DRAFT

Agenda for
Antiviral Drug Products Advisory Committee Meeting on HIV Resistance Testing
November 2 - 3, 1999

DAY 1: TUES. NOV. 2

8:30 Welcome
Conflict of Interest Statements

8:40 Introduction:
Statement of public health importance, set framework for regulatory perspective, *Heidi Jolson*

8:50 SESSION 1

Performance Characteristics and Limitations of Currently Available Genotypic and Phenotypic Assays

Objectives:
1. To describe the methods and accuracy of genotypic assays in discriminating among wild type and viral variants.
2. To describe the methods and accuracy of phenotypic assays in discriminating susceptibility profiles.
3. To obtain scientific input on issues related to sensitivity, specificity, reproducibility and quality control of genotypic and phenotypic assays across a range of HIV RNA levels.
4. To review criteria used for the analytical interpretation of assay results.
5. To explore data that describes comparability between phenotypic assays.
6. To explore data that describes comparability between genotypic assays.
7. To explore data evaluating the correlation between genotype and in vitro phenotype.

8:50-10:00 Presentations
1. CBER's policies on assay regulation; Definitions of Assay Performance Characteristics –*Indira Hewett/Andrew Dayton, CBER (15 min)*
2. Overview of Performance Characteristics of Genotypic and Phenotypic Assays--*Doug Richman (45 min)*

10:00-10:15 Break

10:15-11:45 AC Questions

11:45 Lunch

1:00 SESSION 2

Evaluation of Relationships between Genotype, Phenotype and Treatment Outcome

Objectives:

1. To discuss approaches for categorizing mutational patterns for assessing their prognostic value on treatment outcome.
2. To discuss approaches for categorizing susceptibility profiles for assessing their prognostic value on treatment outcome.
3. To determine whether available evidence supports the clinical utility of HIV genotyping in drug development and to determine what additional information is needed.
4. To determine whether available evidence supports the clinical utility of phenotypic testing in drug development and what additional information is needed.

1:00-3:00 Presentations

Introduction to Session 2-*Heidi Jolson*

Prospective Studies

1. Viradapt Study: *Phillipe Clevenbergh* (include drug concentration data)
2. GART Study: *John Baxter*

Retrospective Studies

3. Introduction to Resistance Collaborative Group re-analysis of selected studies using the RCG Data Analysis Plan (DAP) incl. Development of mutational algorithm: John Mellors
4. DAP Methodology, Statistical: *Victor DeGruttola*
5. Overview of Retrospective and Prospective Studies re-analyzed using the DAP: John Mellors
6. Key retrospective studies analyzed in a standardized fashion (5 min each)—
   - ACTG 333: Michael Para
   - CNAA2007: Mounir Ait-Khaled
   - Frankfurt cohort: Veronica Miller
7. Summary of Key Points (5 min): John Mellors
8. FDA statistical comments of retrospective analyses

3:00-3:30 Break

3:30-5:30 AC Questions:

DRAFT

DAY 2: WED., NOV. 3

8:30 SESSION 3

Practical Considerations for the Use of Resistance Testing in Antiretroviral Drug Development and Use

Objectives

1. To review the prevalence of genotypic variants and/or reduced susceptibility in selected populations.
2. To illustrate possible limitations in the practical clinical use/application of resistance assays in clinical investigations.
3. To examine how other cofactors associated with treatment outcome confound interpretation of resistance testing.

8:30-9:30 Presentations

1. Review of prevalence data on resistance including information on transmission of resistant virus – *Susan Little, UCSD*
2. Overview of other factors that could confound interpretation of resistance data (sampling issues, drug concentrations, compliance, complexity of interpreting results in the setting of combination therapy, compartment issues)—Rich D'Aquilla

9:30-10:30 AC Questions

10:30-10:45 Break

10:45 SESSION 4

Potential Roles of Resistance Testing in Drug Development

Objectives:

1. To obtain committee recommendations on the amount and type of *in vitro* resistance data sufficient to initiate a clinical development program.
2. To obtain committee recommendations on the amount and type of and clinical resistance data sufficient to characterize the clinical activity of an antiretroviral drug against "resistant" viral isolates.
3. To obtain committee recommendations on the amount and type of clinical resistance data appropriate to determine an antiretroviral drug's potential to induce resistance and cross-resistance.
4. To obtain committee recommendations regarding how resistance testing can be optimally incorporated into phase 2/3 clinical trial design.

10:45-11:45 Presentations

1. Historical perspective ("lessons learned") from the antibacterial analogy and contrasts with virology – *Gary Chikami*

2. Overview by DAVDP of the issues (see objectives above) – *Jeff Murray or other DAVDP reviewer*

11:45 Lunch

1:00 – 2:00 p.m.: Open Public Hearing (Patient/community/industry perspectives)

2:00-2:30 Session 4 Presentations (continued)

3. Presentation of Regulatory Proposals—*Katie Laessig*

2:30-4:45 Questions

4:45-5:00 Recap and Summation of the Meeting

Summary—*Scott Hammer*

Adjourn