

Xpert NPM1 Control Panel C194

INTENDED USE:

The Xpert NPM1 Control Panel C194 is intended for use as reference material to monitor the performance of *in vitro* laboratory nucleic acid testing procedures for the quantitative detection of the NPM1 Type A mutant mRNA transcript and ABL1 endogenous control mRNA transcript when analyzed using the Xpert® NPM1 Mutation assay on Cepheid GeneXpert® Instrument Systems.

The nucleophosmin-1 gene (NPM1) encodes for a highly versatile protein, with major functions in nucleocytoplasmic protein shuttling, protein chaperoning, ribosome biogenesis, cell cycle progression and apoptosis. Tetranucleotide insertion mutations in exon 12 of NPM1 are frequently seen in hematopoietic cancers; representing roughly one-third of adult acute myeloid leukemia cases.¹ The 'Type A' NPM1 mutation (TCTG insertion in exon 12) represents nearly 80% of all NPM1 gene alterations.³ These insertions introduce a frameshift in the NPM1 gene that ablates translation of a C-terminal nucleolar localization motif and creates a *de novo* nuclear export signal, ultimately reappportioning NPM1 protein from the nucleus and nucleolus to the cytoplasm.^{1,2} This is associated with instability of the critical tumor-suppressors p53 and ARF, known to be modulated by NPM1.⁴ Mutations in NPM1 represent a recently recognized class of leukemias by the World Health Organization (WHO).⁴ Quantitative monitoring of NPM1 transcripts in patient blood, including the common Type A mutant RNA, is a valuable approach for determining treatment responses.

PRODUCT SUMMARY and PRINCIPLE:

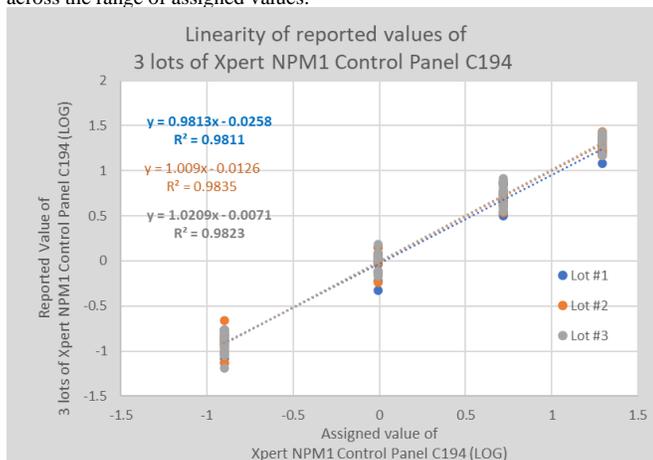
The Xpert NPM1 Control Panel C194 consists of 5 components. Each component contains an increasing concentration of NPM1 Type A mutant RNA transcript mixed with fixed concentrations of ABL1 and wildtype NPM1 transcripts to produce 5 levels of Type A Mutant RNA to ABL1 RNA: 0%, 0.1%, 1%, 5%, and 20%. The 0% level contains wildtype NPM1 and wildtype ABL1 transcripts only.

Validation and Value Assignment

MMQCI manufactured 3 lots of Xpert NPM1 Control Panel C194 and tested the lots across 5 Xpert NPM1 Mutation 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. Figure 1 compares the reported values of each of the 3 lots of C194 to the assigned values and demonstrates linearity across the range of values reported.

Figure 1.

Linearity of the reported values of 3 lots of Xpert NPM1 Control Panel C194 across the range of assigned values.



References

- Falini B, Brunetti L, Sportoletti P, Martelli MP. NPM1-mutated acute myeloid leukemia: from bench to bedside. *Blood*. 2020; 136:1707-1721.
- Grisendi S, Mecucci C, Falini B, Pandolfi PP. Nucleophosmin and cancer. *Nat Rev Cancer*. 2006; 6:493-505.
- Falini B, Nicoletti I, Martelli MF, Mecucci C. Invited review: Acute myeloid leukemia carrying cytoplasmic/mutated nucleophosmin (NMPc+ AML): biological and clinical features. *Blood*. 2007; 109:874-885.
- Heath EM, Chan SM, Minden MD, Murphy T, Shlush LI, Schimmer AD. Biological and clinical consequences of NPM1 mutations in AML. *Leukemia*. 2017; 31:798-807.

COMPOSITION:

Xpert NPM1 Control Panel C194 is comprised of 10 single use bottles, 2 bottles of each % NPM1 mutation level. The C194 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 NPM1 and ABL1 RNA transcript only. Levels 0.1%, 1%, 5%, and 20% contain varying ratios of NPM1 Type A mutant RNA transcript to ABL1 RNA transcript, in a background of NPM1 wildtype RNA.

STORAGE and STABILITY:

The Xpert NPM1 Control Panel C194 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 NPM1 Control Panel C194 components are for single use only. Discard after use according to your local and federal regulations.

INSTRUCTION FOR USE:

- Allow the Xpert NPM1 MUT A controls to be tested to come completely to room temperature (18°C to 25°C) for approximately 30 minutes.
- Immediately before pipetting, thoroughly mix the control bottle by inverting 8 times followed by 2 pulse vortexes, 2-3 seconds each, at maximum speed.
- Add 4mL of the control sample to 100µL of Proteinase K in a conical tube, as you would a blood specimen.
- Continue with the assay procedure according to manufacturer's instructions.
- Discard after use according to 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.
- Quality control materials should be used in accordance with local, state, federal regulations and accreditation requirements.
- Xpert NPM1 Control Panel C194 cannot be cloned, sold, or transferred without the explicit written consent of MMQCI.

EXPECTED VALUES:

Locate the assigned % values on the Xpert NPM1 Control Panel C194 Data Sheet found in each kit box of Xpert NPM1 Control Panel C194. As indicated on the Data Sheet, laboratory reported % values for C194 can be analyzed by linear regression and graphed versus the C194 assigned values to confirm performance. The reported % values of C194 may vary among laboratories, reagent lots, operators and test systems. **Each laboratory should establish their own % ranges and perform a linear regression with an expected correlation coefficient (R²) at or above 0.9.**

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.

ORDERING INFORMATION:

Xpert NPM1 Control Panel C194

Part Number: C194

Kit contains: 10 bottles x 4mL

2 of each % Level (0%, 0.1%, 1%, 5% and 20%)