

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

22-172s000

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: October 2, 2007

TO: Kimberly Updegraff, Regulatory Project Manager
Michelle Chuen, M.D., Clinical Reviewer
Division of Psychiatry Products, HFD-130

THROUGH: Joseph P. 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: #22-172

NME: No

APPLICANT: AstraZeneca

DRUG: Seroquel® SR (quetiapine fumarate) sustained-release tablet

THERAPEUTIC CLASSIFICATION: 6S

INDICATION: (b) (4) schizophrenic patients.

CONSULTATION REQUEST DATE: April 2, 2007

DIVISION ACTION GOAL DATE: October 4, 2007

PDUFA DATE: November 22, 2007

I. BACKGROUND:

The primary objective in this study was to demonstrate superior efficacy of quetiapine fumarate sustained-release (Seroquel SR, hereafter called quetiapine SR) to placebo by evaluating relapse prevention in long-term use in patients with schizophrenia as measured by the time to first psychiatric relapse up to one year (time to relapse will be assessed using randomization and time to first instance of the first psychiatric relapse). Relapse was defined as deterioration in the patient's condition despite study drug dose adjustments. According to at least one of the definitions stated below:

- hospitalization due to worsening of the schizophrenia
- an increase on the Positive and Negative Syndrome Scale (PANSS) score
- a rating of much worse or very much worse (score 6 or 7) on the Clinical Global Impression-Global

- Improvement (CGI-I) scale
- need for any other antipsychotic medication to treat psychosis

Summary Report of Foreign Inspections

II. RESULTS (by protocol/site):

Name of CI and site #, if known	City, State, Country	Protocol #	Insp. Date	EIR Received Date	Final Classification
Natalia Maruta, M.D. Center 1304	Kharkiv, Ukraine	D14444C00004	8/27/2007 to 8/30/2007	pending	pending; probable NAI
Vladislav Demchenko, M.D. Center 1305	Kyiv, Ukraine	D14444C00004	8/20/2007 to 8/24/2007	pending	pending; probable 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.

Protocol # D14444C00004

1. Natalia Maruta, M.D., Center 1304, Kharkiv, Ukraine

- a. There were sixteen subjects enrolled at the site. Twelve subjects were randomized. All records were reviewed in depth for the data audit.
- b. There were no limitations to the inspection.
- c. Six of the twelve subjects had a relapse. Five of the six subjects who relapsed were on placebo. The field investigator verified that blinding was maintained throughout the study. There were no regulatory deficiencies at the site.
- d. The study appears to have been conducted adequately, and the data generated by this site appear acceptable in support of the respective indication.

Observations noted above are based on the Form FDA 483 and communications from field investigator, a inspection summary addendum will be generated if conclusions change upon receipt and review of the EIR.

2. Vladislav Demchenko, M.D., Center 1305, Kyiv, Ukraine

- a. Nineteen subjects were screened. Twelve subjects were randomized. All records were reviewed in depth for the data audit.
- b. There were no limitations to the inspection.
- c. None of the subjects at this site had initial visits within the +/- 2 day window as per protocol. They were supposed to be two weeks apart, but they were sometimes up to three weeks apart.

One subject took diazepam, a prohibited medication, but was allowed to continue on in the trial. This was reported to the sponsor a major protocol deviation at this site.

No other regulatory deficiencies were noted at the site.

- d. The study appears to have been conducted adequately, and the data generated by this site appear acceptable in support of the respective indication.

Observations noted above are based on the Form FDA 483 and communications from field investigator, a inspection summary addendum will be generated if conclusions change upon receipt and review of the EIR.

III. OVERALL ASSESSMENT OF FINDINGS AND GENERAL RECOMMENDATIONS

The study appears to have been conducted adequately, and the data generated by these sites appear acceptable in support of the respective indication. No follow up other than routine surveillance is recommended.

{ See appended electronic signature page }

Dianne 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

**This is a representation of an electronic record that was signed electronically and
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/s/

Dianne Tesch
10/3/2007 09:39:27 AM
CSO

Joseph Salewski
10/3/2007 10:45:15 AM
CSO