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Development of an External Quality Assessment Programme for POCT D-dimer

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Introduction

D-dimer is a fibrin degradation product which is used to determine whether clot formation has occurred as in DVT, PE, or to monitor the progress and treatment of DIC and other thrombotic conditions. A number of Point of Care (POCT) devices are now being used to measure D-dimer to guide immediate patient management.

External Quality Assessment (EQA) is an essential part of providing quality laboratory diagnostic services, and participation in EQA is a requirement for laboratory accreditation to ISO 15189 and for POCT accreditation to ISO 22870.

The aim of this study was to develop an EQA programme for POCT D-dimer users including validation of suitable material for its stability and commutability, and to establish performance specifications.

Method

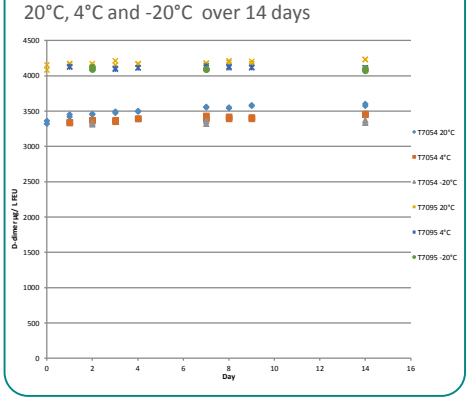
Frozen serum collected from 2 individual donors was thawed, filtered aseptically and aliquoted into 1ml tubes for stability assessment at 20°C, 4°C and -20°C. Samples were stored for specific time periods at the three temperatures and frozen at -70°C prior to analysis. All the samples were analysed in one run using the Roche Cobas 6000 D-dimer method. Further donations were collected, aliquoted and stored at -70°C for homogeneity studies.

Fifteen sites in the UK were recruited to take part in the study. Each site was provided with 3 samples covering a concentration range of 300 – 5000 ng/mL every 2 months. Participants could report both quantitative and qualitative results.

Results - Stability

Sample T7905 showed no significant change in D-dimer concentration when stored at 20°C, 4°C and -20°C for 14 days. Sample T7054 showed no significant change at 4°C or -20°C for 14 days but did show an increase of 7% by day 7 when stored at 20°C. The samples are therefore adequately stable for shipment to users and at the recommended storage temperature of 4°C.

Figure 1 D-dimer stability of 2 samples stored at 20°C, 4°C and -20°C over 14 days



Results - Long Term Stability

Long Term stability will be assessed using overall mean data from EQA results, however, early data suggests no significant change in mean concentration after 3 months.

Results - Homogeneity

Homogeneity data showed excellent between vial reproducibility with a coefficient of variation (CV) of 1.1% observed at a concentration of 497 µg/L FEU, 4.7% at 169 µg/L FEU, and <1% at concentrations above 1000 µg/L FEU.

Table 1 Homogeneity Data

D-dimer Mean (µg/L FEU)	SD (µg/L FEU)	CV(%)	n
169	8.0	4.7	10
497	5.7	1.1	10
1416	8.2	0.6	10
2324	9.9	0.4	10

Results – EQA Programme

Data for the first 5 distributions has highlighted methodological bias with the 3 most commonly used POCT devices on the programme (the Radiometer AQT90, the Roche Cobas h232 and the Siemens Stratus). Table 2 shows the overall mean, SD and CV for 3 pools with overall mean concentrations above and below the common cut-offs.

Table 2 Overall Mean, SD and CV for 3 pools distributed on the EQA programme

	Overall Mean (µg/L FEU)	Overall SD (µg/L FEU)	CV (%)	n
Pool 24	326.1	86.6	26.6	26
Pool 25	583.0	138.7	23.8	27
Pool 11	1085	378	34.8	24

The wide variation seen with the overall mean for all pools is due to the large between method bias. Tables 3-5 shows the method mean, SD and CV for 3 most commonly used POCT devices on the programme. The within method variation is much lower than the overall (between method) variation at all concentrations.

Table 3 Method Mean, SD and CV for pool 24

Method	Method Mean (µg/L FEU)	Method SD (µg/L FEU)	CV (%)	n
AQT90	262.7	30.4	11.6	10
Cobas h232	346.3	44.8	12.9	10
Siemens Stratus	452.3	12.5	2.8	4

Table 4 – Method Mean, SD and CV for pool 25

Method	Method Mean (µg/L FEU)	Method SD (µg/L FEU)	CV (%)	n
AQT90	489.9	36.7	7.5	11
Cobas h232	641.5	42.6	6.6	10
Siemens Stratus	774.3	16.2	2.1	4

Table 5 – Method Mean, SD and CV for pool 11

Method	Method Mean (µg/L FEU)	Method SD (µg/L FEU)	CV (%)	n
AQT90	824	76	9.2	11
Cobas h232	1353	157	11.6	10
Siemens Stratus	1508	11	0.7	4

For pool 24 (overall mean 326.1 µg/L FEU) all users of the Radiometer AQT90, the Roche Cobas h232 and the Siemens Stratus reported negative results (n = 12) for qualitative D-dimer.

For pool 11 (overall mean 1085 µg/L FEU) all users of the Radiometer AQT90, the Roche Cobas h232 and the Siemens Stratus reported positive results (n = 12) for qualitative D-dimer.

For pool 25 (overall mean 583.0 µg/L FEU) for the Radiometer AQT90 there was 1 positive result and 3 negative, for the Roche Cobas h232 there were 3 positive results and 1 negative result, and for the Siemens Stratus there were 2 positive results and no negative results for qualitative D-dimer.

Table 6 - Qualitative Results

Method	Pool 24 %Positive	Pool 25 %Positive	Pool 11 %Positive
AQT90	0	25	100
Cobas h232	0	75	100
Siemens Stratus	0	100	100

Conclusion

The material developed was found to be suitable for use as an EQA material showing good stability and excellent vial to vial reproducibility.

An EQA programme has been successfully established for POCT D-dimer for both quantitative and qualitative POCT D-dimer results.

Samples are distributed at concentrations above and below common cut-offs to provide post analytical assessment of user interpretation.

Additional samples will be distributed over the coming months to provide further evidence as to the "state of the art" of the POCT D-dimer methods used in the UK. This data will be used to establish performance criteria for the EQA programme.