DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 22-479 **TENTATIVE APPROVAL**

Hetero Drugs Limited Unit III
Attention: G. Sangeetha, Regulatory Affairs
22-110, Industrial Development Area
Jeedimetla, Hyderabad-500 055
India

Dear Mr. G. Sangeetha:

Please refer to your new drug application (NDA) 22-479 dated July 14, 2009, received on July 17, 2009, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Lamivudine and Stavudine Tablets, 150 mg/30 mg.

We acknowledge receipt of your submissions dated:

November 17, 2008	April 5, 2010
October 13, 2009	April 28, 2010

This NDA provides for the use of Lamivudine and Stavudine Tablets, 150 mg/30 mg in combination with other antiretrovirals for the treatment of HIV-1 infection in adults.

This NDA was reviewed under the President's Emergency Plan for AIDS Relief (PEPFAR).

We completed our review of this application, as amended. It is **tentatively approved** under 21 CFR 314.105 for use as recommended in the agreed-upon labeling (refer to the enclosed text for the package insert, patient package insert, and immediate container labels). Also, refer to your original submission for the immediate container labels and the agreed-upon labeling emailed on May 12, 2010, for the package insert and patient package insert. Based on the data provided, the expiration dating period is 24 months for Lamivudine and Stavudine Tablets, 150 mg/30 mg in HDPE containers of 30, 60, and 100 tablets fitted with child-resistant plastic caps (b) (4), (b) (4) and desiccan (b) (4)) when stored at 20º-25ºC (68º to 77ºF). HDPE containers of 500 tablets fitted with (b) (4) plastic caps with (b) (4), and desiccant (b) (4) are also included in this action.

The tentative approval is contingent upon information available to the Agency at this time (i.e., information in your application and the status of current good manufacturing practices of the facilities used in manufacturing and testing of the drug product) and is, therefore, subject to change on the basis of any new information that may come to our attention.

We have the following recommendation regarding carton labels:

1. It is our understanding that a few PEPFAR recipient nations have expressed a preference for antiretroviral drugs to be supplied in an individual carton containing a bottle and the package insert. If you wish, you may submit color images of carton label(s) as a labeling amendment for review. If they are found to be acceptable, you would have an option to provide bottles alone and bottles within cartons. No additional stability data would be required because the addition of a cardboard carton is not expected to have a measurable effect on the protection provided by the bottle.

One of the listed reference drug product [Epivir® (lamivudine)] upon which you base your application is subject to a period of patent protection and therefore, final approval of your application under section 505(c)(3) of the Act (21 U.S.C. 355(c)(3)) may not be made effective until the period has expired. If you have questions as to when this date will be, please contact the Agency at the information provided below.

Two or six months prior to the expiration of the patents protection, as appropriate, submit an amendment to this application identifying changes, if any, in the conditions under which your product was tentatively approved. Any changes to the conditions outlined in this NDA require our review before final approval and the goal date for our review will be set accordingly. Your amendment should include updated labeling, chemistry, manufacturing and controls data, and a safety update. This amendment should include draft final printed labels and labeling which comply with all United States regulations (uniqueness of drug product appearance per 21 CFR 206; child-resistant packaging per 16 CFR 1700, etc.). This amendment should be designated clearly in your cover letter as a "**FINAL APPROVAL REQUESTED**."

Failure to submit this amendment will prompt a review of this application that may result in rescission of the tentative approval status of your application, or may result in a delay in the issuance of the final approval letter.

We remind you that you are expected to comply with the reporting requirements provided in 21 CFR 314.80 and 314.81. If the product is to be mass distributed in developing countries, a system of collecting and reporting adverse drug reactions by the distributor would be desirable (e.g., through governmental or nongovernmental agencies distributing the products).

We remind you that, should you intend to market this product in the United States after the period of patents protection, you are required to join the antiretroviral pregnancy registry at that time and make the appropriate labeling change that references the existence of the pregnancy registry. In addition, an updated package insert (PI) must be submitted under the Structured Product Labeling requirements (http://www.fda.gov/oc/datacouncil/spl.html) as defined by the Physician's Labeling Rule [21 CFR 201.56, 201.57].

Before we issue a final approval letter, this NDA is not deemed approved. If you believe that there are grounds for issuing the final approval letter before the expiration of the patents protection, you should amend your application accordingly.

This product may be considered misbranded under the Federal Food, Drug, and Cosmetic Act if it is marketed in the United States before final approval.

If you have any questions, please contact Monica Zeballos, Pharm.D., Senior Program Consultant, at (301) 796-0669 or by email at monica.zeballos@fda.hhs.gov.

Sincerely yours,

{See appended electronic signature page}

Jeffrey Murray, M.D., M.P.H.
Deputy Director
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Enclosures: Draft PI, PPI, and immediate container labels

Email CC: Dr. Sudhakar Rao Vidiyala, U.S. Agent for Hetero Drugs Limited Unit III
Soma Raju, U.S. Regulatory POC
InvaGen Pharmaceuticals Inc.
7 Oser Avenue
Hauppauge, NY 11788

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22479	ORIG-1	HETERO DRUGS LTD	Lamivudine/Stavudine FDC Tabs (150mg/30mg)

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

JEFFREY S MURRAY
05/17/2010