BCR::ABL1 Major Quantification Programme

All Participant Report

Distribution - 252601

Participant ID -

Date Issued - 15 May 2025

Closing Date - 13 June 2025

Trial Comments

The trial was issued to 339 participants; 320 (94.4%) participants returned results. Of the 19 laboratories that did not return results, six pre-notified us of their intention to not return results. Seven participants returned non-International Scale (IS) data only, 142 participants returned IS data only and 171 participants returned both non-IS and IS data.

Sample Comments

Two vials of lyophilised material (BCRQ 197 and BCRQ 198) were issued for quantitative BCR::ABL1 analysis.

Results and Performance - Performance monitoring based on **Single Sample z-score**

	Your Unconverted Results (*BCR::ABL1*/ Reference Gene %)	Your IS Results (%)	Your Log Transformed IS Result	Log Transformed Robust Mean	Uncertainty of the Assigned Value (Log Transformed Robust Mean)
BCRQ 197	Not Returned	0.07	-1.15	-1.05	± 0.02
BCRQ 198	Not Returned	0.409	-0.39	-0.37	± 0.01

Result Type	Log Change Between Samples	Robust Mean Log Change	Uncertainty of the Assigned Value (Robust Mean)	Robust SD Log Change
Unconverted	N/A	-0.67	± 0.01	0.12
IS	-0.77	-0.68	± 0.01	0.14

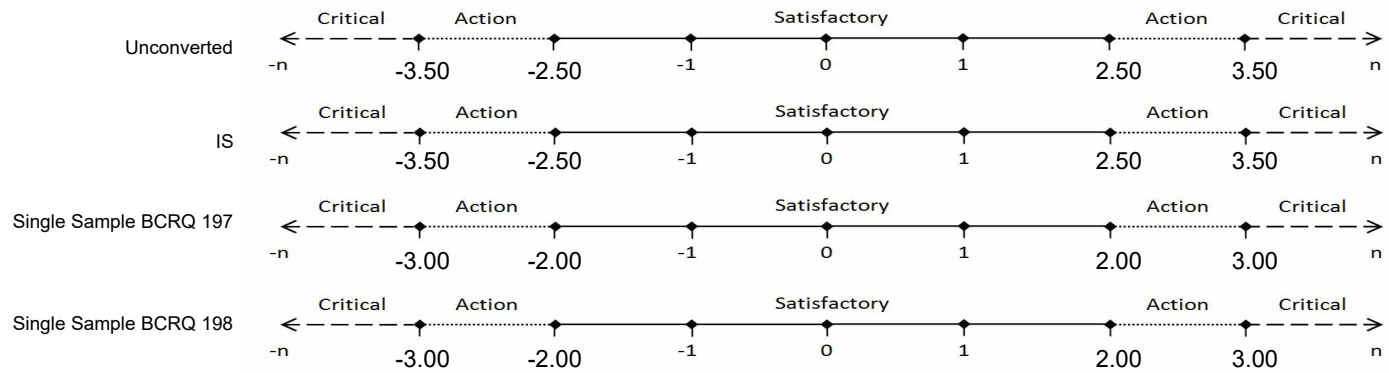
Sample	Single Sample z-score**	Performance Status for this Trial	Performance Status Classification Over 6 Sample Period		
			Satisfactory	Action	Critical
BCRQ 197	-0.42	Satisfactory	6	0	0
BCRQ 198	-0.08	Satisfactory	6	0	0

Reported Log Change	Log Change z-score**	Performance Status for this Trial *	Performance Status Classification Over 3 Trial Period		
			Satisfactory	Action	Critical
Unconverted	N/A	N/A	0	0	0
IS	-0.64	Satisfactory	3	0	0

* Please note, the information in this table is for information only. Performance monitoring is based on Single Sample data only

****z-score Limits Definitions**

Please note the scale below is applicable to the tables above and to the z-score histograms and Shewhart control charts that follow. It is not applicable to the Cusum control charts.

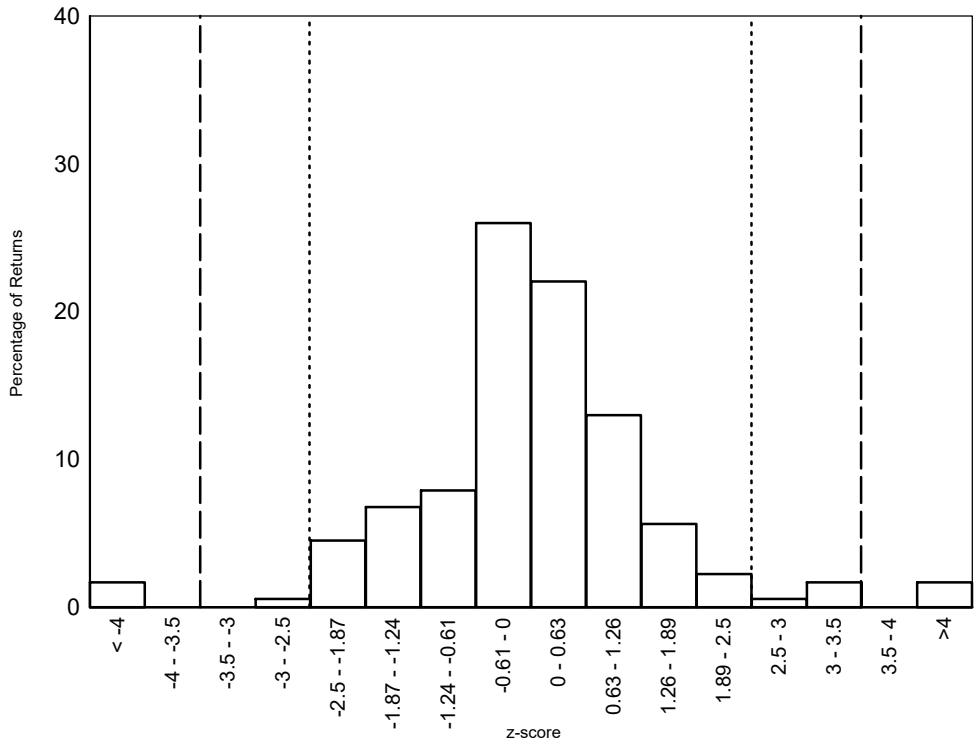


BCR::ABL1 Major Quantification Programme

Histograms of Participant z-scores

Log Change between samples - Unconverted *BCR*::*ABL1*/Reference Gene %

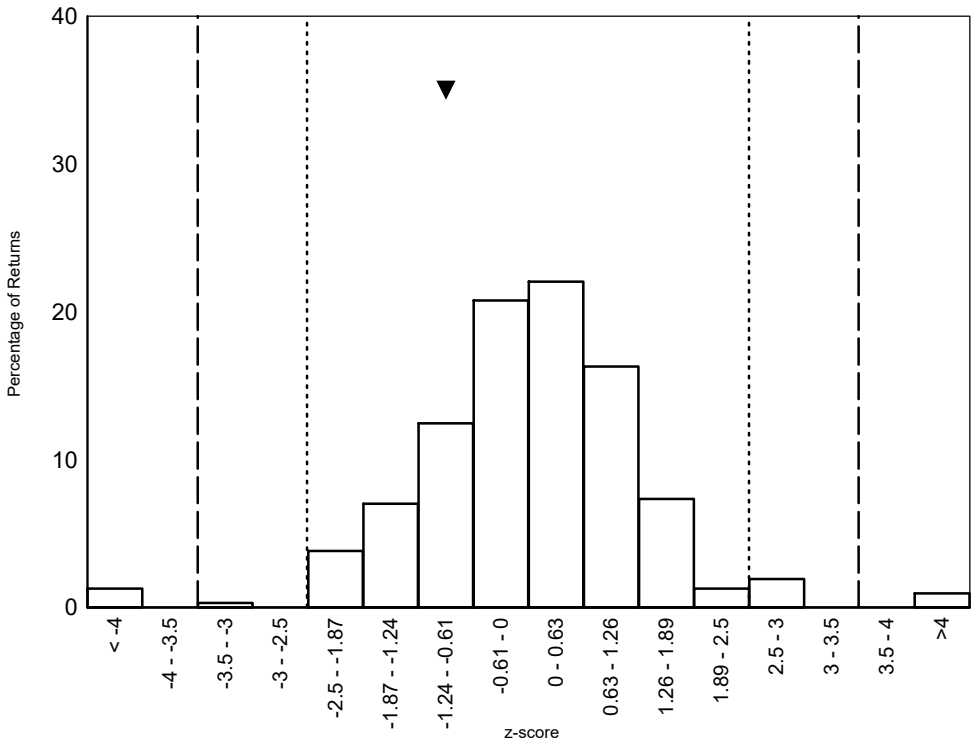
Please note ▼ denotes your result



Histograms of Participant z-scores

Log Change between samples - IS *BCR*::*ABL1*/Reference Gene %

Please note ▼ denotes your result

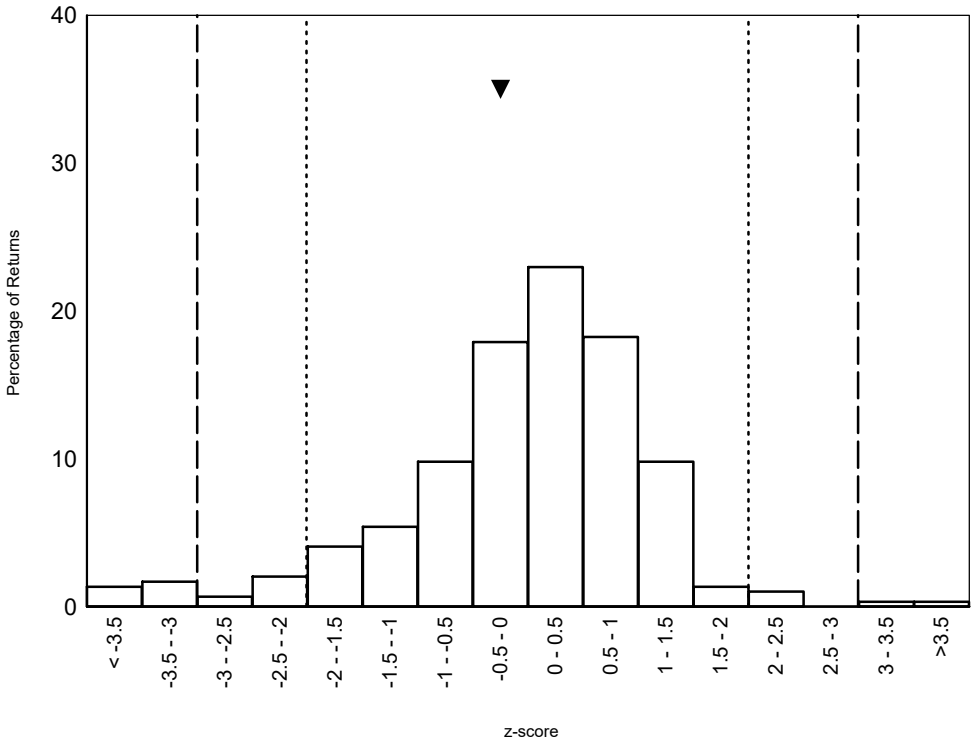


BCR::ABL1 Major Quantification Programme

Histograms of Participant z-scores

BCRQ 197 Single Sample % *BCR*::*ABL1*[IS] z-score

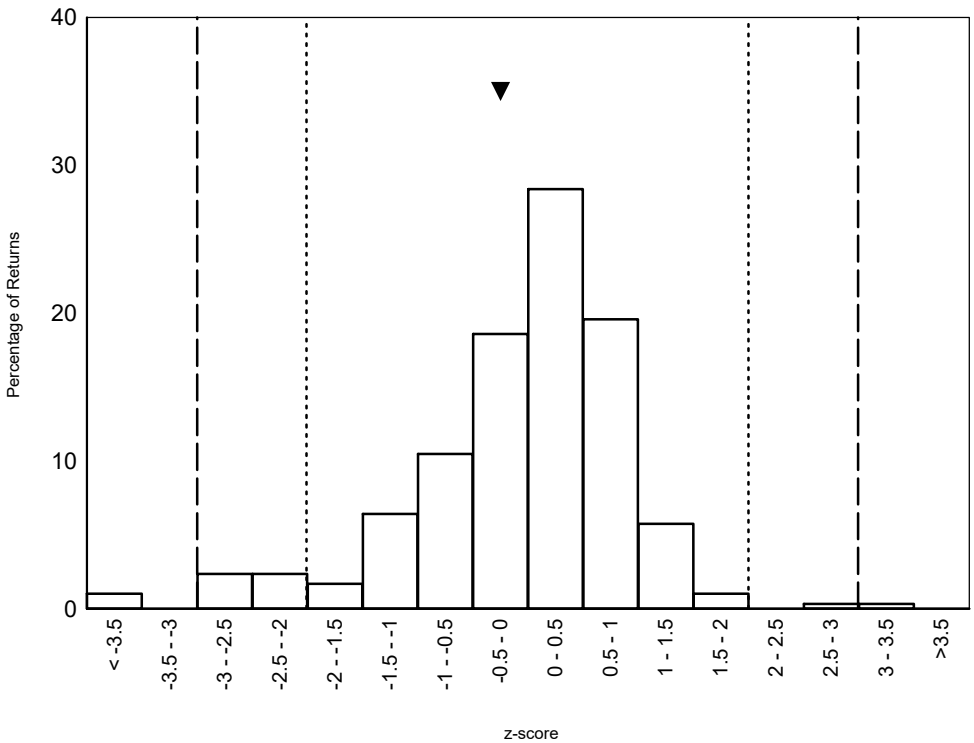
Please note ▼ denotes your result



Histograms of Participant z-scores

BCRQ 198 Single Sample % *BCR*::*ABL1*[IS] z-score

Please note ▼ denotes your result

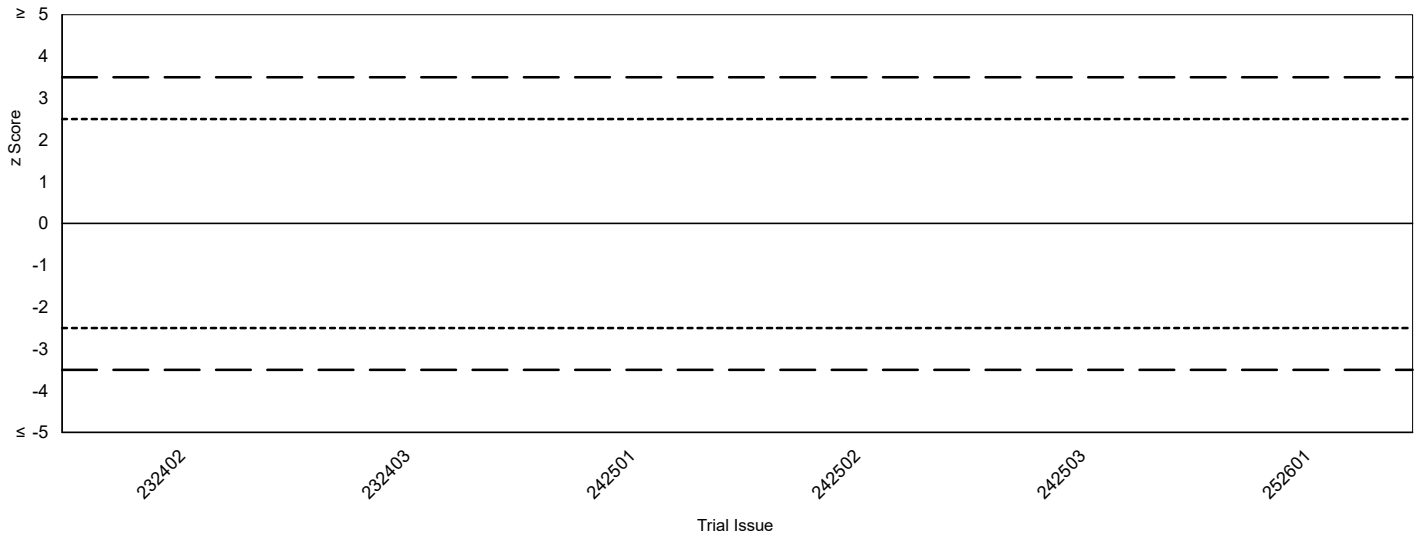


BCR::ABL1 Major Quantification Programme

Shewhart Control Charts

(Please note each data point represents a single trial)

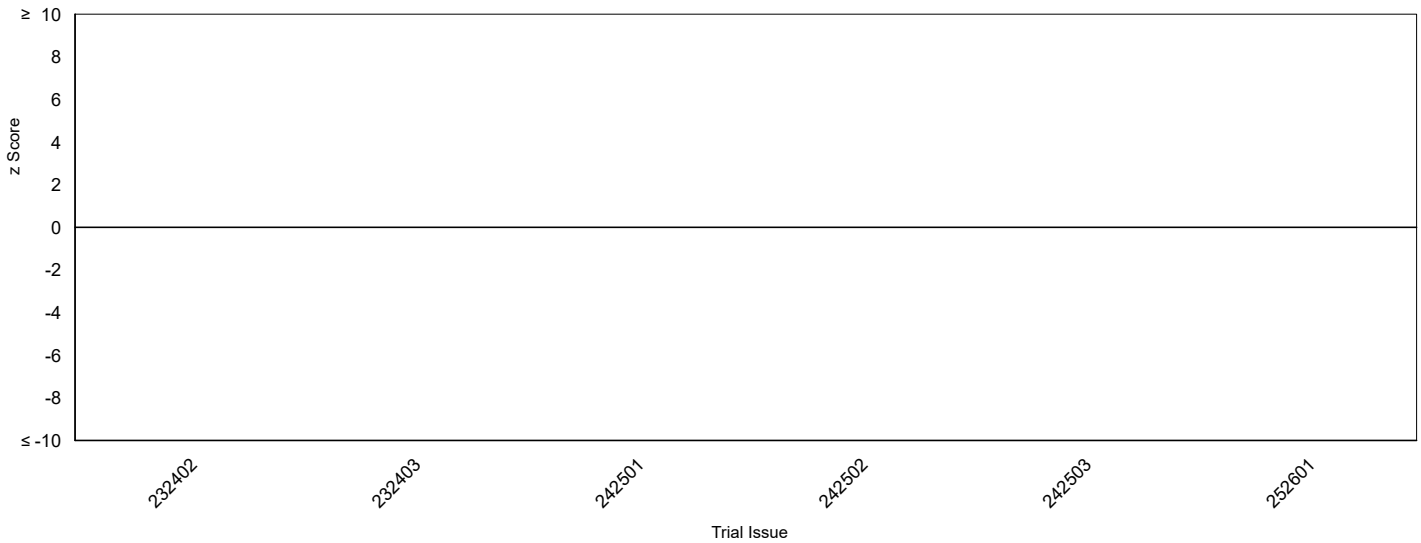
Log Change between samples Unconverted *BCR*::*ABL1*/Reference Gene %



Cusum Control Charts

(Please note each data point represents the sum of the z scores of the current trial and the two previous trials)

Log Change between samples Unconverted *BCR*::*ABL1*/Reference Gene %

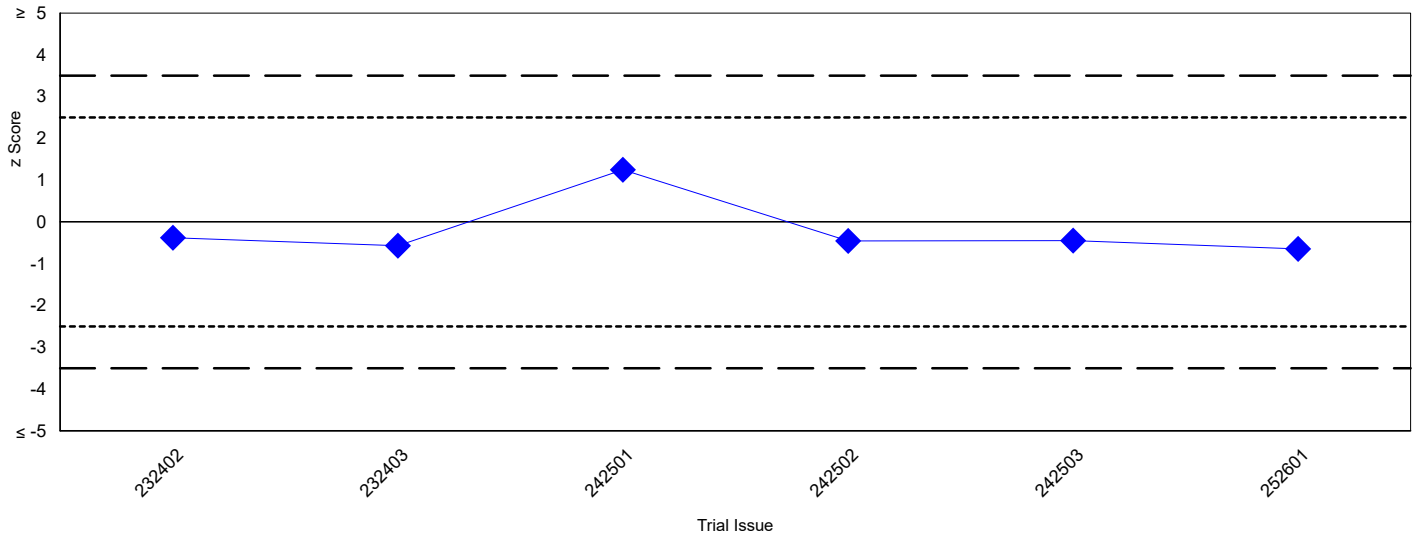


BCR::ABL1 Major Quantification Programme

Shewhart Control Charts

(Please note each data point represents a single trial)

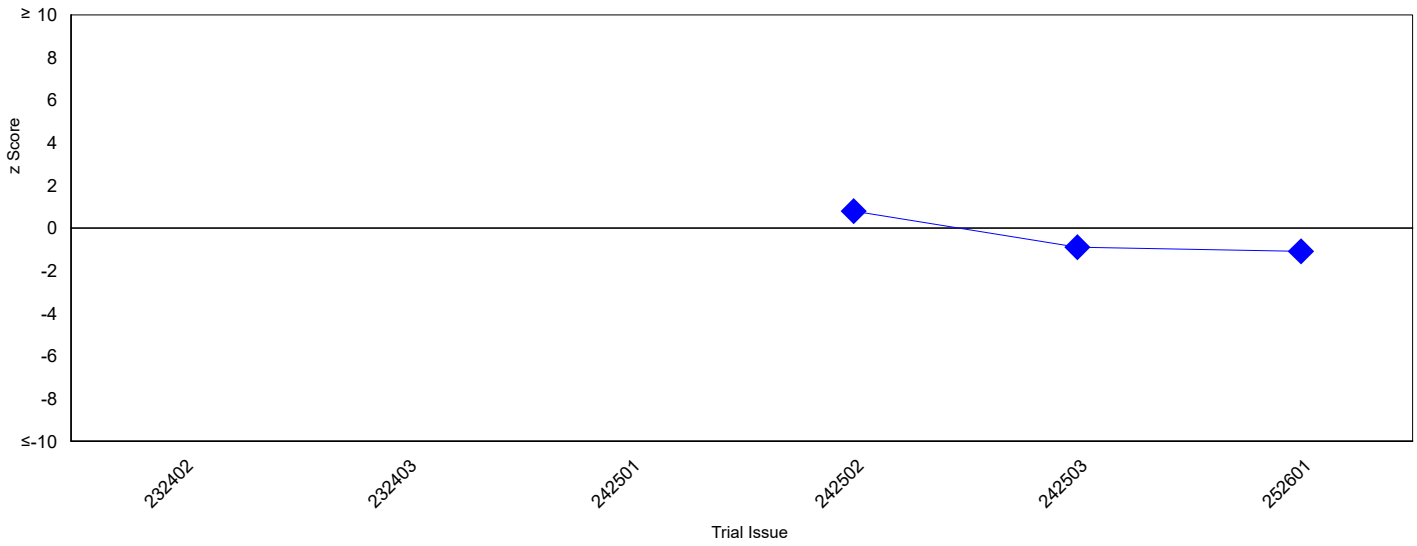
Log Reduction between samples IS *BCR*::*ABL1*/Reference Gene %



Cusum Control Charts

(Please note each data point represents the sum of the z scores of the current trial and the two previous trials)

Log Reduction between samples IS *BCR*::*ABL1*/Reference Gene %

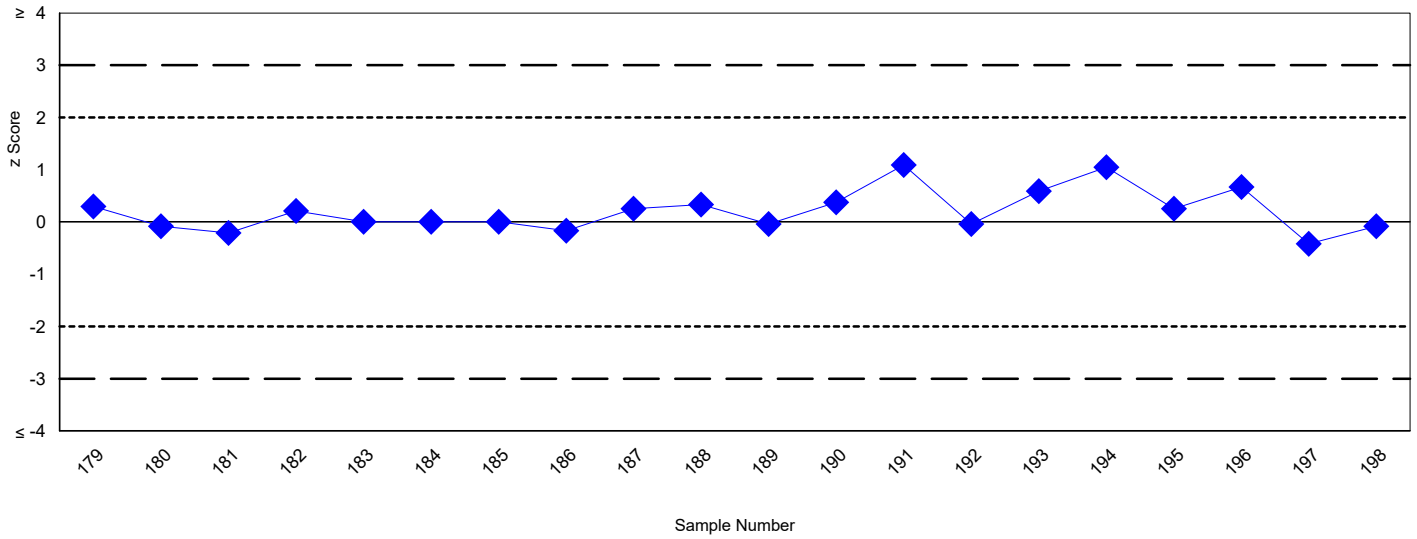


BCR::ABL1 Major Quantification Programme

Shewhart Control Charts

(Please note each data point represents a single sample)

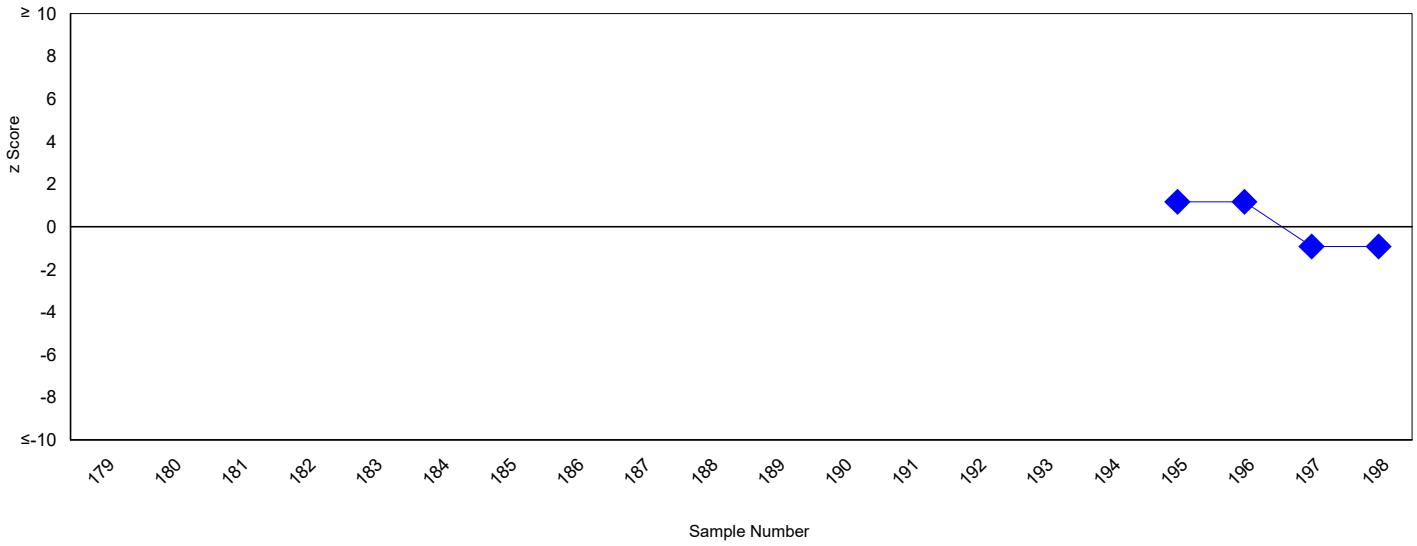
Single Sample % *BCR::ABL1*^{IS}



Cusum Control Charts

(Please note each data point represents the sum of the z scores of the current sample and the two previous samples)

Single Sample % *BCR::ABL1*^{IS}



BCR::ABL1 Major Quantification Programme

Please note, only methods/instruments used by ≥2 participants are included in the tables.

Instrument Data Summary

Method	Returns
Cepheid GeneXpert	131
Qiagen Rotorgene	31
Roche LC 480	26
ABI QuantStudio 5	24
ABI 7500	20
Biorad QX200 Droplet Digital PCR	17
Biorad CFX96	9
ABI QuantStudio 7	8
ABI 7500 FAST	6
ABI Step One Plus	5
Diatech Pharmacogenetics EasyPGX RT800-96	5
ABI 7300	4
Agilent AriaMX Real Time PCR System	4
ABI 7500 FastDx	4
Corbett Rotorgene	3
ABI Vii A7	3
ABI QuantStudio 6 Flex	3
Optolane LOAA Analyzer On-Point	3
ABI 7900HT	2
Roche LC 2.0	2
ELITechGroup ELITe InGenius	2

Standard Dilution Data Summary

Method	Returns
Not Applicable	119
ERM-AD623 Certified Reference Material	43
None	32
Ipsogen IS MMR standards	23
Ipsogen Fusion Quant standards	18
Ipsogen BCR-ABL1 Mbcr IS-MMR Kits single plasmid	18
Ipsogen plasmids	14
BCR-ABL P210 ELITe Standard	9
EasyPGX ready BCR-ABL p210	6
In-house standards	5
Bioclarma SensiQuant P210 Standards	5
BlackBio TRUPCR Standards	5
Ipsogen BCRABL1 Mbcr RGQ RTPCR Single Plasmid	4
Asuragen QuantideX BCRABL IS Kit calibrators	4
Molecular MD standards	3
Genmark geneMAP BC-ABL1 P210 IS MMR	3

BCR::ABL1 Major Quantification Programme

Kit/Method Data Summary

Method	Returns
Cepheid GeneXpert Ultra BCR-ABL assay	131
In-house protocol (EAC)	43
Qiagen (formerly Ipsogen) IS MMR Kit	31
In-house protocol	19
QIAGEN Ipsogen BCR-ABL1 Mbcr RGQ RT-PCR	13
Biorad CE-IVD QXDx BCR-ABL IS Kit	11
In-house (EAC-modified)	10
Qiagen (formerly Ipsogen) Fusion Quant Kit	10
BCR-ABL P210 ELITe MGB Kit (Elitech Group)	8
Diatech Pharmacogenetics Easy PGX p210	6
Bioclarma SensiQuant P210 Kit	5
Ipsogen kit	4
Other	4
3B BlackBio TRUPCR BCR-ABL Quantitative kit	4
REALQUALITY RQ-BCR-ABL p210 One-Step kit	4
Genmark geneMAP BCR-ABL1 p210 IS MMR Kit	3
Optolane Dr. PCR BCR-ABL1 Major IS Detection Kit	3
Asuragen QuantideX qPCR BCRABL IS Kit	2
Entrogen BCR-ABL P210 (Mbcr) One-Step Detection	2
Asuragen Quantidex qPCR BCR-ABL1 IS Kit	2

Reference Gene Data Summary

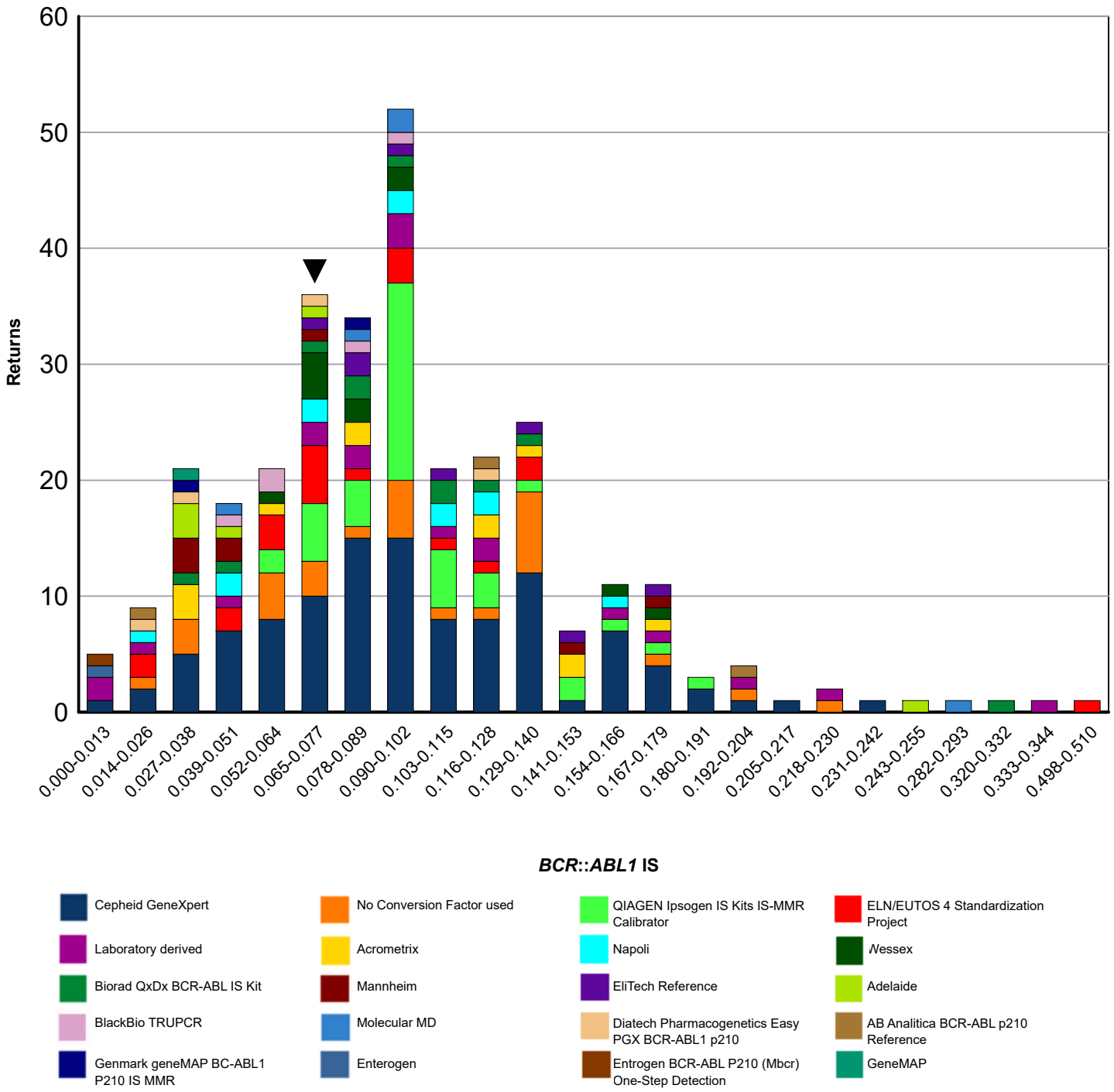
Method	Returns
ABL1	297
GUSB	16
BCR	3

Source of Conversion to the IS Data Summary

Method	Returns
Cepheid GeneXpert	109
QIAGEN Ipsogen IS Kits IS-MMR Calibrator	42
ELN/EUTOS 4 Standardization Project	21
Laboratory derived	20
Acrometrix	12
Biorad QxDx BCR-ABL IS Kit	11
Wessex	11
Napoli	11
Mannheim	8
EliTech Reference	7
Adelaide	6
BlackBio TRUPCR	5
Molecular MD	5
Diatech Pharmacogenetics Easy PGX BCR-ABL1 p210	4
AB Analitica BCR-ABL p210 Reference	3
Genmark geneMAP BC-ABL1 P210 IS MMR	2

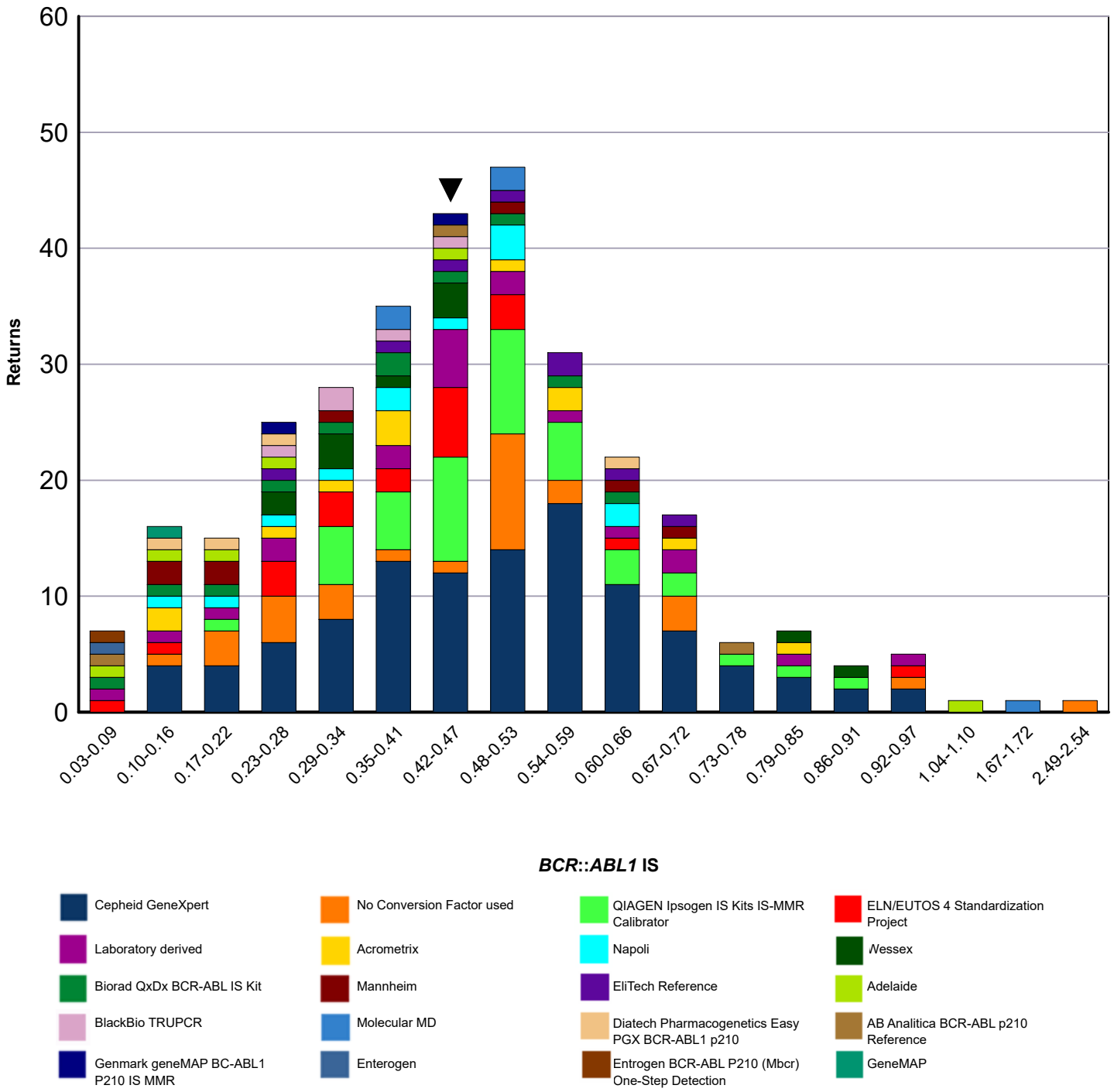
BCR::ABL1 Major Quantification Programme

Frequency distribution histogram showing participant *BCR*::*ABL1*/Reference gene results, classified by IS conversion method for sample 197



BCR::ABL1 Major Quantification Programme

Frequency distribution histogram showing participant *BCR*::*ABL1*/Reference gene results, classified by IS conversion method for sample 198



BCR::ABL1 Major Quantification Programme

Trial Comments

Performance monitoring for participants utilising *ABL1* as a reference gene and selecting to be assessed on the *BCR*::*ABL1*^{IS} is now based on single sample z-scores.

Please note, single sample scoring on the International Scale is only applicable to laboratories using *ABL1* as a reference gene as validation data has suggested that alternative control gene expression (e.g. *GUSB*, *BCR* and *B2M*) in the EQA material is significantly different compared to the WHO standards causing these laboratories to no longer be reporting on the IS. We will no longer be displaying single sample z-scores or performance classifications for non-*ABL1* users for this reason. **The programme does not have a sufficient number of alternative reference gene users to robustly score them as individual user groups on single sample results therefore non *ABL1* users will continue to be scored using log change.**

Since trial distribution 232402, we have removed the option for participants to select whether they are scored on either the unconverted or IS dataset. Following guidance from the UK NEQAS LI molecular specialist advisory group, all laboratories utilising *ABL1* as a reference gene and not submitting results on the International Scale will be an automatic critical result. Laboratories submitting data using a non-*ABL1* reference gene will continue to be performance monitored on the unconverted log change between the samples.

Laboratories performing *BCR*::*ABL1* quantification can express results on the International Scale (IS) using one of three approaches[1]. They may employ laboratory-specific conversion factors (CF) obtained through sample exchange with an established reference laboratory, derive the CF from secondary reagents calibrated to the 1st WHO International Genetic Reference Panel[2], or use validated diagnostic kits calibrated to the WHO panel.

If you have further questions, please contact admin@uknegasli.co.uk.

BCR::ABL1 Major Quantification Programme

IS single sample data

- The median *BCR*::*ABL*^{IS} for sample BCRQ 197 was 0.094%, with an IQR of 0.053%.
- For BCRQ 197, 11 participants incurred a critical trial score with a z-score of <-3.0 / >3.0. Of these, four utilised the Cepheid GeneXpert Ultra BCR-ABL assay, two used the Entrogen BCR-ABL P210 (Mbcr) One-Step Detection kit, two used the Bioclarma SensiQuant P210 kit, one the Qiagen (formerly Ipsogen) Fusion Quant kit, one a REALQUALITY RQ-BCR-ABL p210 One-Step kit and one the Diatech Pharmacogenetics Easy PGX p210 kit.
- The median *BCR*::*ABL*^{IS} for sample BCRQ 198 was 0.45%, with an IQR of 0.24%.
- Four participants incurred a critical trial score with a z-score of <-3.0 / >3.0, all of which also incurred a critical score for BCRQ 197 (two Entrogen BCR-ABL P210 (Mbcr) One-Step Detection users, one Cepheid GeneXpert Ultra BCR-ABL user and one REALQUALITY RQ-BCR-ABL p210 One-Step user.
- The robust mean IS log change between sample BCRQ 197 and BCRQ 198 was -0.68 with a robust SD of 0.14. This information is provided for interest only.
- One participant did not detect any *BCR*::*ABL1* transcript in sample BCRQ 197. This participant utilised *BCR* as the reference gene with an in-house protocol.

Unconverted log change data

- The robust mean unconverted log change between sample BCRQ 197 and BCRQ 198 was -0.67 with a robust SD of 0.12.
- Given the move away from performance monitoring participants utilising *ABL1* on unconverted log change data, out of consensus information will only be provided for non-*ABL1* participants.

ABL1 Data

- The unconverted median for participants using *ABL1* as a reference gene for sample BCRQ 197 was 0.11% *BCR*::*ABL1/ABL1,* with an IQR of 0.072%.
- The unconverted median for participants using *ABL1* as a reference gene for sample BCRQ 198 was 0.55% *BCR*::*ABL1/ABL1,* with an IQR of 0.34%.
- One hundred and sixty two out of 297 participants utilising *ABL1* as the sole reference gene for *BCR*::*ABL1* quantification returned reference gene information. Median *ABL1* reference gene levels were 143,900 and 144,179 for samples BCRQ 197 and BCRQ 198, respectively.
- For BCRQ 197, there were 10 (6.2%) participants and for BCRQ 198, 11 (6.8%) participants that reported *ABL1* levels <10,000. Amplification resulting in <10,000 *ABL1* molecules per sample is considered sub-optimal[3]. Please do not submit results from testing that has not met internal quality standards. Participants are reminded that repeat samples are available for all trials. To request repeat samples, please contact repeatsamples@uknegasli.co.uk

BCR::ABL1 Major Quantification Programme

GUSB Data

- Sixteen participants reported utilising *GUSB* as the sole reference gene for *BCR*::*ABL1* quantification.
- The unconverted median for participants using *GUSB* as a reference gene for sample BCRQ 197 was 0.033% *BCR*::*ABL1/GUSB,* with an IQR of 0.034%.
- The unconverted median for participants using *GUSB* as a reference gene for sample BCRQ 198 was 0.14% *BCR*::*ABL1/GUSB,* with an IQR of 0.11%.
- Median *GUSB* reference gene levels were 546,631 and 566,373 for samples BCRQ 197 and BCRQ 198, respectively.
- No participants utilising *GUSB* as the reference gene reported levels <24,000[4] for sample BCRQ 197 and 198.

Reference(s)

1. Cross, NCP. *et al*. European LeukemiaNet laboratory recommendations for the diagnosis and management of chronic myeloid leukemia. *Leukemia* **37**, 2150-2167 (2023).

2. White, HE. *et al.* Establishment of the first World Health Organization International Genetic Reference Panel for quantitation of BCR-ABL mRNA. *Blood* **116**, e111–117 (2010).

3. Foroni, L. *et al.* Guidelines for the measurement of BCR-ABL1 transcripts in chronic myeloid leukaemia. *Br J Haematol* **153**, 179–90 (2011).

4. Cross, NCP. *et al*. Laboratory recommendations for scoring deep molecular responses following treatment for chronic myeloid leukemia. *Leukemia* **29**, 999-1003 (2015).

BCR::ABL1 Major Quantification Programme

Information with respect to compliance with standards BS EN ISO/IEC 17043:2010

4.8.2 a) The proficiency testing provider for this programme is:
UK NEQAS for Leucocyte Immunophenotyping
Pegasus House, 4th Floor Suite
463A Glossop Road
Sheffield, S10 2QD
United Kingdom
Tel: +44 (0) 114 267 3600
e-mail: amanda.newbould@ukneqasli.co.uk

4.8.2 b) The coordinator(s) of UK NEQAS LI programmes: Mr Stuart Scott (acting Director).

4.8.2 c) Person(s) authorising this report: Mr Stuart Scott (acting Director) of UK NEQAS LI.

4.8.2 d) Administration and shipping for this programme is provided by EQA International Limited.

4.8.2 d) Pre issue and post closure testing of samples for this programme is externally provided, although the final decision about sample suitability lies with the EQA provider; no other activities in relation to this EQA exercise were externally provided.

4.8.2 d) Where externally provided products or services are used in the delivery of EQA, a competent supplier is used, the EQA provider is responsible for this work and participants are informed accordingly.

4.8.2 g) The UK NEQAS LI Privacy Policy can be found at the following link: https://sheffield-ukneqas.ipassportqms.com/document_download/NjRlNTgxYzctMTI4ZS00MTg4LWI2ZDMtZDdkYzJhMTFlZTg3. Participant details, their results and their performance data remain confidential unless we are required by law to share this information. Where required by law or authorised by contractual arrangements to release confidential information, UK NEQAS LI will notify those concerned of the information released, unless prohibited by law. For UK participants, the relevant National Quality Assessment Advisory Panel is informed when a UK participant is identified as having performance issues.

4.8.2 i) All EQA samples are prepared in accordance with strict Standard Operational Procedures by trained personnel proven to ensure homogeneity and stability. Where appropriate/possible EQA samples are tested prior to issue. Where the sample(s) issued is stabilised blood or platelets, pre and post stability testing will have proved sample suitability prior to issue.

4.8.2 l), n), o), r) & s) Please refer to the UK NEQAS LI website at www.ukneqasli.co.uk for detailed information on each programme including the scoring systems applied to assess performance (for BS EN ISO/IEC 17043:2010 accredited programmes only). Where a scoring system refers to the 'consensus result' this means the result reported by the majority of participants for that trial issue. Advice on the interpretation of statistical analyses and the criteria on which performance is measured is also given. Please note that where different methods/procedures are used by different groups of participants these may be displayed within your report, but the same scoring system is applied to all participants irrespective of method/procedure used.

4.8.2 m) We do not assign values against reference materials or calibrants.

4.8.2 q) Details of the programme designs as authorized by The Steering Committee and Specialist Advisory Group can be found on our website at www.ukneqasli.co.uk. The proposed trial issue schedule for each programme is also available.

4.8.2 t) If you would like to discuss the outcomes of this trial issue, please contact UK NEQAS LI using the contact details provided. Alternatively, if you are unhappy with your performance classification for this trial, please find the appeals procedure at www.ukneqasli.co.uk/contact-us/appeals-and-complaints/

4.8.4) The UK NEQAS LI Policy for the Use of Reports by Individuals and Organisations states that all EQA reports are subject to copyright, and, as such, permission must be sought from UK NEQAS LI for the use of any data and/or reports in any media prior to use. See associated policy on the UK NEQAS LI website: http://www.ukneqasli.co.uk/eqa-pt-programmes/new-participant-information/