

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
50-813

OTHER REVIEW(S)

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

CLINICAL INSPECTION SUMMARY

DATE: November 29, 2007

TO: Susmita Samanta, Regulatory Project Manager
Menfo Imoisili, M.D., Clinical Reviewer
Division Of Anti-Infective And Ophthalmology Products, HFD-520

THROUGH: Joseph Salewski
Acting Branch Chief
Good Clinical Practice Branch 2, HFD-47
Division of Scientific Investigations

FROM: Dianne Tesch, Consumer Safety Officer

SUBJECT: Evaluation of Clinical Inspections

NDA: 50-813

NME: No

APPLICANT: Advancis Pharmaceutical Corporation

DRUG: APC-111 MP Tablet

THERAPEUTIC CLASSIFICATION: Standard Review

INDICATION: Treatment of tonsillitis or pharyngitis — *Streptococcus pyogenes*

CONSULTATION REQUEST DATE: June 18, 2007

DIVISION ACTION GOAL DATE: October 8, 2007

PDUFA DATE: January 23, 2008

b(4)

I. BACKGROUND:

Advancis Pharmaceutical Corporation (Advancis) is developing a once-a-day pulsatile-release multiparticulate formulation of amoxicillin (APC-111 MP Tablet, 775 mg or APC-111) for a 10-day regimen for tonsillitis and/or pharyngitis — *Streptococcus pyogenes* (*S. pyogenes*) in adolescents and adults. APC-111 MP Tablet is designed to sequentially deliver an immediate release and two delayed release pulses of amoxicillin. In summary, APC-111 is intended to provide a lower treatment dose, once-a-day alternative to current approved penicillin and amoxicillin regimens for the treatment of tonsillitis or pharyngitis.

b(4)

Both sites were chosen for inspection because they were high enrollers. Their results were pivotal for FDA's decision regarding this NDA.

NDA 50-813 Product Name APC-111 Amoxicillin
Summary Report of U.S. Inspections

II. RESULTS (by protocol/site):

Name of CI and site #, if known	City, State*	Protocol #	Insp. Date	EIR Received Date	Final Classification
Stanley Block, M.D.	Bardstown, KY	111.302	7/16/07-7/20/07	8/23/07	VAI
Dan Henry, M.D.	Salt Lake City, UT	111.302	10/1/07-10/4/07	11/8/07	NAI

Key to Classifications

NAI = No deviation from regulations. Data acceptable.

VAI-No Response Requested= Deviations(s) from regulations. Data acceptable.

VAI-Response Requested = Deviation(s) from regulations. See specific comments below for data acceptability

OAI = Significant deviations for regulations. Data unreliable.

A. Protocol #111.302

1. Stanley Block, M.D., Bardstown, KY Center 0391

- a. At this site, 117 subjects were screened; 58 subjects were randomized and 52 subjects completed the study. There were no deaths or SAEs reported. Six subjects discontinued due to lack of efficacy.
- b. There were no limitations to the inspection.
- c. An audit of 16 subjects' records was conducted. There were three instances of subjects who were enrolled who met exclusion criteria, and multiple instances of study interval telephone calls not being made. It is unlikely that any of these protocol violations affected data integrity.
- d. The study appears to have been conducted adequately, and the data generated by this site appear acceptable in support of the respective indication.

2. Dan Henry, M.D., Salt Lake City, UT Center 0388

- a. At this site, fifty-one subjects were screened, forty-eight subjects were randomized, and forty-six subjects completed the study. There were seven treatment failures. One subject withdrew due to an allergic reaction.
- b. There were no limitations to the inspection.
- c. An audit of all subjects' records for informed consent and assent for minor subjects was conducted. No regulatory violations were noted. An in depth audit of eight subjects' records for adherence to protocol, reporting of adverse events (AEs), and drug accountability was conducted. No regulatory violations were noted.
- d. The study appears to have been conducted adequately, and the data generated by this site appear acceptable in support of the respective indication.

III. OVERALL ASSESSMENT OF FINDINGS AND GENERAL RECOMMENDATIONS

The study appears to have been adequately conducted. There were minor regulatory violations at one of the sites. The violations are unlikely to have had an effect on data integrity.

{See appended electronic signature page}

Dianne D. Tesch
Consumer Safety Officer

CONCURRENCE:

Supervisory comments

{See appended electronic signature page}

Joseph P. Salewski
Acting Branch Chief
Good Clinical Practice Branch II
Division of Scientific Investigations

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/s/

Dianne Tesch
12/4/2007 09:30:11 AM
CSO

Joseph Salewski
12/4/2007 10:27:48 AM
CSO