Research Use Only
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Xpert NPM1 MUT 0%

INTENDED USE:
The Xpert NPM1 MUT 0% is intended for use as an assayed external quality control to monitor the performance of *in vitro* laboratory nucleic acid testing procedures for the quantitative detection of the NPM1 mutant mRNA transcripts and ABL1 endogenous control mRNA transcript when analyzed using the Xpert® NPM1 Mutation assay on Cepheid GeneXpert® 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] The 'Type B' (CATG insertion) and 'Type D' (CCTG insertion) are found in 10% and 5% of cases, respectively.[2] 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 reapportioning NPM1 protein from the nucleus and nucleolus to the cytoplasm.[1,3] 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 is a valuable approach for determining treatment responses.

PRODUCT SUMMARY and PRINCIPLE:
The Xpert NPM1 MUT 0% is composed of one level, Xpert NPM1 MUT 0%, which contains wildtype NPM1 and wildtype ABL1 transcripts only. This control is designed to represent a sample with no mutations of the NPM1 gene. Xpert NPM1 MUT 0% is also a component of Xpert NPM1 Control Panel C194v1.1, part number C194v1.1.

Quality controls can be used for routine monitoring of test systems, validation, verification, proficiency assessment, and training procedures. Quality controls that are consistent from lot to lot assist 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.

COMPOSITION:
Xpert NPM1 MUT 0% contains 5 single-use bottles of Xpert NPM1 MUT 0% consisting of synthetic wildtype NPM1 and ABL1 RNA transcripts, suspended in a stabilizing matrix with a non-infectious solution of buffers and preservatives.

STORAGE and STABILITY:
Xpert NPM1 MUT 0% 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 MUT 0% is for single use only. Discard after use according to your local and federal regulations.

PRECAUTIONS, WARNINGS, and LIMITATIONS:
- 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.
- Xpert NPM1 MUT 0% cannot be cloned, sold, or transferred without the explicit written consent of MMQCI.
- Quality control materials should be used in accordance with local, state, and federal regulations and accreditation requirements.

INSTRUCTION FOR USE:
1. Allow the Xpert NPM1 MUT 0% component to be tested to come completely to room temperature (18°C to 25°C), approximately 30 minutes, until bottles are warm to the touch.
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 100µL 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:
The expected result of Xpert NPM1 MUT 0% when tested with the Xpert NPM1 Mutation assay on the Cepheid GeneXpert system is: Negative (sufficient ABL transcript).

Control	Test Result
Xpert NPM1 MUT 0%	Negative (sufficient ABL transcript)

ORDERING INFORMATION:
Xpert NPM1 MUT 0%
Part Number: C19512-5
Kit contains: 5 bottles x 4mL

References
[1] Falini B, Brunetti L, Sportoletti P, Martelli MP. NPM1-mutated acute myeloid leukemia: from bench to bedside. *Blood*. 2020; 136:1707-1721.
[2] 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.
[3] Grisendi S, Mecucci C, Falini B, Pandolfi PP. Nucleophosmin and cancer. *Nat Rev Cancer*. 2006, 6:493-505.
[4] 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