FOOD AND DRUG ADMINISTRATION
Center for Drug Evaluation and Research
ANTIVIRAL DRUGS ADVISORY COMMITTEE (AVAC) MEETING

QUESTIONS TO THE COMMITTEE

August 6, 2002

Holiday Inn, 8120 Wisconsin Avenue, Bethesda, MD

NDA 21-449, adefovir dipivoxil tablets, Gilead Sciences, Inc., proposed for treatment of chronic hepatitis B infection

1. Has the applicant demonstrated the safety of adefovir 10-mg in patients with chronic hepatitis B (CHB)? Please discuss patients with decompensated liver disease and/or baseline renal insufficiency. Also include in your discussion proposals for patient monitoring of adefovir-associated toxicity.

2. Has the applicant demonstrated the efficacy of adefovir 10-mg for the treatment of CHB? Please comment on the efficacy in patients with the following characteristics: compensated liver disease; decompensated liver disease; lamivudine resistance disease; presumed precore mutant disease; and co-infection with HBV and HIV.

3. Based on the risk/benefit profile of adefovir, does the Committee recommend approval of adefovir (10-mg daily) for the treatment of CHB in adults?

4. Are there any issues with the safety and efficacy data that should be highlighted in the product labeling? In particular, please discuss the use of adefovir in HIV/HBV coinfection and the potential risk of inducing NRTI resistance.

5. Please recommend appropriate Phase 4/postmarketing studies for adefovir in CHB patients. In particular, please discuss the adequacy of the applicant's current program to detect adefovir-resistant HBV and the optimal strategy for long-term resistance surveillance.