DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Antimicrobial Products
Division of Special Pathogen and Transplant Products

FDA Briefing Document Addendum and Errata

TO: AIDAC Committee Members

RE: Addendum and Errata to the FDA Briefing Document for the September 12, 2006 Advisory Committee Meeting

Drug: Factive® (gemifloxacin) 320 mg Tablets

Proposed Indication: Treatment of Acute Bacterial Sinusitis (ABS)

NDA: 21-158/S-006

This addendum provides clarifications regarding statements made in the FDA briefing document.

1. On page 10 of the FDA briefing document, the statement regarding protocol OP-634-501 states that "…a complete consultation is included as an appendix to this document." There is no corresponding appendix; instead the actual comments are presented on pages 35-37.

2. On page 12 of the FDA briefing document, it states "Four clinical studies have been conducted in which gemifloxacin was evaluated for the treatment of ABS." The actual number of studies is five, as summarized in Table 1 on page 12. The fifth study, Study 333, is an open-label, noncomparative study of 5 days of gemifloxacin for ABS and is discussed in the applicant's submission.

3. Oscient has requested that we clarify what appears to be a discrepancy between the Oscient and FDA briefing documents regarding the number of patients studied in clinical trials. The Oscient briefing document (e.g., Tables 29, 30, 31) lists the total clinical trial safety population of 8119 patients who received gemifloxacin. The FDA agrees this number is correct. The 8119 number cited by Oscient includes the 6775 patients studied as part of the earlier application, NDA 21-158, and the 1344 patients studied in two recent trials of community-acquired pneumonia and one open-label trial of ABS. The FDA briefing document concentrates on presenting the cutaneous safety data in 2 parts: (a) the 6775

(NDA 21-158, 2002) database because of the extensive analyses performed on these data; and (b) an examination of the cutaneous adverse events in the five ABS clinical trials (009, 010, 186, 206, 333), in which 1122 patients received gemifloxacin for 5 days and 724 patients received gemifloxacin for 7 days.

4. We also wish to bring to your attention the following clarification between "serious" and "severe" adverse reactions. In the FDA briefing document on page 23, the following statement is included: "Thirteen percent of subjects with rash (or 0.4% of the total population exposed to gemifloxacin) experienced a serious rash…" The term 'serious' should be changed to 'severe.'

   A serious adverse event is specifically defined in the regulations, 21 CFR 312.32 (a) and 21 CFR 314.80 (a), as an adverse drug experience occurring at any dose that results in any of the following outcomes: death, a life-threatening adverse drug experience, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity, or a congenital anomaly/birth defect.

   A severe adverse event reflects the severity or degree of an adverse effect, which may or may not be serious, and is defined by the clinical protocol.