CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 20-154/S-029, S-030
20-155/S-021
20-156/S-022

APPROVAL LETTER

NDA 20-154/S-029, S-030
NDA 20-155/S-021
NDA 20-156/S-022

Bristol-Myers Squibb Company
Attention: Cynthia F. Piccirillo
Associate Director, Worldwide Regulatory Affairs
5 Research Parkway
Wallingford, CT 06492

Dear Ms. Piccirillo:

Please refer to your supplemental new drug applications dated April 30, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for VIDEX® (didanosine) Chewable/Dispersible Tablets, Buffered Powder for Oral Solution, and Pediatric Powder for Oral Solution.

We acknowledge receipt of your submissions dated:

May 18, 1999	May 19, 1999	June 18, 1999
June 24, 1999	July 20, 1999	July 21, 1999
July 23, 1999	August 2, 1999	August 11, 1999
August 12, 1999	August 19, 1999	August 20, 1999
September 2, 1999	September 8, 1999	September 14, 1999
September 22, 1999	October 13, 1999	October 19, 1999
October 25, 1999	October 26, 1999	October 27, 1999
October 28, 1999		

These supplemental new drug applications provide for a new strength of VIDEX® tablets (200 mg) as well as allowing a change in dosing interval to once-daily administration, when used in combination therapy for the treatment of HIV-1 infection.

We have completed the review of these applications and have concluded that adequate information has been presented to demonstrate that VIDEX® is safe and effective for use as recommended in the draft labeling dated October 26, 1999. Accordingly, these applications are approved effective on the date of this letter. A 24 month expiration dating period is granted for this product.

We acknowledge your intent to distribute, within 15 days, the agreed upon Dear Health Care Professional and Dear Investigator letters regarding revisions to the pancreatitis warning in the VIDEX package insert, and guidance on appropriate patient management.

The final printed labeling (FPL) must be identical to the submitted draft labeling (package insert and patient package insert submitted October 26, 1999). Marketing the product with FPL that is

not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit 16 paper copies and one diskette that includes a PDF version of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FINAL PRINTED LABELING" for approved NDA 20-154/S-029, S-030, NDA 20-155/S-021, and NDA 20-156/S-022. Approval of this submission by FDA is not required before the labeling is used.

In addition, we note the following Phase 4 commitments, specified in your submissions dated September 14, 1999, and September 23, 1999. These commitments include:

1. To conduct appropriate studies to evaluate the safety and activity of: (a) once daily dosing regimens in the pediatric population, and (b) the use of the 200 mg tablet as part of a dosing regimen in the appropriate pediatric populations.

2. To submit within 60 days a comprehensive risk assessment for fatal and non-fatal pancreatitis in patients treated with VIDEX® alone or in combination with other antiretroviral agents, including stavudine and hydroxyurea. This assessment will be based on all sources of clinical information currently available to Bristol-Myers Squibb Co., including, but not limited to clinical trials. Also, to provide an outline of proposed pharmacoepidemiologic studies investigating this problem, with a proposed timeline for completing such studies, within the aforementioned 60 day time frame.

3. To submit the 48 week data from study AI454-148 as soon as it is available.

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 *FR* 66632). We note that you have not fulfilled all the requirements of 21 CFR 314.55 (or 601.27), and therefore we are deferring submission of your pediatric studies until June 1, 2001.

If you believe that this drug qualifies for a waiver of the pediatric study requirement, you should submit a request for a waiver with supporting information and documentation in accordance with the provisions of 21 CFR 314.55 within 60 days from the date of this letter. We will notify you within 120 days of receipt of your response whether a waiver is granted. If a waiver is not granted, we will ask you to submit your pediatric drug development plans within 120 days from the date of denial of the waiver.

Pediatric studies conducted under the terms of section 505A of the Federal Food, Drug, and Cosmetic Act may result in additional marketing exclusivity for certain products (pediatric exclusivity). Please refer to the Pediatric Written Request dated August 5, 1999. Please note that satisfaction of the requirements in 21 CFR 314.55 alone may not qualify you for pediatric exclusivity.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, contact Destry M. Sillivan, M.S., Regulatory Project Manager, at (301) 827-2335.

Sincerely,

Heidi M. Jolson, M.D., M.P.H.
Director
Division of Antiviral Drug Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research