 Corporate Boulevard
Rockville, Maryland 20850

Response to FDA List of Chemistry Deficiencies and Comments
Response to FDA Labeling Questions

Dear Dr. Soreth:

We are writing with regard to our New Drug Application for Amoxil® (amoxicillin) for Oral Suspension, NDA 50-761, submitted April 15, 1998, which provides for a change in the dosing regimen of amoxicillin from thrice daily to twice daily dosing in pediatric patients, and to provide for new strength suspensions.

At this time, we are amending the NDA with the complete response to the chemistry deficiencies and comments, as cited in the facsimile transmission of March 12, 1999, sent by Mr. José Cintron. For your convenience, the FDA questions/requests precede our responses and are presented in boldface type. Included as part of the chemistry response are updated immediate container labels for the commercial product and sample product.

If you have any questions regarding NDA 50-761, please do not hesitate to contact me at (215) 751-6318.

Sincerely,

Deneen R. Stewart

Deneen R. Stewart, Ph.D.
Regulatory Associate
U.S. Regulatory Affairs

Desk copy: J. Cintron (HFD-520)
A. Yu (Chemistry Reviewer)
H. Sun (Biopharm Reviewer)

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

NDA 50-761

APPLICANT INFORMATION

NAME OF APPLICANT
SmithKline Beecham Pharmaceuticals

DATE OF SUBMISSION
31 March 1999

TELEPHONE NO. *(Include Area Code)*
(215) 751-6318

FACSIMILE (FAX) Number *(Include Area Code)*

APPLICANT ADDRESS *(Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued):*
One Franklin Plaza, P.O. Box 7929
Philadelphia, PA 19101-7929

AUTHORIZED U.S. AGENT NAME & ADDRESS *(Number, Street, City, State, ZIP Code, telephone & FAX number)* IF APPLICABLE
Deneen R. Stewart, Ph.D
Regulatory Associate, U.S. Regulatory Affairs

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER *(If previously issued)*

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

PROPRIETARY NAME *(trade name)* IF ANY
Amoxil®

CHEMICAL/BIOLOGICAL/BLOOD PRODUCT NAME *(If any)*

CODE NAME *(If any)*

DOSAGE FORM:
Chewable Tablets

STRENGTHS:
200mg and 400mg

ROUTE OF ADMINISTRATION:
oral

(PROPOSED) INDICATION(S) FOR USE:
The treatment of infections caused by susceptible strains of designated organisms in the following infections: ear, nose, and throat infections, lower respiratory infections, skin and soft tissue infections, genitourinary tract infections and gonorrhea

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
Response to FDA Chemisrty Reviewer

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

NUMBER OF VOLUMES SUBMITTED

THIS APPLICATION IS ☒ PAPER ☐ PAPER AND ELECTRONIC ☐ ELECTRONIC

ESTABLISHMENT INFORMATION

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

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)*	
X	1. Index
x	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) (2) (i), 21 CFR 601.2)
	C. Methods validation package (e.g. 21 CFR 314.50 (e) (2) (i), 21 CFR 601.2)
	5. Nonclinical pharmacology and toxicology section (e.g. 21 CFR 314.50 (d) (2), 21 CFR 601.2)
	6. Human pharmacokinetics and bioavailability section (e.g. 21 CFR 314.50 (d) (3), 21 CFR 601.2)
	7. Clinical Microbiology (e.g. 21 CFR 314.50 (d) (4))
	8. Clinical data section (e.g. 21 CFR 314.50 (d) (5), 21 CFR 601.2)
	9. Safety update report (e.g. 21 CFR 314.50 (d) (5) (vi) (b), 21 CFR 601.2)
	10. Statistical section (e.g. 21 CFR 314.50 (d) (6), 21 CFR 601.2)
	11. Case report tabulations (e.g. 21 CFR 314.50 (f) (1), 21 CFR 601.2)
	12. Case report forms (e.g. 21 CFR 314.50 (f) (2), 21 CFR 601.2)
	13. Patent information on any patent which claims the drug (21 U.S.C. 355 (b) or (c))
	14. A patent certification with respect to any patent which claims the drug (21 U.S.C. 355 (b) (2) or (j) (2) (A))
	15. Establishment description (21 CFR Part 600, if applicable)
	16. Debarment certification (FD&C Act 306 (k)(1))
	17. Field copy certification (21 CFR 314.5 (k) (3))
	18. User Fee Cover Sheet (Form FDA 3397)
X	19. OTHER (Specify) Response to Chemisrty Reviewer's questtions received by facsimile

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, 315.72, 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
Deneen R Stewart	Deneen R. Stewart, Ph.D., Regulatory Assoc., U.S. Regulatory Aff.	March 31, 1999

ADDRESS *(Street, City, State and ZIP Code)*	Telephone Number
One Franklin Plaza, P.O. Box 7929 Philadelphia, PA 19101-7929	(215) 751-6318

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DHHS, Reports Clearance Officer
Paperwork Reduction Project (0910-0338)
Hubert H. Humphrey Building, Room 521-H
200 Independence Avenue, S.W.
Washington, DC 20201

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