

# UK NEQAS (Blood Coagulation) Performance Analysis

The purpose of the scheme is to identify centres obtaining results different to their “peer group”, and to offer help in identifying the cause of these differences.

## 1. Assignment of target values.

Measurement of haemostatic analytes is a process subject to a large number of variables, particularly for screening tests. Therefore, it is extremely difficult to assign “target values” for any analyte or test. Analysis of samples in the NEQAS laboratory prior to dispatch will give only an approximate indication of expected results. Target values to assess performance are therefore assigned by a consensus of participating centre results. To avoid undue influence of outlying results, whilst avoiding the exclusion or truncation of any participants’ results, the median value is used to define the central or target value. For “screening tests” PT/INR, PTD, APTT, HDA and TT several studies have identified significant differences in results obtained by different reagents. Therefore, median values are determined both for all returned results (overall median) and for specific reagent groups (reagent median). For the Quick’s PT/INR, only those centres calculating a locally derived mnpt are used to determine the median INR.

## 2. Performance Analysis

### 2.1 Registration

Registration for specific tests is requested, participation being recommended for all tests laboratories offer as a service. Registration may be amended at any time on survey forms or by written notification to the Scheme. Where tests are carried out for which participants have not previously registered, it will be assumed that registration is required in future surveys.

#### 2.1.1 Non>Returns

A failure to return a results for a registered test will lead to a non-return designation for that test. Unless a valid reason is given for the failure to return, this will count towards cumulative performance analysis.

### 2.2 Performance Analysis for Screening Tests

For PT/INR, PTD, and APTT, the percentage deviation of each individual laboratory’s results from the reagent and overall medians are calculated, and the following criteria for performance are applied:

Performance is considered “*within consensus*” if the deviation is <15% from:

the **reagent median** if the number of users of that reagent is equal to or greater than 10 or

the **overall median** if the number of users of the reagent is less than 10.

Results >15% deviation from the median are considered “*outwith consensus*”. If results are outwith consensus on three consecutive occasions (including failure to return results), the scheme director sends a letter of concern to the head of department.

For thrombin times, the same performance criteria apply, but due to the greater imprecision between results, the target range is +/- 20% from the median.

For Heparin Dosage Assessment (HDA), modified criteria apply. . For HDA, assay precision is poor, and approximately 20-25% of centres would be outwith consensus if 15% deviation from the median was used to define outwith consensus grading. In addition, marked differences in the heparin sensitivity of APTT reagents have led to the conclusion that it is inappropriate to assess minority reagent users against the overall median. Therefore the criteria applied for HDA are:

Results >20% deviation from reagent medians for majority groups are considered *outwith consensus*.

No performance analysis is applied to minority groups, although their % deviation from reagent and overall medians is recorded on individual reports.

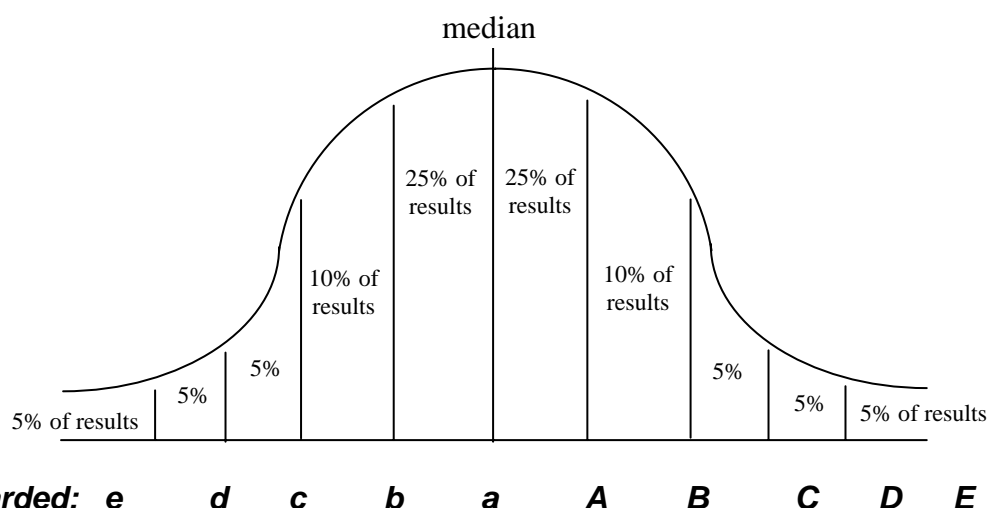
For Fibrinogen estimations, results performed by the Clauss method are assessed against the overall median, as above. Users of the Dade-Behring Multifibrin U method are assessed as a separate group, on the basis that this method differs from the traditional Clauss fibrinogen method.

### 2.3 Performance Analysis for Assays

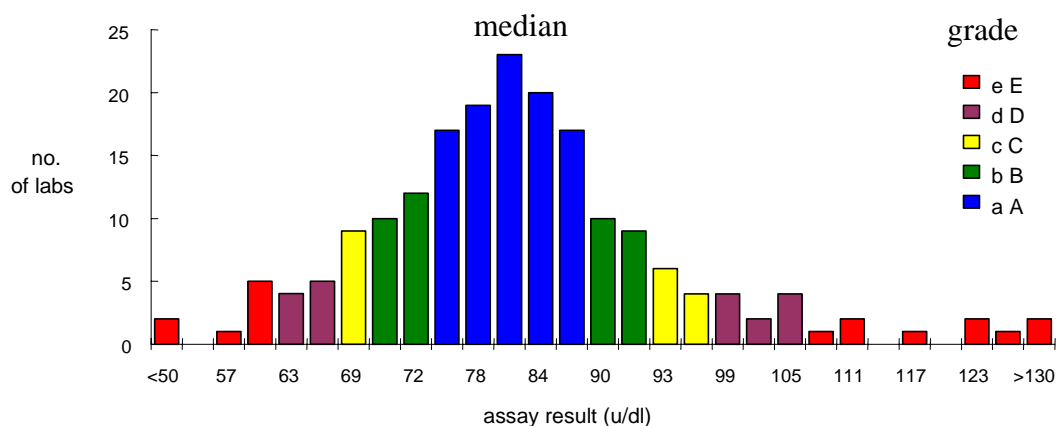
For all other assays the variable nature of the concentration of each analyte means that the % deviation from the median cannot be used as a means of defining performance. A ranked grading analysis to evaluate performance was devised by Professor S Thomson, (Director of the MRC Biostatistics Unit, Cambridge UK, and honorary professor of biostatistics at the University of Cambridge).

For this system, the overall consensus median is taken as the central reference point or “target value”. Individual results are divided into 5 groups above and 5 groups below the median. Grades between “A” and “E” are then assigned as shown overleaf. Using this scoring system, if 100 laboratories performed a factor VIII:C assay, the 50 laboratories reporting results closest to the median would receive an “A” grade, 20 laboratories would receive a “B” grade, and 10 laboratories each would receive a “C” OR “D” grade. The 10 laboratories with results furthest from the median receive an “E” grade. Grades below the median are shown in lower case, and above the median in upper case, to aid in assessment of bias.

**A-E grading system for a distribution of results:**



An example of this distribution for a factor VIII:C assay is given below:



Where a result falls on a dividing limit between groups, it is assigned to the 'higher' category.

Performance designation (*"within"* or *"outwith"* consensus) is based on grades obtained in two consecutive exercises for any particular test. **Performance "outwith consensus"** is defined as any of the following combination of grades: **DD, CE, EC, DE, ED, and EE**. The overall probability of obtaining any such combinations of grades by chance alone is 0.06 (ie. 6%).

**Persistent "outwith consensus" performance** is defined as two consecutive **"outwith consensus"** performances, where the sequence of grades does not alter

the grade classification. The sequences of three grades which provoke this designation are therefore:

<b>DDD</b>	<b>DED</b>	<b>ECE</b>	<b>EEC</b>	<b>DDE</b>	<b>DEE</b>
<b>EDD</b>	<b>EED</b>	<b>CEE</b>	<b>EDE</b>	<b>EEE</b>	

The overall probability of obtaining any such combinations of grades by chance alone is 0.011 (ie 1.1%).

**A non-return** for a registered test will be graded as “F” and taken as equivalent to an E grading. Thus, designations which include 'F' grades are based on performance over 2 or 3 exercises, respectively.

In some cases, significant differences have been noted between different methodologies. Where this occurs on a consistent basis, separate analysis of the groups is carried out, using medians specific to each method group. However, the system is only effective if the number of participants is greater than 20 - consequently, grading analysis is not applied to groups of results from fewer than 20 centres.

At present, the following groups are considered:

- D-Dimers – by different kit sources
- FVIII:C (1-stage, 2-stage & chromogenic assays)
- AT antigen (results expressed in u/dl and mg/dl)
- AT activity – by substrate source (human thrombin/ bovine thrombin/ Xa)
- Protein C activity (clotting and chromogenic assays)
- APCr – by different kit source and units for reporting
- VWF:RCo/Activity – ELISA, non ELISA, Turbidometric

These groupings are regularly reviewed.

Protein S activity is currently not assessed, on recommendation of the Steering Committee.

A further set of analytes are not at present incorporated into formal grading analysis. These include:

- Lupus assays: interpretive
- FVIII:C inhibitors: non-obligatory participation for HCV+ve samples
- FXIII:C: interpretive