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IMMUNOLOGY

Proficiency testing in immunopathology: establishing the homogeneity of test material

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Summary

Aims: To develop a technique for homogeneity testing of serum aliquot samples suitable for use in the Quality Assurance Program in Clinical Immunology (QAP Pty Ltd).

Methods: Albumin was selected as the surrogate protein marker for the product to be tested and the coefficient of dispersion (COD) calculated as the measure of homogeneity. To detect changes in the average level of homogeneity, cumulative sum control (cusum) charts were used.

Results: The COD(%) for each triplicate reading of albumin obtained from 34 specimens was normally distributed with a mean of 0.49% and a standard deviation of 0.25%. In industrial quality control schemes the action line is generally set at the upper 99% confidence limits, hence any triplicate sample would be considered to have acceptable homogeneity if the COD was $\leq$1.08%. Cusum charts were created to monitor albumin homogeneity over time.

Conclusions: The use of albumin measurement as the surrogate appears statistically suitable for homogeneity testing in QAP programs for immunodiagnostic testing. CUSUM charts are particularly useful to monitor such homogeneity testing.

Key words: Quality assurance program, albumin, homogeneity testing, coefficient of dispersion, CUSUM charts.

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INTRODUCTION

Pathology laboratories have the prime function of generating test results used for critical decision making in disease diagnosis and patient management. Quality assurance is that process which measures the validity and precision of those tests generated in the laboratory. One of the most important aspects in assessing performance is the participation of laboratories in an external proficiency testing scheme (EPTS). Quality Assurance Programs Pty Ltd is a company formed under the auspices of the Royal College of Pathologists of Australasia (RCPA) to provide such schemes, and currently operates these in all pathology subdisciplines including clinical immunology.

The Immunology Quality Assurance Program (QAP) is an EPTS based at Flinders Medical Centre in Adelaide, South Australia, that distributes serum or plasma specimens to all laboratories enrolled in the scheme. Laboratories are asked to perform prescribed tests and return their results to the organisers. Results are analysed by the organisers who then compare them with a target result that is either pre-designated or may be derived from the returned data. Allowable limits around this target or acceptable result variants are also determined and reports are issued to the participating laboratories. In particular, comments are provided on their performance compared with all other laboratories and with peer groups using similar methodology. Regulatory health authorities and QAP organisers are in the process of defining limits that indicate poor and acceptable performance for assays, and laboratories showing consistently poor performance will in the future possibly come under challenge from these regulatory bodies. As EPTS programs are used in this way it is essential that they are accredited by the National Association of Testing Authorities Australia (NATA).

It is a requirement for accreditation of external proficiency testing providers that the test material they supply is 'appropriately' homogeneous for the purposes of the scheme. That is, the test material should not be a disproportionate source of variation in the final test result. To eliminate heterogeneity of material sent to participants as a cause of result discrepancy (and thus possible perceived poor performance), it is vital that each aliquot received by each participant is essentially identical in composition. The QAP must be able to ensure the homogeneity of the material it distributes for testing, as far as is practicably possible. An important aspect of this is to strictly control all processing and dispensing of the material to minimise any opportunity for homogeneity to be compromised. This includes such measures as mixing well throughout the processing, and maintaining traceability through all stages of production. However, it is of equal importance that any heterogeneity inherently present or unavoidably introduced through the processing is detected by developing a protocol for testing the finished product (in the format presented to participants). In this way rules can be established that are used to define and designate materials as 'homogeneous' or 'non-homogeneous' and the rationale and statistics used will provide more tangible information in support of the validity of a material's homogeneity if challenged.

The nature of some of the immunological analytes and the limited volumes of material from which individual aliquots are prepared, renders the use of conventional established homogeneity testing protocols impossible,

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resulting in the need to develop a novel approach to the problem. With this background in mind we report our experiences in developing a statistical approach to ensure that heterogeneity in test material will be detected.

Definitions

Specimen A stock of material designated as a single challenge within the Program.

Aliquot A small sub-unit of specimen dispensed and distributed to participants for testing.

Batch Group of one or more specimens dispensed into aliquots by a single operator in a single session of dispensing.

Sample An aliquot selected at random for homogeneity testing.

Existing recommendations for homogeneity testing

Recommendations for the statistical testing of the homogeneity of samples are provided in the analysis of *The International Harmonized Protocol for the Proficiency*

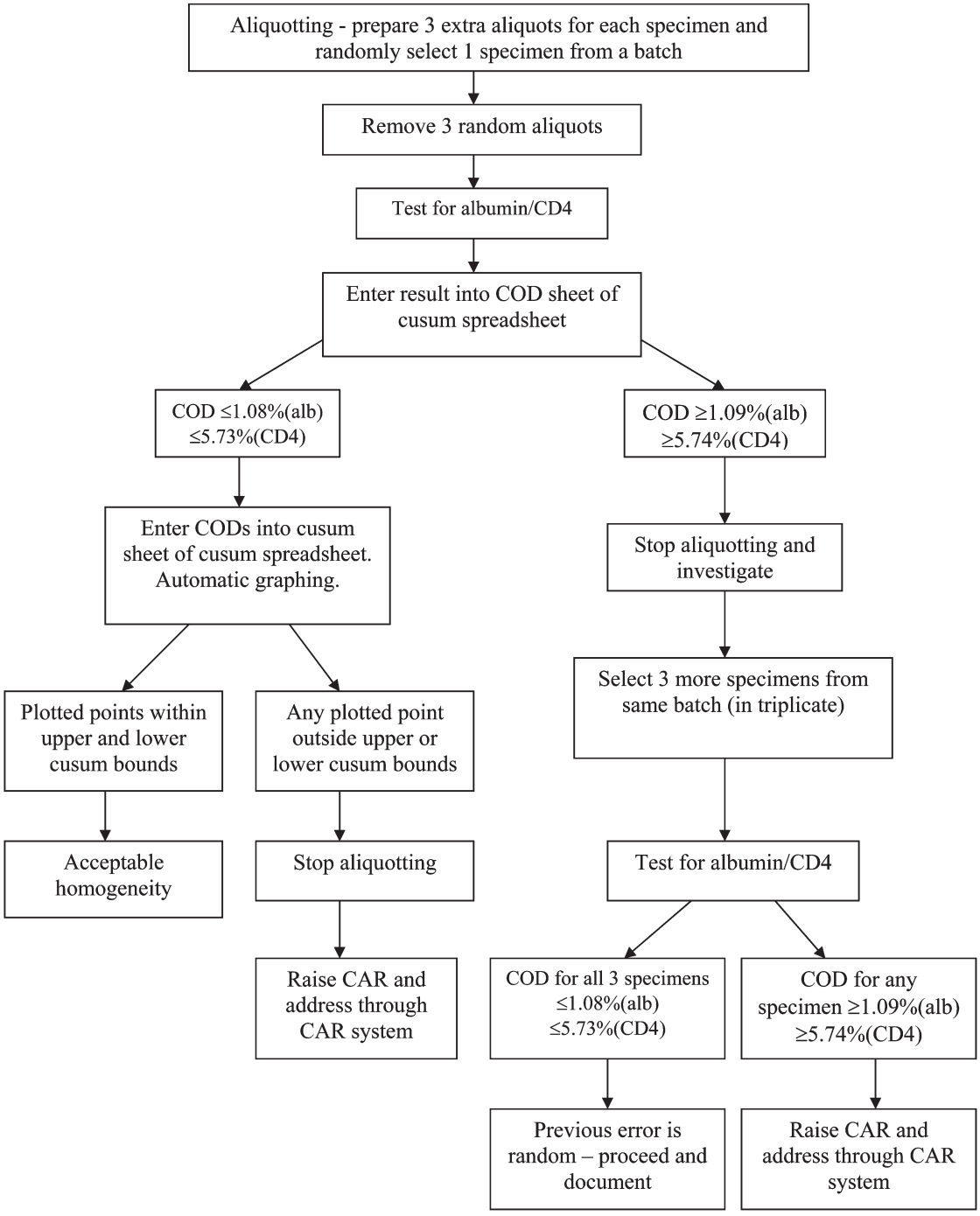

Fig. 1 Homogeneity testing flowchart. COD, coefficient of dispersion; CAR, corrective action response.