IVD

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Birlinn™ BCR-ABL1 p210 IS Panel C230

INTENDED USE:

The Birlinn™ BCR-ABL1 p210 IS Panel C230 is intended to monitor the detection and quantification of *BCR-ABL1* (p210) fusion gene using molecular test systems. The Birlinn BCR-ABL1 p210 IS Panel C230, with assigned values traceable to World Health Organization (WHO), allows calculation of a Conversion Factor (CF) necessary to express quantification results (M-bcr transcript of *BCR-ABL1* p210 relative to the *ABL1* transcript) according to the International Scale (IS).

The Philadelphia chromosome, a translocation between the *ABL1* gene on chromosome 9 and the *BCR* gene on chromosome 22, designated as t(9;22), generates the fusion gene *BCR-ABL1* which is present in most chronic myelogenous leukemia patients. Quantitative monitoring of *BCR-ABL1* transcripts in patient blood is an important tool for measuring response to therapy. In 2009, the WHO developed a panel of four *BCR-ABL1* primary standards to establish an international scale (IS), a standardized method for reporting assay results as a ratio of fusion transcripts to control gene transcripts (%IS), useful to the harmonization of patient care across laboratories worldwide.[1,2] The %IS can also be expressed as molecular response (MR), the log reduction from a standardized baseline of 100% on the IS. The Birlinn BCR-ABL1 p210 IS Panel C230 kit is traceable to the WHO International Genetic Reference Panel for Quantitation of *BCR-ABL1* Translocation (WHO Reference Panel), NIBSC code 09/138, and designed to enable laboratories to report on the international scale.

PRODUCT SUMMARY and PRINCIPLE:

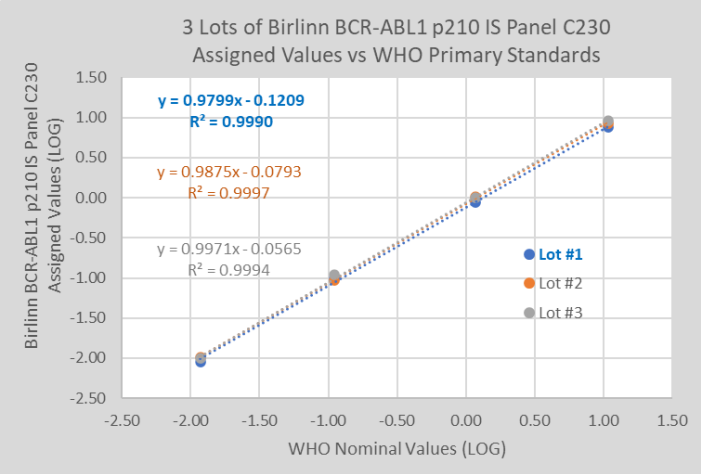
The Birlinn BCR-ABL1 p210 IS Panel C230 consists of five components. Each component contains an increasing concentration of *BCR-ABL1* (e14a2/b3a2) RNA transcript mixed with a fixed concentration of *ABL1* RNA transcript to produce five levels, 0.0032%, 0.01%, 0.1%, 1% and 10%. The %IS values provided are traceable to WHO Reference Panel, NIBSC code 09/138, and are assigned to each lot of the Birlinn BCR-ABL1 p210 IS Panel C230 according to NIBSC Instructions for Use.[3,4]

Quality controls can be used for routine monitoring of test systems, validation, verification, proficiency assessment, and training procedures. Consistent 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 Birlinn BCR-ABL1 p210 IS Panel C230 and tested them alongside the WHO Reference Panel, using one reagent lot of the REALQUALITY RQ-BCR-ABL p210 One-Step assay. Linear Regression was applied and a lot-specific Correction Factor (CF) was calculated to assign WHO-traceable %IS values to each level of Birlinn BCR-ABL1 p210 IS Panel C230 for all 3 lots according to NIBSC Instructions for Use.[4] Figure 1 compares the 3 lots of Birlinn BCR-ABL1 p210 IS Panel C230 to the 4 members of the WHO Reference Panel. New lots of Birlinn BCR-ABL1 p210 IS Panel C230 will be assigned lot-specific %IS values in the same manner.

Figure 1. Three lots of Birlinn BCR-ABL1 p210 IS Panel C230 calibrated to the WHO International Genetic Reference Panel for Quantitation of BCR-ABL Translocation.



COMPOSITION:

The Birlinn BCR-ABL1 p210 IS Panel C230 is comprised of 5 tubes, 1 tube of each %IS level. The tubes contain 20µL of synthetic *BCR-ABL1* RNA transcript and synthetic *ABL1* control gene RNA transcript provided in a ready-to-use solution. Each of the components can be directly used in a reverse transcription reaction followed by amplification of cDNA for detection of BCR-ABL1/ABL1 using the laboratory's system. The Birlinn BCR-ABL1 p210 IS Panel C230 materials are provided in a background of total RNA at a concentration of 400ng/µL and may be diluted as a patient sample to provide the recommended sample input for the assay to be used.

STORAGE and STABILITY:

The Birlinn BCR-ABL1 p210 IS Panel C230 should be stored at -25°C to -15°C and is stable through the expiration date printed on the kit label when stored frozen. Do not freeze/thaw more than 5 times. Discard after use according to your local and federal regulations.

PRECAUTIONS and WARNINGS:

- This product is intended for *in vitro* diagnostic use only.
- This product is clear in appearance.
- Do not freeze/thaw more than 5 times.
- This product does not contain any biological material of human or animal origin. Universal Precautions are NOT required when handling this product.
- The Birlinn BCR-ABL1 p210 IS Panel C230 cannot be cloned, sold, or transferred without the explicit written consent of MMQCI.

RECOMMENDED INSTRUCTION FOR USE:

1. Allow the Birlinn BCR-ABL1 p210 IS Panel C230 component to be tested to come completely to room temperature (18°C-25°C), approximately 10-15 minutes.
2. Immediately before pipetting, thoroughly mix the samples by flicking the tube 20x followed by 2 pulse vortexes, 2-3 seconds each at maximum speed. Quick spin tube to remove droplets from cap.
3. Carefully pipette each component according to the assay Manufacturer's instructions for patient samples. If a dilution is required for sample concentrations of 400ng/µL, dilute the Birlinn BCR-ABL1 p210 IS Panel C230 components in the same manner. *Note: It is recommended to use a minimum of 5µL of the* Birlinn *BCR-ABL1 p210 IS Panel C230 material for optimal performance.*
   Dilution Protocol Example:
   1. In a labeled 1.5mL LoBind tube, pipette 5µL of well-mixed Birlinn BCR-ABL1 p210 IS Panel C230 component into 45µL of molecular grade H2O to make a 1:10 dilution.
   2. Mix dilution by 20x inversions, followed by 2 pulse vortexes, 3-5 seconds. Quick spin to remove all liquid from cap prior to use.
4. Continue with the assay procedure according to manufacturer's instructions.
5. See the Lot Specific Data Sheet and assay Manufacturer's instructions to calculate a Correction Factor to correlate the assay ratios of *BCR-ABL1*/ *ABL1* to %IS.[3,4]Assigned values for Birlinn BCR-ABL1 p210 IS Panel C230 are provided in the Data Sheet of the specific kit lot, to be used as secondary standards to calculate an assay-specific CF traceable to the WHO Primary Panel.
6. Discard after use according to local and federal regulations, or store remaining material at -25°C to -15°C.

EXPECTED VALUES:

Locate the appropriate WHO-traceable %IS values assigned to your lot of Birlinn BCR-ABL p210 IS Panel C230 on the Data Sheet found in each kit box. It is important to notice that the WHO-traceable values were assigned by testing with one lot of REALQUALITY RQ-BCR-ABL p210 One-Step assay. Each laboratory should establish their own Correction Factor and %IS ranges independently for the assay to be used. Linearity can be confirmed by performing a linear regression with an expected correlation coefficient (R^2) at or above 0.97.

ORDERING INFORMATION:

Birlinn BCR-ABL1 p210 IS Panel C230
Part Number: C230
Kit Contains: 5 tubes x 20µL;
1 tube each of 0.0032%IS, 0.01%IS, 0.1%IS, 1%IS and 10%IS

References
[1]Branford S et al. Desirable performance characteristics for BCR-ABL measurement on an international reporting scale to allow consistent interpretation of individual patient response and comparison of response rates between clinical trials. Blood 2008, 112:3330-38.
[2]White HE et al. Establishment of the first World Health Organization International Genetic Reference Panel for quantitation of BCR-ABL mRNA. Blood 2010, 116:e111-117.
[3]Cross et al. Development and evaluation of a secondary reference panel for BCR_ABL1 quantification on the International Scale. Leukemia 2016 30, 1844-1852.
[4]1st WHO International Genetic Reference Panel for Quantitation of BCR-ABL Translocation, NIBSC code: 09/138 Instructions for use (Version 9.0, Dated 22/10/2020).

C230 IVD Issued: January 2025 Rev.01