UK NEQAS LI *BCR*::*ABL1* Minor Quantitation – Molecular Programme

Performance Scoring System

Aim

The scoring system is a rolling scheme that will identify unsatisfactory performance or persistent unsatisfactory performance of any participant. This is in order that UK NEQAS for Leucocyte Immunophenotyping (LI) can provide support and guidance where needed and ensure that the Genetics National Quality Assurance Advisory Panel (NQAAP) are informed as appropriate. Please note that each programme is scored independently.

Outline

Two samples are issued in each trial that may be positive or negative for the *BCR*::*ABL1* (minor) transcript. There are a maximum of 3 trials per annum.

The *BCR::ABL1* minor (e1a2, p190) fusion transcript is identified using molecular techniques and requires a quantitative response. Therefore, participants are asked, using their normal laboratory technique, to produce a % ratio *BCR::ABL1* minor/reference (control) gene result for each sample. It has not been possible to devise a scoring system to assess participants performance based on the % ratio *BCR::ABL1* minor/reference gene data returned for individual samples. This is due to participants using a multitude of unstandardised methodological approaches (including different reference genes) in the absence of an international scale (as used for the major *BCR*::*ABL1* fusion), each of which produce very different median values. Since a single scoring system which can be applied to all participants is required, the scoring system implemented is a quantitative approach based upon the $\log_{10}$ change of the % ratio *BCR::ABL1* (minor)/reference gene result calculated from the data returned by the participants for the two samples.

From the participant's submitted results for each sample a $\log_{10}$ change is calculated using the following formula:

$$log10\left(\frac{\text{normalised } BCR :: ABL1 \text{ (minor)} Ratio \text{ (\%) } Sample\ 2}{\text{normalised } BCR :: ABL1 \text{ (minor) } Ratio \text{ (\%) } Sample\ 1}\right)$$

The $\log_{10}$ change value is then used in conjunction with the robust mean and robust standard deviation to calculate a z score using the following formula:

$$z = (x - X)/\hat{\sigma}$$

where x is the result returned by the testing laboratory ($\log_{10}$ change), X is the assigned value (robust mean) and $\hat{\sigma}$ is the standard deviation for proficiency assessment (robust SD).

The robust mean and robust SD are derived from participant data using Algorithm A (ISO 5725-5) that ensures that all data is included in the generation of the robust mean and robust SD but also minimizes the effect of outliers upon the final values. The robust mean and SD are calculated to 2 decimal places (d.p.).

Interpretation of z-scores in the context of this programme is as follows:

- A result between 2.5 and -2.5 will be classed as satisfactory.
- A result between >2.5 and 3.5 or <-2.5 and -3.5 will be classed as an 'Action' result, which highlights a potential issue to the laboratory. Two 'Action' results in a period of 3 samples would result in classification as a 'Critical'.

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- A result >3.5 or <-3.5 is considered to be a 'Critical' result requiring immediate investigation by the laboratory.

Due to the nature of how z scores are generated a positive z score highlights a positive bias in a laboratory's results, whereas a negative z score shows a negative bias. As such, this adds value to the performance monitoring information provided to laboratories because the z score immediately highlights to the participating centre if their result is above or below the expected consensus value.

If a trial distribution features a *BCR*::*ABL1* minor negative sample it will not be possible to calculate a $\log_{10}$ change value for each participant. As such, participants will be scored qualitatively only for this exercise. If a participant falsely detects *BCR*::*ABL1* minor transcript in a *BCR*::*ABL1* minor negative sample or fails to detect *BCR*::*ABL1* minor transcript in a *BCR*::*ABL1* minor positive sample it is deemed a 'Critical' result.

Samples producing a median % ratio *BCR::ABL1*/*ABL1* <0.1% will be scored qualitatively.

Any laboratory who fails to return a result by the closing date will be classified as 'Critical' for the trial. Please note, results should not be submitted if samples fail internal quality control (QC) measures. Repeat samples are available for all trials, if required. If following repeat sample(s) processing, results obtained still do not pass local internal QC please contact UK NEQAS LI. If results are submitted based on the suboptimal extraction and/or assay they will be subjected to the same performance monitoring mechanisms as all other participants.

Unsatisfactory performance in this programme is defined as any occurrence of 'Critical' performance and this will be initially communicated to participants on their trial report. This will be followed with an email and notification on the participant hub on each occurrence of unsatisfactory performance and offering support and guidance. This may take the form of repeat/additional samples, communications by email, telephone conversations or face to face communications.

If a participant's status is elevated to persistent unsatisfactory performance (defined as a 'Critical' classification on 2 or more occasions within a 12-month period (3 trial issues (6 samples)) then a further email and hub notification will be issued, and the Genetics NQAAP informed (for UK participants only).

Participant's results will be reviewed by the lead scientist and the participant may, at the discretion of the Director and Specialist Advisory Group chairperson, be referred Genetics NQAAP even if they have not met the criteria for persistent unsatisfactory performance in any individual EQA.

As with all scoring systems it is important to note that the limits will be constantly reviewed to determine whether they are providing the information required. The Director of the programme retains the right to determine if an individual trial should not be scored.