UK NEQAS

Leucocyte Immunophenotyping

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Performance Monitoring System for Measurable Residual Disease for ALL by Flow Cytometry

Outline

The term measurable residual disease (MRD) refers to the small number of remaining leukaemia cells present in a patient after treatment. MRD detection is used clinically for a variety of reasons such as: ensuring patients are disease free, or to decide upon treatment regimes. MRD detection can be performed using a variety of different techniques however this programme is only intended for laboratories performing MRD detection by flow cytometry.

Sample Frequency

Three samples are issued at each trial (send out) (minimum 3 times and maximum 4 times per annum). The samples consist of one presentation sample and 2 follow up samples. Participants are required to return the percentage MRD population in each of the follow up samples.

Scoring System Description

The scoring system is based upon the use of z scores as described in ISO 13528. This involves the calculation of a robust mean and robust standard deviation from the returned results. Then using these values and the individual results returned a z score can be calculated for each participant.

Scoring System Operation

Three samples are issued each trial, one presentation sample and two follow up samples. A participant's submitted result for each follow up sample is then used in conjunction with the robust mean and robust standard deviation to calculate a z score using the following formula:

$z = (x-X)/\sigma$

where x is the result returned by the testing laboratory, X is the assigned value (robust mean) and σ 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.

Interpretation of z-scores is as follows:

- A result between 2.5 and -2.5 would be classed as satisfactory
- A result between >2.5 and 3.5 or <-2.5 and -3.5 is seen as an 'Action' result, that highlights a potential issue to the laboratory. Two 'Action' results in a period of 3 samples would result in classification as a 'Critical'
- A result above 3.5 or below -3.5 is 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. In addition to the z-score all methodological data featured on reports will be in the format of robust mean and robust SD. This will give participants the option to use the extra provided data to calculate additional "in-house" z-scores based on machine types, methodologies etc and allow them to monitor if there are any "in-house" technical biases. **However, it is important to stress that the z-score issued by UK NEQAS for Leucocyte Immunophenotyping based on all methods will remain the only parameter that is used for performance monitoring.**

Please note UK NEQAS LI uses z score limits of 2.5 and 3.5 for performance monitoring to ensure that the proportion of laboratories identified as outside of the expected range of results is in line with that expected by ISO 13528. This approach has been validated by in-house analysis of historical results and approved by an independent scientific advisory committee. These limits are continually monitored as part of routine programme operation.

Any laboratory who fails to return a result by the closing date will be regarded as an action for each sample. As such any laboratories that do not return results for both samples within a trial will be classified as critical.

Unsatisfactory performance 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. The support and guidance offered will be tailored to the needs of the participant but may include the provision of repeat/additional samples plus telephone, email or face-to-face communications.

If a participant's status is elevated to persistent unsatisfactory performance (defined as a critical classification on 3 or more occasions within a 12 month period) then a further letter will be issued and the Haematology National Quality Assurance Advisory Panel informed (for UK participants only).

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