DEPARTMENT OF HEALTH AND HUMAN SERVICES **Public Health Service**

Division of Antiviral Products
Food and Drug Administration
Silver Spring, MD 20993

DATE: **September 8, 2008**

TO: **NDA 22-141 (Lamivudine and Tenofovir Disoproxil Fumarate Tablets)**

FROM: **Russell Fleischer, PA-C, MPH**
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RE: **PEPFAR NDA Clinical Review**

Background

The purpose of these submissions is to gain tentative approval of Matrix Pharmaceuticals' registration application for a fixed-dose combination containing Tenofovr Disoproxil Fumarate 300 mg and Lamivudine 300 mg.

Use of simplified anti-HIV regimens in the form of co-packaged drugs (such as blister packs) or fixed-dose combinations (FDCs) may facilitate distribution and improve patient adherence in the US and developing countries. To facilitate more rapid development of FDCs or co-packaging of antiretroviral agents, FDA issued Guidance for Industry on Fixed Dose Combination and Co-packaged Drug Products for Treatment of HIV under the PEPFAR program. This guidance is intended to encourage sponsors to submit applications to the FDA for approval of FDC and co-packaged versions of previously approved antiretroviral therapies.

Matrix's application for a FDC containing tenofovir and lamivudine were submitted in response to this guidance. Because the individual components of these FDCs are under patent, the applications cannot be approved but are eligible to receive *tentative approval*, which recognizes that, at the time the tentative approval action is taken, the application meets the technical and scientific requirements for approval, but final approval is blocked by patent or exclusivity.

Labeling Review

- The labeling for the proposed FDC was reviewed and compared to the currently approved US labeling for the individual products: lamivudine (Epivir®, GlaxoSmithKline, NDA 20-564) and tenofovir disoproxil fumarate (Viread®, Gilead Sciences Inc, NDA 21-356). Minor revisions were required to make the labeling for the FDC product consistent with the US labeling of the individual products.

Recommended Regulatory Action

The labeling for Matrix's Lamivudine and Tenofovir Disoproxil Fumarate Tablets and the currently approved US labeling for the individual products are comparable and allow for safe use of this FDC. Based on acceptable bioequivalence data, labeling, and chemistry, manufacturing and controls information, this application should be granted tentative approval.

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/s/

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9/12/2008 03:18:54 PM
MEDICAL OFFICER