European Concerted Action on Anticoagulation. Quality Assessment of the CoaguChek Mini and TAS PT-NC Point-of-Care Whole-Blood Prothrombin Time Monitors

Leon Poller,†* Michelle Keown,† Nikhil Chauhan,† Anton M.H.P. van den Besselaar,‡ Armando Tripodi,§ Caroline Shiach,∥ and Jorgen Jespersen∥

Background: International Normalized Ratios (INRs) for prothrombin time obtained with the CoaguChek Mini and TAS (RapidPointCoag) PT-NC systems are markedly different and also differ from the “true” INR. There is therefore a need for local quality assessment (QA) of the two systems.

Methods: A set of 60 lyophilized artificially depleted and 60 lyophilized coumarin plasmas were tested at 10 centers on both point-of-care testing monitors. Subsets of three and five plasmas were selected as QA plasmas and compared with the remaining 55 to assess the relative ability of the systems to characterize performance at the individual centers. The incidence of aberrant results (outliers; >15% deviation from the true INR) was also recorded. The expected incidence with the QA plasmas was calculated and compared.

Results: On both systems, INR with the common sets of 55 lyophilized plasmas varied considerably between centers. With the TAS PT-NC, subsets of five and three European Concerted Action on Anticoagulation (ECAA) artificially depleted plasmas gave good correlation with the 55 plasmas, but the coumarin plasmas performed less well. With the CoaguChek Mini, correlation was good with sets of five artificially depleted QA plasmas and reasonable with three but was less satisfactory with the coumarin plasmas. Outliers were detected with both types of plasmas on both test systems but with variable success.

Conclusions: With the TAS PT-NC, three ECAA artificially depleted lyophilized plasmas provided reliable QA, but five lyophilized coumarin plasmas were required. With the CoaguChek Mini, five artificially depleted plasmas gave reliable QA but coumarin plasmas gave poorer results. ECAA QA plasmas provide a local system for checking INRs obtained with monitors of both types.

© 2004 American Association for Clinical Chemistry

Whole-blood point-of-care testing (POCT) prothrombin time (PT) monitors are being used on an increasing scale to regulate warfarin dosage to meet increasing worldwide demands for anticoagulation and for greater convenience of patients and medical staff. For evaluating the safety and effectiveness of warfarin administration in preventing thrombotic and hemorrhagic complications, it is therefore essential that these monitors conform to the WHO PT standardization scheme (1, 2) and provide reliable International Normalized Ratios (INRs). External quality as-

1 European Concerted Action on Anticoagulation Central Facility, School of Biological Sciences, The University of Manchester, Manchester, United Kingdom.
2 Haemostasis and Thrombosis Research Centre, Leiden University Medical Center, Leiden, The Netherlands.
3 A Bianchi Bonomi, Haemophilia and Thrombosis Centre, IRCCS Maggiore Hospital, University of Milan, Milan, Italy.
4 Department of Haematology, Manchester Royal Infirmary, Oxford Road, Manchester, United Kingdom.
5 Department for Thrombosis Research, University of Southern Denmark and Department of Clinical Biochemistry, Ribe County Hospital, Esbjerg, Denmark.
†Member of ECAA Steering Group.
*Address correspondence to this author at: ECAA Central Facility, School of Biological Sciences, The University of Manchester, Manchester M13 9PT, United Kingdom. Fax 44-161-275-5316; e-mail ecaa@man.ac.uk.
Received April 4, 2003; accepted December 1, 2003.
Previously published online at DOI: 10.1373/clinchem.2003.019653

6 Nonstandard abbreviations: POCT, point-of-care testing; PT, prothrombin time; INR, International Normalized Ratio; QA, quality assessment; ISI, International Sensitivity Index; and ECAA, European Concerted Action on Anticoagulation.
sessment (QA) is therefore required because calibration of individual monitors by use of the International Sensitivity Index (ISI) is not feasible. In addition, a POCT system consists of the monitor and a specific lot of test strips/cards. A manufacturer’s calibration of each individual lot of test strips/cards is performed with a limited number of individual monitors, but the ISI is used for all individual monitors of the same make.

It would not be possible for the users of all POCT monitors to participate in existing national or regional external QA schemes because of the massive numbers of POCT monitors in use (>80,000) patients in Germany are believed to already be involved in a self-monitoring/self-dosage program with the CoaguChek alone.

A reliable but simple local QA procedure that could be widely available and applied to individual whole-blood PT monitors by their users is therefore required, which ideally should be performed by the patients under supervision at their primary care centers.

The CoaguChek Mini and TAS PT-NC, two widely used whole-blood POCT PT monitoring systems marketed by European Union manufacturers, have been studied in previous European Concerted Action on Anticoagulation (ECAA) reports (3–10) and have been found to show marked differences in mean INR and from the “true” INR on the same blood samples, as established by WHO methodology (11).

In a previous ECAA study (12), the ISI of both monitor systems, based on a multicenter calibration exercise using the modified WHO procedure devised by Tri podi et al. (13), was substituted for the manufacturers’ ISI, but this only partly corrected the INR differences between the two systems and from the true INR. There therefore is a need for an additional step using external QA of individual monitors and their users in addition to the manufacturer’s initial ISI calibration of a POCT system.

The present report considers the results of such an exercise with the two monitor systems. The QA plasmas were subsets of 3 and 5 from the full sets of 60 lyophilized artificially depleted and 60 coumarin plasmas and were selected to give a representative range of INR values across the therapeutic interval (1.5–4.5). These subsets were tested at the 10 centers.

The performance of individual instruments of both systems and their operators at seven ECAA centers was assessed by use of these selected subsets of three and five lyophilized ECAA plasmas. INRs had been assigned independently at three “certifying” centers. The mean INR results for the QA plasmas were compared with the mean INR of the remaining 55 lyophilized ECAA samples tested by the same operators at the same centers to assess the relative ability to characterize performance at the individual centers. This was to assess whether a few test samples would be representative of and would characterize the performance of a larger number of samples. It would also provide a comparison of the reliability of three and five QA plasmas when assayed on both test systems.

### Materials and Methods

#### TEST SYSTEMS

Ten monitors of each type were loaned to the study by Roche Diagnostics and Bayer AG, respectively, to provide a single monitor system (combination of a brand of instrument with a single lot of test strips/cards) of both types (CoaguChek Mini and TAS PT-NC) to all 10 centers.

The CoaguChek system consisted of the meter and lot 164 of “Mini” test strips, incorporating rabbit thromboplastin. The TAS, now redesignated the RapidPointCoag system, incorporated lot 30706002 “PT-NC” test cards, which contain human placental thromboplastin.

#### LYOPHILIZED PLASMAS

Plasma from individual donors was obtained and lyophilized in 0.5-mL volumes.

#### ARTIFICIALLY DEPLETED PLASMA SAMPLES

Sixty artificially depleted lyophilized plasmas were prepared according to ECAA methodology (14) from plasmapheresis donations. Values spanned the 1.5–4.5 INR range when tested with the ECAA rabbit reference thromboplastin, the ISI of which had been determined previously in a multicenter calibration against the WHO rabbit International Reference Preparation (15). All plasmas had a fibrinogen content >1.5 g/L and factor V concentrations >50%, with intervial CV <3%.

Twenty vials of one arbitrarily selected plasma were tested on one CoaguChek Mini and one TAS PT-NC test system by one operator. Each vial was analyzed in duplicate. The imprecision, expressed as the CV, was calculated from the duplicate measurements by fitting a random-effects model, so that the INR variation among vials could be compared with the total variation. Results of this analysis are summarized in Table 1. With both monitors there was no evidence of between-vial variation. The total variation was greater on the TAS monitor.

#### INDIVIDUAL COUMARIN PLASMA SAMPLES

Venous blood samples (20 mL) were collected from 60 adult patients in the Anticoagulant Clinic of Manchester Royal Infirmary, after ethics approval had been granted and informed consent had been obtained from patients.

**Table 1. Interval study results.**

<table>
<thead>
<tr>
<th>Plasma Type</th>
<th>Monitor System</th>
<th>Mean INR</th>
<th>CV, %</th>
<th>Between-vial</th>
<th>Total</th>
<th>Total variation from between-vial variation, % (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Artificially depleted</td>
<td>CoaguChek</td>
<td>2.49</td>
<td>0.0</td>
<td>4.5</td>
<td>0</td>
<td>0 (0–34)</td>
<td>0.67</td>
</tr>
<tr>
<td></td>
<td>TAS PT-NC</td>
<td>3.38</td>
<td>0.0</td>
<td>9.8</td>
<td>0</td>
<td>0 (0–21)</td>
<td>0.86</td>
</tr>
<tr>
<td>Coumarin</td>
<td>CoaguChek</td>
<td>1.99</td>
<td>1.8</td>
<td>2.6</td>
<td>49</td>
<td>1–79)</td>
<td>0.02</td>
</tr>
<tr>
<td></td>
<td>TAS PT-NC</td>
<td>3.02</td>
<td>1.2</td>
<td>7.7</td>
<td>2</td>
<td>0–51)</td>
<td>0.46</td>
</tr>
</tbody>
</table>

*CV, confidence interval.*
The patients had been stabilized on long-term warfarin treatment and were within the 1.5–4.5 INR range.

For ethical reasons, the volume of blood collected from each patient had to be limited and was insufficient for interval studies. There was, however, sufficient volume of one plasma (15 vials) to perform further studies as described above for the artificially depleted plasmas. These were performed by the same operator. The between-vial variation (see Table 1) was not significant on the TAS (between-vial CV = 1.2%; total CV = 7.7%). Although the between-vial variation on the CoaguChek was acceptably small (CV = 1.8%), it was statistically detectable because the between-vial variation was almost one-half the total variation (CV = 2.6%).

**RECONSTITUTION AND TESTING OF LYOPHILIZED PLASMAS ON POCT PT MONITORS**

Sets of 60 ECAA plasmas of both types (artificially depleted and coumarin) were provided to all centers. A training course in the procedures for the two POCT monitors was held before the start of the study, and the same operator at each center performed the laboratory studies. Each plasma was to be reconstituted with 0.5 mL of distilled water and left at room temperature for 10 min before testing within 30 min of reconstitution.

Reconstituted plasma (0.1 mL) was transferred to a plastic tube, and 0.1 mL of 17 mmol/L calcium chloride was added and mixed. The plasma was applied within 15 s of recalcification to the test strip/cards, and the monitor-displayed INR was recorded. A standard solution of calcium chloride (17 mmol/L) was provided to all centers.

All 60 artificially depleted and 60 individual coumarin plasma samples were tested on both POCT monitor systems at all centers. Only single tests could be performed because the number of manufacturers’ test strips/cards of the same lot was limited.

**MONITOR-ASSIGNED INR**

Monitor-assigned INRs were obtained for both types of lyophilized plasmas for both the TAS PT-NC and the CoaguChek Mini systems. These were the means of the respective monitor-displayed INRs at three centers (Leiden, Milan, and Manchester). These certifying centers had special experience in the testing of recalcified plasmas because they had performed ISI calibration exercises with two POCT systems before the present study (3, 8).

**SELECTION OF QA PLASMAS**

Subsets of five QA plasmas were chosen from the full sets of 60 plasmas of each type to give a good distribution of assigned INRs across the 1.5–4.5 range on both monitor systems. The CV of the monitor-displayed INR values for all plasmas were <15% at the three certifying centers.

The effect of reducing the number of plasmas of both types from five to three on the reliability in QA of the two monitor systems was also investigated. The sets of five plasmas were numbered in order of increasing monitor-assigned INR. For the sets of three plasmas, the first, the third, and the fifth plasmas were chosen.

**STATISTICAL ANALYSIS**

At each center the mean monitor-displayed INRs of the sets of five and three QA plasmas were plotted against the mean monitor-displayed INRs of the remaining 55. The results with the 55 plasmas were regarded as the center’s benchmark value for each monitor. The Pearson correlation coefficient was calculated to measure the degree of association between the mean INRs of the QA plasmas and test samples.

To assess the reliability of the individual monitors and their users on the basis of the QA plasmas, the monitor-displayed INRs of all 55 plasmas at the seven centers (excluding Leiden, Milan, and Manchester) were compared with the monitor-assigned INRs of the QA subsets. The percentage deviation of the monitor-displayed INRs from the assigned INR was calculated for all sets of plasmas. From the 55 test plasmas at each center, the number with absolute INR deviations >15% (i.e., ±15%) was determined, this being considered to be a clinically relevant difference. The WHO revised guidelines regard a 10% INR difference as clinically relevant (2), but we have previously found that the POCT PT systems are less precise than conventional PT testing (3), and some additional margin of error was allowed.

Individual plasmas with absolute INR deviations exceeding 15% were therefore classified as "outliers".

The expected numbers of outliers from the sets of three and five QA plasmas were estimated. The estimates were derived by multiplying the proportion of the 55 test plasmas giving outlying INRs by the number of QA plasmas in the set, i.e., three or five. This value was then rounded to the nearest whole number and compared with the actual number of outliers observed with the sets of three and five QA plasmas.

**Results**

The assigned INRs of the five artificially depleted lyophilized plasmas ranged from 2.02 to 4.77 with the TAS PT-NC and from 2.01 to 4.48 with the CoaguChek. The corresponding values with the lyophilized coumarin plasmas ranged from 2.15 to 5.47 with the TAS PT-NC and 1.71 and 4.39 with the CoaguChek (see Table 2).

As shown in Figs. 1 and 2 for the TAS PT-NC and CoaguChek Mini, respectively, there was a considerable between-center difference in mean INR with both artificially depleted or coumarin plasmas when the same 55 samples were tested.

The subsets of five and three plasmas also demonstrated considerable variability in performance at the individual centers. The three certifying centers are identified in Figs. 1 and 2 by an asterisk. Their inclusion in the analysis did not appear to have biased the mean displayed INR.
With the TAS PT-NC, these differences were reliably reflected by both subsets of three and five artificially depleted QA plasmas, as shown by the correlation coefficients of 0.95 and 0.96, respectively. After exclusion of a single outlying point, the correlation coefficients were 0.82 and 0.74, respectively, for the sets of five and three plasmas. With the TAS PT-NC, the three and five artificially depleted QA plasmas gave a better correlation with the set of 55 plasmas than the corresponding sets of coumarin plasmas, as shown by the linear regression lines and correlation coefficients (see Fig. 1).

With the CoaguChek Mini system, the between-center variability in results obtained for the full sets was also reflected by the subsets of both types of QA plasmas, but the correlation was not as good, particularly with the coumarin plasmas (correlation coefficients of 0.58 and 0.30, respectively, for the subsets of five and three coumarin plasmas).

Outliers (i.e., defined in this report as exceeding a 15% absolute deviation in INR from assigned values) were detected with variable success with the subsets of three and five QA plasmas of both types, as shown in Tables 3 and 4. With the full sets of 55 lyophilized plasmas on the TAS PT-NC, the number of outliers was slightly less with the artificially depleted plasmas (18.4%) than with the coumarin plasmas (21.3%). With the CoaguChek Mini, the corresponding values were reversed, 25.4% with the full set of 55 artificially depleted plasmas and 16.9% with the 55 coumarin plasmas.

With both the TAS PT-NC and CoaguChek Mini monitor systems, the greatest number of outliers in both full sets of 55 plasma samples (artificially depleted and coumarin) were found at two centers (centers 1 and 2). At the remaining five centers, the numbers of outliers expected and detected with both types and subsets of QA plasma were similar.

With the CoaguChek Mini, the artificially depleted plasmas underestimated the relatively small numbers of outliers, whereas coumarin plasmas slightly overestimated the incidence of outliers.

Discussion
A simple method of external QA for the two POCT monitor systems is required, and this should be readily available and performed easily by individual monitor users, preferably in primary care clinics or possibly at home.

Reliable INR monitoring during warfarin treatment is critical because clinical events of thrombosis and hemorrhage, respectively, are greatly increased when patients’ INRs are outside the conventional 2.0 and 4.5 INR limits (16). Previously, the ECAA reported that there is a considerable problem with the reliability of displayed INRs but to a different degree with the two types of monitors (11). Local ISI calibration, however, is not feasible for individual monitor users even with the simplified method devised by the ECAA (17). Even if a local calibration is performed, the ISI encoded on the test strip/card is fixed by the manufacturer and could not be changed by the user to amend the displayed INR. For individual monitors and their users, the only solution for testing the reliability of the displayed INR is therefore to use some reliable system of external QA.

Existing national or regional QA schemes could not in most countries deal with this problem. This is because of the massive numbers of such instruments involving many thousands of users in some countries, which would overwhelm the facilities performing such schemes.

There is the added problem, which the present report reveals, of the need for a multiplicity of external QA test samples to be tested on each occasion. Three samples have been shown to be required for the TAS (RapidPointCoag) PT-NC and a minimum of five for the CoaguChek Mini.

The results of the present study are encouraging in the attempt to devise such a simple local system of QA for the users of the two types of POCT monitor systems. The procedure has been developed from previous ECAA reports showing that lyophilized plasmas, when suitably adapted for use on the two monitor systems, can be used to calibrate these two whole-blood POCT PT monitors (10, 17, 18).

National/regional external QA studies are performed at intervals of several months and usually involve one test sample. It would take several exercises to characterize system performance. Furthermore, this would assume that there would therefore be no change in test strip or monitor performance in the intervening period.

The present study shows that considerable overall differences in mean displayed INRs were obtained on the

Table 2. Monitor-assigned INRs (mean of three monitor-displayed INRs) and CV for the sets of five artificially depleted and coumarin ECAA QA plasmas.

<table>
<thead>
<tr>
<th>Plasma</th>
<th>Artificially depleted</th>
<th>Coumarin</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TAS PT-NC</td>
<td>CoaguChek Mini</td>
</tr>
<tr>
<td></td>
<td>Monitor-assigned INR</td>
<td>CV, %</td>
</tr>
<tr>
<td>1</td>
<td>2.02</td>
<td>8.1</td>
</tr>
<tr>
<td>2</td>
<td>2.80</td>
<td>5.3</td>
</tr>
<tr>
<td>3</td>
<td>3.52</td>
<td>8.3</td>
</tr>
<tr>
<td>4</td>
<td>4.16</td>
<td>5.7</td>
</tr>
<tr>
<td>5</td>
<td>4.77</td>
<td>7.7</td>
</tr>
<tr>
<td></td>
<td>2.15</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>2.90</td>
<td>1.8</td>
</tr>
<tr>
<td></td>
<td>3.48</td>
<td>3.6</td>
</tr>
<tr>
<td></td>
<td>4.08</td>
<td>9.3</td>
</tr>
<tr>
<td></td>
<td>5.47</td>
<td>3.6</td>
</tr>
</tbody>
</table>

With the TAS PT-NC, these differences were reliably reflected by both subsets of three and five artificially depleted QA plasmas, as shown by the correlation coefficients of 0.95 and 0.96, respectively. After exclusion of a single outlying point, the correlation coefficients were 0.82 and 0.74, respectively, for the sets of five and three plasmas. With the TAS PT-NC, the three and five artificially depleted QA plasmas gave a better correlation with the set of 55 plasmas than the corresponding sets of coumarin plasmas, as shown by the linear regression lines and correlation coefficients (see Fig. 1).

With the CoaguChek Mini system, the between-center variability in results obtained for the full sets was also reflected by the subsets of both types of QA plasmas, but the correlation was not as good, particularly with the coumarin plasmas (correlation coefficients of 0.58 and 0.30, respectively, for the subsets of five and three coumarin plasmas).

Outliers (i.e., defined in this report as exceeding a 15% absolute deviation in INR from assigned values) were detected with variable success with the subsets of three and five QA plasmas of both types, as shown in Tables 3 and 4. With the full sets of 55 lyophilized plasmas on the TAS PT-NC, the number of outliers was slightly less with the artificially depleted plasmas (18.4%) than with the coumarin plasmas (21.3%). With the CoaguChek Mini, the corresponding values were reversed, 25.4% with the full set of 55 artificially depleted plasmas and 16.9% with the 55 coumarin plasmas.

With both the TAS PT-NC and CoaguChek Mini monitor systems, the greatest number of outliers in both full sets of 55 plasma samples (artificially depleted and coumarin) were found at two centers (centers 1 and 2). At the remaining five centers, the numbers of outliers expected and detected with both types and subsets of QA plasma were similar.

With the CoaguChek Mini, the artificially depleted plasmas underestimated the relatively small numbers of outliers, whereas coumarin plasmas slightly overestimated the incidence of outliers.
same sets of 55 lyophilized plasma samples (whether artificially depleted or coumarin plasmas) tested at the 10 centers. Similar variability in performance of both the TAS PT-NC and CoaguChek Mini monitor systems was also shown by the small subsets of five and three lyophilized artificially depleted ECAA QA plasmas.

With the TAS PT-NC, subsets of five and three ECAA artificially depleted QA plasmas gave a good correlation (correlation coefficients of 0.96 and 0.95, respectively) with the results for the full set of 55 plasmas tested at the same centers, but the subsets of coumarin plasmas, although reflecting the variability of performance, did not correlate as closely (correlation coefficients of 0.68 and 0.49 for sets of five and three plasmas, respectively).

With the CoaguChek Mini, subsets of 5 artificially depleted QA plasmas gave good correlation (correlation...
coefficient, 0.87) with the results for the full sets of 55 plasmas, but the sets of 3 were less satisfactory (correlation coefficient, 0.67). However, the subsets of coumarin QA plasmas did not perform well in reflecting the between-center differences observed with the full sets (correlation coefficients of 0.58 and 0.30 for sets of five and three plasmas, respectively).

Outlying results (exceeding a 15% absolute deviation from the assigned INR) were recorded in a proportion of results with the full sets of both artificially depleted and coumarin plasmas with both monitor systems. The ability to detect outliers is therefore an important additional component of a local QA procedure. The success of the sets of three and five QA plasmas of the two types in detecting outliers was therefore examined in this study.

For both POCT systems, the use of QA subsets of both types of plasma allowed detection of outliers. When full sets of both types of plasmas were used, more than one-half of the outliers were found to be present at two of the seven centers. With sets of 5 QA plasmas of both types

Fig. 2. Plots of mean monitor-displayed INRs for CoaguChek Mini at 10 centers. Also shown are the linear regression line and Pearson correlation coefficient. * indicate results obtained at certifying centers. (A), subset of five artificially depleted QA plasmas. (B), subset of three artificially depleted QA plasmas. (C), subset of five coumarin QA plasmas. (D), subset of three coumarin QA plasmas.
on the TAS PT-NC, the number of outliers closely agreed with the predicted numbers from the full sets of 55; however, with the sets of 3 QA plasmas of both types there was a trend to overdetection. With the CoaguChek Mini, both sets of artificially depleted QA plasmas tended to underestimate the number of outliers, whereas the coumarin plasma sets slightly overestimated the expected number. The use of small subsets of ECAA-certified lyophilized QA plasmas therefore appears to offer a reasonable approach to the QA of the considerable variability of performance of individual monitors.

The present study was performed by experienced scientific staff at selected established centers. It is reasonable, therefore, to assume that the need for a QA procedure would be even greater with less experienced monitor users, e.g., patients engaged in self-testing, than with the experienced staff of the seven centers. Operator differences are undoubtedly an important component of the observed between-center variability. The degree of difference observed in our study therefore reflects not only the differences in performance of the instruments but also of the use of plasmas rather than whole blood, which is the sample type usually tested on these monitors, by the operators. The reliability of lyophilized plasmas in determining the ISI of these two POCT monitor systems was established previously in ECAA studies (10, 17, 18).

One limitation of the study involved the assignment of INRs to the QA plasmas; the limited supply of test strips/cards of the same lots restricted the number of tests that could be performed to assign INRs to single tests on the three monitors at the three certifying centers. A more accurate assignment of INRs could be obtained by multiple tests on a larger number of instruments.

The present study therefore demonstrates the feasibility of a simple practical QA procedure for checking the reliability of INR results with individual monitors of both the CoaguChek Mini and TAS PT-NC systems that could be made available to all users of these monitors. Depending on the monitor system, sets of three or five plasmas with assigned INRs are proposed for this purpose. Individual users would test these and compare results with the assigned INR. If the INR of one or more plasmas deviates by ≥15% from the assigned value, the procedure should be repeated.

According to WHO guidelines (2), a 10% difference in INR is clinically relevant, but because the two POCT systems studied have been shown to be less precise than conventional manual PT testing (3), a 15% limit is recommended. If problems persist, the monitor manufacturer or a local expert anticoagulant center should be contacted to ascertain whether the error is attributable to the instrument or the user. A QA procedure is designed solely as a measure of performance and detection, not for correction of instrument or technical faults. A local expert center or the manufacturer should be able to perform an ISI calibration using the simplified procedure based on general

<table>
<thead>
<tr>
<th>Center</th>
<th>55 test plasmas</th>
<th>5 QA plasmas</th>
<th>3 QA plasmas</th>
<th>55 test plasmas</th>
<th>5 QA plasmas</th>
<th>3 QA plasmas</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>17</td>
<td>3 (2)</td>
<td>2 (1)</td>
<td>25</td>
<td>2 (2)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>2</td>
<td>21</td>
<td>1 (2)</td>
<td>1 (1)</td>
<td>18</td>
<td>1 (2)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>3</td>
<td>12</td>
<td>1 (1)</td>
<td>1 (1)</td>
<td>13</td>
<td>2 (1)</td>
<td>2 (1)</td>
</tr>
<tr>
<td>4</td>
<td>4</td>
<td>1 (0)</td>
<td>0 (0)</td>
<td>9</td>
<td>0 (1)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>5</td>
<td>8</td>
<td>1 (1)</td>
<td>1 (0)</td>
<td>5</td>
<td>1 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>6</td>
<td>3</td>
<td>1 (0)</td>
<td>1 (0)</td>
<td>8</td>
<td>1 (1)</td>
<td>1 (0)</td>
</tr>
<tr>
<td>7</td>
<td>6</td>
<td>0 (1)</td>
<td>0 (0)</td>
<td>4</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>All</td>
<td>71 (of 385 tests)</td>
<td>8 (7)</td>
<td>6 (3)</td>
<td>82 (of 385 tests)</td>
<td>7 (7)</td>
<td>5 (3)</td>
</tr>
</tbody>
</table>

*Numbers in parentheses are the number of QA plasmas that would be expected to have outlying INRs based on results for the 55 test plasmas.

---

<table>
<thead>
<tr>
<th>Center</th>
<th>55 test plasmas</th>
<th>5 QA plasmas</th>
<th>3 QA plasmas</th>
<th>55 test plasmas</th>
<th>5 QA plasmas</th>
<th>3 QA plasmas</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>25</td>
<td>1 (2)</td>
<td>1 (1)</td>
<td>18</td>
<td>3 (2)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>2</td>
<td>30</td>
<td>1 (3)</td>
<td>1 (2)</td>
<td>27</td>
<td>4 (2)</td>
<td>3 (1)</td>
</tr>
<tr>
<td>3</td>
<td>7</td>
<td>1 (1)</td>
<td>1 (0)</td>
<td>5</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>4</td>
<td>7</td>
<td>0 (1)</td>
<td>0 (0)</td>
<td>9</td>
<td>0 (1)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>5</td>
<td>11</td>
<td>0 (1)</td>
<td>0 (1)</td>
<td>2</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>6</td>
<td>10</td>
<td>0 (1)</td>
<td>0 (1)</td>
<td>2</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>7</td>
<td>8</td>
<td>0 (1)</td>
<td>0 (0)</td>
<td>2</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>All</td>
<td>98 (of 385 tests)</td>
<td>3 (10)</td>
<td>3 (5)</td>
<td>65 (of 385 tests)</td>
<td>7 (5)</td>
<td>4 (2)</td>
</tr>
</tbody>
</table>

*Numbers in parentheses are the number of QA plasmas that would be expected to have outlying INRs based on results for the 55 test plasmas.
provision of certified lyophilized plasmas proposed by the ECAA (10, 11, 18).

Both types of monitor systems used in this study are based on the same principle of clot detection, i.e., the movement of iron oxide particles in a magnetic field. Other types of available monitors rely on different methods of end-point detections, e.g., optical detection of blood flow. QA procedures specifically adapted to their individual methodologies may be required, but there is no reason to suppose that suitable QA materials could not be developed.

This study was supported by the EC Standards Measurements and Testing Program (Grant SMT4-CT98-2269) and an additional grant from the Manchester Thrombosis Research Foundation. We thank Roche Diagnostics (Mannheim, Germany) and Bayer AG (Leverkusen, Germany) for the loan of the CoaguChek and TAS instruments and donation of test strips/cards, respectively. We are also grateful to the following scientific staff for their valuable assistance: G. Anthi (Athens), M. Clerici (Milan), H. Fitzgerald (Dublin), M.H. Horellou (Paris), J. Meeuwisse-Braun (Leiden), E.M. Norberg and L. Söderblom (Stockholm), K. Overgaard (Esbjerg), and M. Vacas Rius (Bilbao). Additional multicenter study participants included J. Conard, Laboratoire Central D’Hematologie, Hôtel-Dieu de l’île de Paris (Paris, France); D. Dias, Service Immunotherapie, Hospital de S. Joao (Porto, Spain); N. Egberg, Department of Clinical Chemistry, Karolinska Hospital (Stockholm, Sweden); J.A. Iriarte, Instituto de Epidemiologia y Prevencion de Enfermedades Cardiovasculares, Hospital Civil de Basurto (Bilbao, Portugal); I. Kontopoulou-Griva, Anticoagulant Unit, Hippocratie General Hospital (Athens, Greece); and B. Otridge, Hematology Department, Mater Misericordiae Hospital (Dublin, Ireland).

References