Performance Monitoring System for Immune Monitoring Programme

Outline

The enumeration of lymphocyte subsets is important in a variety of conditions such as primary immunodeficiency (e.g. Severe Combined Immunodeficiency/SCID) or the monitoring of drug therapies such as Rituximab in autoimmune disorders. However, the most common use is in the monitoring Human Immunodeficiency Virus/HIV, a secondary immunodeficiency disorder. To ensure that the programme meets the requirements of all users the programme issues stabilised whole blood with laboratories required to determine the lymphocyte subsets (CD3+, CD3+/CD4+, CD3+/CD8+, CD19+ and CD16+/56+). Laboratories are requested to report both percentage and absolute values (in cells per microlitre), and performance scores are generated using this data.

Sample Frequency

Two samples are issued at each trial (send out) bimonthly (minimum 4 times and maximum 6 times per annum).

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 from participants using a single platform approach (the predicate method). Then using these values and the individual results returned a z score can be calculated for each participant. Please note that z scores are generated for both absolute and percentage values and both are used for performance monitoring as they are both used in clinical practice.

Please note - Non-flow cytometric systems and those that include electronic volume measurement to identify cells will be scored as separate cohorts to allow for the performance monitoring of these systems.

Scoring System Operation

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

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

where x is the result returned by the testing laboratory, 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.

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 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. 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.**

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 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 up with a letter on each occurrence of unsatisfactory performance highlighting that performance on the last sample(s) was out of consensus and offering support and guidance to assist in returning to satisfactory performance. 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 3 or more occasions within a 12 month period) then a further letter will be issued and the Immunology 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.