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

# QUESTIONS TO THE COMMITTEE
March 19, 2002

Holiday Inn, Two Montgomery Village Avenue, Gaithersburg, MD

NDA 21-245, Picovir™ (pleconaril), ViroPharma Incorporated, proposed for treatment of acute picornaviral upper respiratory illness (common cold) in adults

1. Please discuss the efficacy of pleconaril for treatment of acute VRI in adults.

Please consider the following points as you discuss this issue:

- the efficacy results from studies 843-043 and 843-044
- the efficacy results across the phase 2 studies
- the manner in which pleconaril will likely be used in clinical practice
  - prescribed to symptomatic patients with no rapid diagnostic test available to identify infected patients
  - prescribed to asymptomatic patients with intention for self initiation at onset of symptoms
- the need to administer pleconaril with food
- the need to institute pleconaril within 24 hours of onset of the first symptoms
- the efficacy results in smokers

2. Please discuss the safety of pleconaril in adult patients with symptoms of acute VRI.

Please consider the following points as you discuss this question:

- pleconaril's effect on cytochrome CYP3A4
- the frequency of menstrual disorders occurring in females using OCs while being treated with pleconaril, and the potential risk for unintended pregnancy
- the apparent pharmacodynamic interaction with theophylline. The reports of tachycardia and palpitations reported in otherwise healthy patients treated with pleconaril
- the general types and frequencies of adverse events observed in clinical studies

3. Based on your discussion, does the safety and efficacy profile of pleconaril support its approval for treatment of VRI in adults?

4. If the answer to question 3 is yes, are there any safety or efficacy issues that you would like to see addressed in product labeling? This may include issues in specific sub-populations and/or any risk communication strategies.

5. If the answer to question 3 is no, please discuss what additional data should be provided to establish pleconaril's safety and efficacy.

6.Should you agree that the safety and efficacy of pleconaril have been established, please comment on the applicant's proposed phase 4 studies, and provide suggestions for other types of studies (clinical and/or pharmacologic), including designs and patient populations, that should be conducted as phase 4 commitments.

7. Please discuss any additional suggestions that you have regarding the design of future clinical trials for this indication. Please include in your discussion diagnostic criteria, patient populations, endpoints, and the potential for drug interactions.