

Xpert BCR-ABL1 p190 Linearity Panel C208

INTENDED USE:

The Xpert BCR-ABL1 p190 Linearity Panel C208 is intended for use as reference material to monitor the reportable range of *in vitro* quantitative detection of the p190 BCR-ABL1 translocation mRNA transcript and the ABL1 endogenous control mRNA transcript when analyzed using the Xpert® BCR-ABL Ultra p190 assay on Cepheid GeneXpert® Instrument Systems.

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 (CML) patients and “Philadelphia positive” acute lymphoblastic leukemia of B-cell lineage (Ph⁺ALL)¹. Depending on the translocation breakpoint in BCR, different BCR-ABL protein isoforms are expressed, which all contain exons 2-11 of the ABL1 gene, but differ in the length of their BCR component. The most common BCR-ABL isoforms are the major p210 and minor p190 translocations, corresponding to a 210kD protein and a 190kD protein, respectively². The major p210 BCR-ABL1 translocation is the hallmark of CML, whereas the minor p190 BCR-ABL1 occurs in the majority of B-cell acute lymphoblastic leukemia patients³. Quantitative monitoring of BCR-ABL1 transcripts in patient blood is an important tool for measuring response to therapy.

PRODUCT SUMMARY and PRINCIPLE:

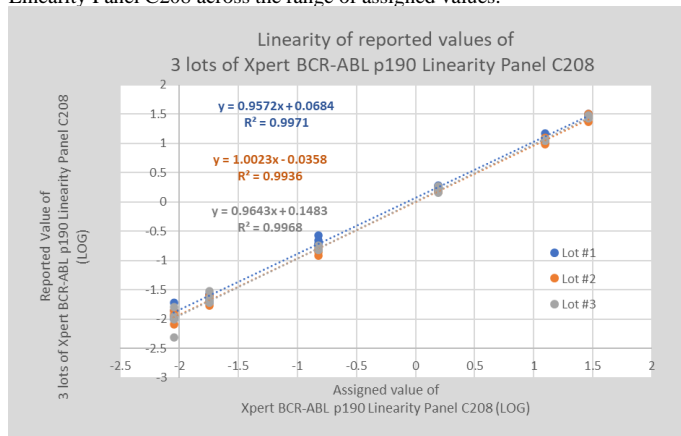
The Xpert BCR-ABL1 p190 Linearity Panel C208 consists of 6 components. Each component contains an increasing concentration of BCR-ABL1 (e1a2) RNA transcript mixed with a fixed concentration of ABL1 RNA transcript to produce 6 levels, 0.008%, 0.02%, 0.1%, 1%, 10%, and 20%. Each ratio of e1a2 RNA to ABL1 RNA has been confirmed by digital PCR.

Assessing the linearity of an assay is a crucial part of good laboratory practice, as it confirms that the test system accurately measures patient samples throughout the manufacturer’s designated reportable range. Linearity testing can help identify problems related to reagents, sample handling, and instruments, enabling prompt action which may avoid failed assay runs.

Validation and Value assignment

MMQCI manufactured 3 lots of Xpert BCR-ABL1 p190 Linearity Panel C208 and tested the lots across 5 Xpert BCR-ABL1 p190 Ultra 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 C208 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 BCR-ABL1 p190 Linearity Panel C208 across the range of assigned values.



References

- Chan LC, Karhi KK, Rayter SI, Heisterkamp N, Eridani S, Powles R, Lawler SD, Groffen J, Foulkes JG, Greaves MF, Wiedemann LM. A novel *abl* protein expressed in Philadelphia chromosome positive acute lymphoblastic leukaemia. *Nature*. 1987;325: 635–637.
- Fainstein E, Marcelle C, Rosner A, Canaan E, Gale RP, Dreazen O, Smith SD, Croce CM. A new fused transcript in Philadelphia chromosome positive acute lymphocytic leukaemia. *Nature*. 1987; 330:386–388.
- Shaoguang, L et al. The P190, P210 and P230 Forms of the BCR/ABL Oncogene Induce a Similar Chronic Myeloid Leukemia-like Syndrome in Mice but Have Different Lymphoid Leukemogenic Activity. *Blood* 2008, 112:3330-38

COMPOSITION:

Xpert BCR-ABL1 p190 Linearity Panel C208 is comprised of 12 single-use bottles, 2 bottles of each % ratio level. Each bottle contains 4 mL of synthetic RNA transcripts, suspended in a stabilizing matrix with a non-infectious solution of buffers and preservatives. Levels 0.008%, 0.02%, 0.1%, 1%, 10% and 20% contain ratios of BCR-ABL1 RNA transcript and ABL1 RNA transcript.

STORAGE and STABILITY:

Xpert BCR-ABL1 p190 Linearity Panel C208 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 BCR-ABL1 p190 Linearity Panel C208 components are for single use. Discard after use according to your local and federal regulations.

PRECAUTIONS and WARNINGS:

- Use the Xpert BCR-ABL1 p190 Linearity Panel C208 components 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, 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 BCR-ABL1 p190 Linearity Panel C208 cannot be cloned, sold, or transferred without the explicit written consent of MMQCI.

INSTRUCTION FOR USE:

- Allow the Xpert BCR-ABL1 p190 Linearity Panel C208 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.
- Immediately before pipetting, thoroughly mix the Xpert BCR-ABL1 p190 Linearity Panel C208 component by inverting 8 times followed by 2 pulse vortexes, 2-3 seconds each at maximum speed.
- Add 4mL of the Xpert BCR-ABL1 p190 Linearity Panel C208 component 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.

EXPECTED VALUES:

Each kit of Xpert BCR-ABL1 p190 Linearity Panel C208 contains a lot specific Data Sheet that details the assigned % values for that lot number of C208. Once the laboratory has tested all levels of the C208 panel using the Xpert BCR-ABL Ultra p190 assay (replicates are recommended for linearity assessment), perform a linear regression analysis to calculate a correlations coefficient (R²), and graph the data by plotting the reported % values against the assigned values. See Figure 1 of the Data Sheet for an example of a linear regression graph. An R² of 0.9 or higher confirms linearity across the reportable range of the assay. **It is important to note that reported % values may vary among laboratories due to different reagent lots, operators, and test systems. Each laboratory should establish their own % ranges for the C208 panel.**

ORDERING INFORMATION:

Xpert BCR-ABL1 p190 Linearity Panel C208

Part Number: C208

Kit contains: 12 bottles x 4mL

2 of each % Level (0.008%, 0.02%, 0.1%, 1%, 10% and 20%)