## PROJECT: Evaluation of two chemiluminescent immunoassays for IgG and IgM antibodies towards human cytomegalovirus

**Study abstract**

The objective of the study is to broadly assess CMV testing results from diagnostic routine as obtained with the Elecsys methods and other commercially available assays in the field. Data will be generated in parallel at ≥1 external study site in the current routine setting. The agreement rates, relative specificity and the relative sensitivity will be compared to at least one other commercially available CMV assay family (e.g. respective corresponding DiaSorin Liaison® CMV assays). Approx. 10000 (target 12000) routine samples with CMV request will be tested.

**Overview experimental part**

The experimental part is subdivided into the following main sections: Study Familiarization (see 9.1) In this part of the Study Protocol the site personnel should get acquainted with the system and reagents, the experimental design and/or WinCAEv (if used). - Check the barcode recognition of routine vials: Run 10 routine vials with routine barcodes - Check data transfer into Roche analysis system WinCAEv and data manager: Perform 5 tests with negative and 5 tests with positive control material (e.g. Preci Control 1 and 2 of CMV IgG or CMV IgM.

The participation in the Main Trial is mandatory. The Main Trial consists of method comparison experiments using routine samples with CMV request. The testing algorithm of the respective PI shall be followed.

**Method comparison**

Relative sensitivity and relative specificity as depicted in the method sheet of the respective assay. Values need to be within the respective confidence ranges of the respective method sheet. Additional analyses may be performed (e.g. Avidity, COI levels, infection status, …) if applicable.

**General note**

The product given to you for the purpose of this study is CE-marked and approved for diagnostic purposes in your country, depending on local regulations. Use of the assays is described in respective method sheets and will be performed accordingly.

**Objective of the study**

Broad assessment of CMV testing results under routine conditions using different commercially available methods

**Intended use**

*Elecsys CMV IgM (07027133190) Immunoassay* for the in vitro qualitative determination of IgM antibodies to cytomegalovirus in human serum and plasma. Results obtained with this assay are used as an aid in the diagnosis of recent CMV infections. The electrochemiluminescence immunoassay "ECLIA" is intended for use on the cobas e 801 immunoassay analyzer.

*Elecsys CMV IgG (07027117190) Immunoassay* for the in vitro quantitative determination of IgG antibodies to cytomegalovirus in human serum and plasma. Results with this assay are used to indicate past or recent infection with CMV. The electrochemiluminescence immunoassay "ECLIA" is intended for use on the cobas e 801 immunoassay analyzer.

**DATA MANAGEMENT PROCEDURES**

Testing results of Elecsys are captured, analyzed, stored and archived in WinCAEv. An electronic archiving system will be used for long term archiving of the data. Calibration and testing results from comparison methods will be stored and archived as hard copies or electronically. Testing results from comparison methods will be entered manually or by Host File Import in WinCAEv. Results from confirmatory testing will be entered manually in WinCAEv or respective datasheets. The manually entered data will be 100% source data verified according to the 4–eye principle. The data will be submitted to Roche Diagnostics and monitored on a regular basis as defined in the respective monitoring plan in order to become aware of unexpected results early on. Retain all samples tested until the CRA allows disposal of the specimens

(store frozen at below -15°C) Data will be validated and locked in WinCAEv by the investigator and monitor after each experiment.

**STATISTICAL METHODS**

Validated software tools (e.g. WinCAEv and/or WinMC) and validated exports thereof into Excel will be used for data analysis. Agreement, relative specificity, relative sensitivity and confidence intervals (95%, two-sided) will be calculated using the validated SAS intranet tool from the Biostatistics department (http://rpzms000543/prgbio/power/KI_1assay.htm) The sensitivity/specificity of this assay is determined relatively to a diagnostic algorithm using additional serologic and/or molecular test(s) and further resolution methods, creating a combined gold standard as a surrogate (refered to as relative/diagnostic sensitivity and specificity).

**Method comparison**

Reagents Roche Elecsys CMV assays and corresponding commercial assays e.g. from DiaSorin Liaison Sample material Approx. 10000 (target: 12000) routine samples with CMV request Preparation/ Aliquotting Volume depending on the number and dead volumes of Roche assays and comparison assays Calibration & QC According to the instructions in the method sheets Measurement Comparison methods in parallel according to the established routine of the laboratory. - Test all samples with routine CMV IgG and IgM as well as with Elecsys CMV IgG and IgM - Test applicable samples from both routine & Elecsys CMV IgG/IgM testing with CMV avidity assays (i.e. routine method as well as on Elecsys / cobas e). - Further second level testing may also comprise on-site virology testing and/or site-specific blot testing, where applicable - If samples are not clinically characterized, further testing needs to be performed in case of discrepancies (on-site or at Roche Diagnostics).

In case of discrepant samples, please also store some excess material at 15°C or below for further testing (on-site or samples will be shipped to Roche for further testing/investigation, as required.) Documentation Datasheet “Main Trial” or WinCAEv. Validation & data calculation Check that controls are within specified ranges. Calculation of relative sensitivity and relative specificity for each single parameter. Agreement rates between assays will be calculated. Additional analyses may be performed (e.g. COI levels, infection status,…) if applicable.

**Figura 1. Piano delle attività**