



## Xpert PML-RARA Control Panel C215

### INTENDED USE:

The Xpert PML-RARA Control Panel C215 is an external reference material used to monitor the performance of *in vitro* laboratory nucleic acid testing procedures for the quantitative detection of PML-RARA transcript isoforms, bcr1, bcr2, bcr3, and ABL1 endogenous control mRNA transcript when analyzed using the Xpert® PML-RARA assay on Cepheid GeneXpert® Instrument Systems.

The translocation t(15;17) (q24;q21) of the promyelocytic leukemia gene (PML) and retinoic acid receptor- $\alpha$  protein (RARA) gene results in PML-RARA, an oncogenic fusion gene. PML-RARA is a driver for acute promyelocytic leukemia (APL), a subtype of acute myeloid leukemia (AML) and is found in over 98% of APL patients<sup>2</sup>. PML-RARA represses the transcription of multiple genes involved in myeloid differentiation and confers a survival and proliferative advantage to leukemic cells, resulting in accumulation of promyelocytes in bone marrow.<sup>1</sup> There are three typical PML-RARA isoforms: bcr1 (L or long), bcr2 (V or variant), and bcr3 (S or short). Bcr1 and bcr3 isoforms are most common and found in 90-95% of APL patients<sup>1</sup>. Treatment involving all-trans-retinoic acid (ATRA), arsenic trioxide (ATO), and/or chemotherapy has been largely successful for pediatric and adult patients. Measurable residual disease monitoring (MRD) with qPCR-based detection of PML-RARA transcript is an important tool for use as a prognostic/predictive biomarker to inform treatment decision-making, a monitoring tool to identify impending relapse, and a potential surrogate end point for overall survival in clinical trials to accelerate the development of novel treatment strategies<sup>2</sup>.

### PRODUCT SUMMARY and PRINCIPLE:

The Xpert PML-RARA Control Panel C215 consists of 5 components. Each component contains varying concentrations of PML-RARA isoforms; bcr1, bcr2 or bcr3, mixed with a fixed concentration of ABL1 to produce five levels: PML-RARA 0%, PML-RARA bcr1 1%, PML-RARA bcr2 1%, PML-RARA bcr3 1%, and PML-RARA bcr1 20%. The 0% level contains only wildtype ABL1 transcript.

Quality controls can be used for routine monitoring of test systems, validation, verification, proficiency assessment, and training procedures. Routine use of quality controls assists the laboratory in identifying shifts, trends, and increased frequency of random errors caused by variations in the test system, such as failing reagents or malfunctioning equipment. Early investigation can prevent failed assay runs.

#### Validation and Value Assignment

MMQCI manufactured 3 lots of Xpert PML-RARA Control Panel C215 and tested the lots across 3 Xpert PML-RARA assay cartridge lots, incorporating multiple days and operators. Grubb's outlier test was applied to remove statistical outliers and the remaining data was used to assign % values to each level.

### COMPOSITION:

Xpert PML-RARA Control Panel C215 is comprised of 10 single-use bottles, 2 bottles of each % PML-RARA level. The C215 bottles contain 4 mL of synthetic RNA transcripts, suspended in a stabilizing matrix with a non-infectious solution of buffers and preservatives. Level 0% contains wildtype ABL1 RNA transcript only. Levels PML-RARA bcr1 1%, PML-RARA bcr2 1%, PML-RARA bcr3 1%, and PML-RARA bcr1 20% contain varying ratios of PML-RARA RNA transcript to ABL1 RNA transcript.

### STORAGE and STABILITY:

The Xpert PML-RARA Control Panel C215 should be stored at -25°C to -15°C. Unopened material is stable through the expiration date printed on the kit label when consistently stored frozen. Xpert PML-RARA Control Panel C215 components are for single use only. Discard after use according to your local and federal regulations.

### PRECAUTIONS and WARNINGS:

- Use the control as provided. Do not dilute or transfer to another storage tube.
- This product is intended for *in vitro* analytical testing and is provided for Research Use Only. It is not for use in diagnostic procedures.
- This product is slightly cloudy in appearance.
- This product does not contain any biological material of human or animal origin. Universal Precautions are NOT required when handling this product.
- Reference materials should be used in accordance with local, state, federal regulations and accreditation requirements.
- Xpert PML-RARA Control Panel C215 cannot be cloned, sold, or transferred without the explicit written consent of MMQCI.

### INSTRUCTION FOR USE:

1. Allow the Xpert PML-RARA controls to be tested to come completely to room temperature (18°C to 25°C) for approximately 30 minutes.
2. Immediately before pipetting, thoroughly mix the control bottle by inverting 8 times followed by 2 pulse vortexes, 2-3 seconds each, at maximum speed.
3. Add 4mL of the control sample to 100 $\mu$ L of Proteinase K in a conical tube, as you would a blood specimen.
4. Continue with the assay procedure according to manufacturer's instructions.
5. Discard after use according to local and federal regulations.

### EXPECTED VALUES:

Locate the assigned % values on the Xpert PML-RARA Control Panel C215 Data Sheet found in each kit box of Xpert PML-RARA Control Panel C215. The reported % values of C215 may vary among laboratories, reagent lots, operators and test systems. **Each laboratory should establish their own % ranges.**

#### References

<sup>1</sup> Liquori A, Ibañez M, Sargac C, Sanz MÁ, Barragán E, Cervera J. Acute Promyelocytic Leukemia: A Constellation of Molecular Events around a Single PML-RARA Fusion Gene [published correction appears in *Cancers (Basel)*. 2021 Jul 09;13(14)]. *Cancers (Basel)*. 2020;12(3):624.

<sup>2</sup> Heuser M, Freeman SD, Ossenkopppele GJ, et al. 2021 Update on MRD in acute myeloid leukemia: a consensus document from the European LeukemiaNet MRD Working Party. *Blood*. 2021;138(26):2753-2767.

### ORDERING INFORMATION:

Xpert PML-RARA Control Panel C215

**Part Number: C215**

Kit contains: 10 bottles x 4mL

2 of each % Level:

(0%, bcr1 1%, bcr2 1%, bcr3 1% and bcr1 20%)