Background of CMV Regulatory Path and Intended Use

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What Is the Purpose of The First Session of this Panel Meeting?

- For the panel to address whether quantitative Cytomegalovirus (CMV) viral load devices classified as class III (PMA) should be reclassified to class II (510(k)). You will be asked to recommend whether they should remain in Class III (PMA), or be reclassified to Class II (510(k)).

Why Have CMV Viral Load Assays for Transplantation Been Regulated as Class III

Background

Device	Cytomegalovirus (CMV) DNA quantitative assay
Definition	Cytomegalovirus (CMV) DNA quantitative assay is an *in vitro* nucleic acid assay for the quantitative measurement of CMV DNA in human plasma or whole blood. The assay can be used to measure CMV DNA levels serially at baseline and during the course of antiviral treatment to assess virological response to treatment. The test results must be interpreted within the context of all relevant clinical and laboratory findings.
Physical State	IVD
Technical Method	In vitro nucleic acid based assay using real-time PCR for the quantitative measurement of CMV DNA
Date of Approval	07/05/2012

Original Intended Use

The COBAS® AmpliPrep/COBAS® TaqMan® CMV Test is an *in vitro* nucleic acid amplification test for the quantitative measurement of cytomegalovirus (CMV) DNA in human EDTA plasma using the COBAS® AmpliPrep Instrument for automated specimen processing and the COBAS® TaqMan Analyzer or the COBAS TaqMan 48 Analyzer for automated amplification and detection.

The COBAS® AmpliPrep/COBAS® TaqMan® CMV Test is intended for use as an **aid in the management of solid-organ transplant patients who are undergoing anti-CMV therapy**. In this population serial DNA measurements can be used to assess virological response to antiviral treatment. The results from the COBAS® AmpliPrep/COBAS® TaqMan® CMV Test must be interpreted within the context of all relevant clinical and laboratory findings.

The COBAS® AmpliPrep/COBAS® TaqMan® CMV Test is not intended for use as a screening test for the presence of CMV DNA in blood or blood products.

Clinical Effectiveness

This clinical usefulness study is a retrospective, longitudinal cohort study of 211 kidney transplant recipients diagnosed with CMV disease or CMV syndrome (referred to collectively as CMV disease below) and treated with anti-CMV drugs (ganciclovir or valganciclovir). The overall objective of this study was to assess whether CMV viral load measured with the CAP/CTM CMV Test is **informative** in aiding in the management of CMV disease in **kidney** transplant recipients with active CMV disease undergoing anti-CMV drug treatment. The **usefulness of this test in this clinical setting** was assessed on the basis of its performance in predicting resolution of CMV disease when measured at Baseline and in assessing virological response to treatment when measured at subsequent time points…

Notes…

- Solid organ transplant patients
- Analytical studies *included* WHO standard
- Data available from the Victor study
  - Identical sponsor for device and drug
  - Prospective collection of specimens from study available for testing
- Study established **clinical effectiveness** of the device for the proposed intended use
- Patient risk from erroneous results believed to warrant classification as Class III
- Dr. Whitaker will later discuss classification of devices, and particularly, the differences between Class III and Class II

Why Consider Reclassification…

- Far more information available on the use of viral load in transplant patients
- Clinical effectiveness unequivocally established
- Reduced assay variability across assays (with caveats)
- *FDA regulatory mandate to be least burdensome and to appropriate classify devices*
- However:
  - as to be discussed, there are differences in the regulatory oversight between Class III and Class II devices
  - a 'lowered' barrier to entry may have risks
  - remains a high-risk population at significant clinical risk from inaccurate results
  - There remain clinical issues that need to be resolved

The Remainder of the CMV Presentations…

- Clinical perspective from Dr. Ajit Limaye
- Analytical/laboratory perspective from Dr. Linda Cook
- FDA presentation by Dr. Kathleen Whitaker
- Open Public Hearing
- Committee Discussion


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