Department of Health and Human Services

Survey of Hospital Coagulation Laboratory Practices, United States–2001

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This report can be downloaded in either HTML or PDF format by visiting the site for the 2001 National Survey of Hospital Coagulation Laboratories at **http://www.phppo.cdc.gov/mlp/coag2001.asp**

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EXECUTIVE SUMMARY

We present findings from a 2001 survey of U.S. hospital coagulation laboratories. (See the Appendix for a copy of the actual survey used.) We sent this questionnaire to 800 hospital laboratories, stratified into large (≥200 beds) and small (<200 beds) hospitals. Study sample was a random selection of the large and small hospitals from the 1999 directory of the American Hospital Association (AHA). The selected large and small hospitals constituted 26% and 9% of the large and small hospitals listed in this directory, respectively. We administered this survey and collected results between June and October 2001. Respondents had the option of mailing a completed survey or submitting one via the Internet. We received 632 responses (corresponding to a response rate of 79% including 20 responses submitted electronically).

Our findings show great variability in certain laboratory practices. Although in most cases, response patterns from the large and small hospital laboratories were not significantly ($P > 0.050$) different, several questions solicited significantly different responses from these 2 groups. For most of these questions, a greater proportion of large hospitals adhered to published laboratory practice recommendations and guidelines. The following is a summary of major findings.

Performance of Coagulation Testing

Ninety-seven percent of the respondents performed coagulation testing.

Test Requisition and Specimen Management

Test requisition. The respondents noted the following usage information on their test requisition forms: coumadin, 53%; unfractionated heparin, 39%; heparinoid, 33%; low molecular weight heparin (LMWH), 23%; and salicylate, 16%. The large hospital respondents noted significantly more requests for information on requisition forms for using unfractionated heparin ($P = 0.003$), heparinoid ($P = 0.044$) and LMWH ($P = 0.045$).

Rejection of specimens. The proportions of the respondents below did not note the following reasons for rejecting a coagulation specimen in their laboratories: specimen collected via indwelling catheter, 68%; label not having hospital medical record number, 55%; specimen stored at an inappropriate temperature, 15%; specimen hemolyzed, 14%; requisition form and specimen label having conflicting patient information, 8%; and specimen transport time exceeding recommended time frame, 8%. The College of American Pathologists (CAP) has recommended that specimens used for monitoring heparin therapy be collected from a different extremity than the one used for heparin infusion (*Arch Pathol Lab Med*. 1998;122:782–798). A significantly greater proportion of the large hospital respondents (59%) rejected coagulation specimens because of the lack of hospital medical record number compared to the small hospital respondents (31%); $P < 0.001$. These results suggest a need for improvement in certain laboratory practices relating to test requisition and specimen collection procedures.

Practices Relating to Prothrombin Time (PT) Assay

Anticoagulant concentration. Based on the recommendation of the World Health Organization (WHO) and the NCCLS guidelines, 3.2% (109 mmol/L) citrate is the anticoagulant of choice for coagulation testing (*Arch Pathol Lab Med*. 1998;122:768–781). Eighty percent of the large hospital respondents stated exclusively using 3.2% sodium citrate as the anticoagulant compared to 66% of the small hospital respondents ($P < 0.001$).

Reporting of results. Reporting PT results in seconds may lead clinicians to inappropriately compare results between institutions (*Am J Clin Pathol*. 1998;109:589–594) and relying on PT ratio has been documented to cause errors in anticoagulant therapy (*Arch Intern Med*. 1992;152:278–282). Almost all the respondents

(99.8%) used international normalized ratio (INR) to report PT; however, 97% also reported PT in seconds and/or as therapeutic PT ratio. Three percent of the respondents reported PT results in INR only.

Reference interval. Ninety-two percent of the respondents conducted in-house evaluations to establish the reference interval for their PT assay. Most respondents (46% of the large hospitals and 74% of the small hospitals, $P < 0.001$) used less than 40 subjects to establish their PT reference intervals. According to the NCCLS, a minimum of 120 subjects for each reference population or subclass is recommended to establish reference intervals for quantitative laboratory tests (*NCCLS approved guideline–2nd edition*. Document C28-A2. Vol 15; No. 4). Five percent of the respondents noted using at least 120 subjects to establish their reference ranges for PT assay.

Sensitivity of PT assay to heparin. According to the CAP, laboratories should determine sensitivity of their PT assays to heparin (*Arch Pathol Lab Med*. 1998;122:782–798). Seventeen percent of the respondents determined the sensitivity of their PT assays to heparin. Also according to the CAP guideline, laboratories should, where possible, select a thromboplastin that is insensitive to heparin in the therapeutic range (*Arch Pathol Lab Med*. 1998;122:768–781). Fifty-nine percent of the large hospital respondents selected a PT-thromboplastin reagent that was insensitive to heparin in the heparin therapeutic range, compared to 40% of the small hospital respondents ($P < 0.001$).

The CAP recommends that thromboplastins with a manual ISI between 0.9 and 1.7 be used (*Arch Pathol Lab Med*. 1998;122:768–781). The large hospital respondents reported an average ISI of 1.52 (median, 1.56) while the small hospitals reported an average of 1.70 (median, 1.89). Of the large hospital respondents, 50% reported ISI values of ≤1.70 compared to 42% of the small hospital respondents ($P = 0.037$). Forty-two percent of the large hospital respondents reported ISI values of ≤1.20 compared to 24% of the small hospital respondents ($P < 0.001$) as recommended by the American College of Chest Physicians (*Chest.* 1995;108(4 Suppl):231S–246S).

Practices Relating to Activated Partial Thromboplastin Time (aPTT) Assay

Therapeutic range. According to the CAP guideline, adjusted dose and therapeutic heparin require anticoagulant monitoring using a method with a defined therapeutic range (*Arch Pathol Lab Med*. 1998;122:782–798). Seventy-three percent of the large hospital respondents noted having an aPTT therapeutic range for heparin compared to 53% of the small hospital respondents ($P < 0.001$). While 64% of the respondents stated they reported the aPTT therapeutic range for heparin when monitoring heparin therapy, 9% included the corresponding heparin concentration with aPTT results.

How the aPTT therapeutic range for heparin was determined. The CAP recommends that therapeutic range of unfractionated heparin for the aPTT reagent-instrument system should be determined with each change in reagent (lot number or manufacturer) or instrument (*Arch Pathol Lab Med*. 1998;122:782-798). This may be accomplished by (1) comparison of *ex vivo* specimens with an appropriately validated heparin assay or (2) comparison of *ex vivo* specimens to a previously calibrated aPTT using a method to control for reagent drift. The respondents adhered to the following practices to determine the aPTT therapeutic range for heparin:

- using samples from patients on heparin therapy to compare a new to an old reagent lot, 59% (66% of the large hospital respondents versus 50% of the small hospital respondents, P = 0.007);
- using heparin-spiked samples to compare a new to an old reagent lot, 46%;
- using heparin-spiked samples to compare a new to an old heparin lot, 15% (12% of the large hospital respondents versus 21% of the small hospital respondents, P = 0.038);
- using samples from patients on heparin therapy to compare a new to an old heparin lot, 12%;
- performing anti-Xa assay, 37% (47% of the large hospital respondents versus 18% of the small hospital respondents, $P < 0.001$) and performing protamine sulfate titration, 9%.

When the aPTT therapeutic range for heparin was reconfirmed. The respondents reconfirmed the aPTT therapeutic range for heparin under the following circumstances:
- when new instrumentation is used, 79%;
- when new reagent lots are used, 75%;
- when new reagents are used, 51%; and
- after a specified time period, 22%.

Specimen management. According to the NCCLS, samples can be assayed up to 4 hours after phlebotomy if centrifuged within 1 hour of collection (*NCCLS approved guideline–3rd edition*. Document H21-A3. Vol 18; No. 20). The respondents indicated they adhered to the following practices to manage specimens before aPTT analysis:
- specimens assayed within 4 hours after phlebotomy, 96%;
- specimens centrifuged within 1 hour of collection, 88% (84% of the large hospital respondents versus 92% of the small hospital respondents, P = 0.007);
- specimens kept at room temperature prior to testing, 82%; and
- specimens kept at 4 °C prior to testing, 22%.

Practices Relating to Assays for von Willebrand Disease (vWD)

Performance of von Willebrand factor (vWF) assays. Ten percent of the large hospital respondents stated that they provided results for von Willebrand factor antigen (vWF Ag) compared to 0.4% of the small hospital respondents ($P < 0.001$). Fourteen percent of the large hospital respondents noted that they provided results for von Willebrand factor activity (Ristocetin cofactor activity) compared to 0.3% of the small hospital respondents ($P < 0.001$). Finally, 3% of the large hospital respondents stated that they provided results for vWF multimers compared to 0.4% of the small hospital respondents ($P = 0.007$). The following proportions of the respondents performed the 3 vWF assays:
- 38% for vWF Ag and vWF activity,
- 25% for vWF activity only,
- 15% for vWF Ag, vWF activity and vWF multimers,
- 15% for vWF Ag only, and
- 6% for vWF multimers only.

Reporting of ABO specific reference interval for vWF antigen assay. Nineteen percent of the respondents that performed vWF Ag assay reported an ABO specific reference interval for this assay.

Provision of vWF multimers results. Eighty-nine percent of the respondents noted that they performed vWF multimers assay only when ordered by a clinician; 38% did so when Ristocetin cofactor was decreased; 29% performed this assay when Ristocetin cofactor was disproportionately decreased relative to vWF Ag; 25% did so when vWF Ag and vWF activity were both low; and 13% did so only if Ristocetin-induced platelet aggregation indicated a Type II B vWD.

Practices Relating to Thrombosis/Hypercoagulability Workup

Protein S assays. Ten percent of the large hospital respondents usually performed the assay for protein S activity (functional test) before the antigenic assay compared to 0.3% of the small hospital respondents ($P < 0.001$). If the results of the functional test were decreased, 17% performed antigenic assay to differentiate Type I deficiency from Type II while 20% performed free and total protein S antigen assay.

Performance of activated protein C (APC) resistance and factor V mutation assays. Eleven percent of the large hospital respondents performed activated protein C (APC) resistance assay compared to 1% of the small hospital respondents ($P < 0.001$). If, after performing the APC resistance assay, results indicated resistance to APC, 61% obtained results for factor V Leiden mutation. Long-term anticoagulation in carriers of factor V Leiden, on the basis of the carrier state alone, is not indicated (*Blood*. 1997;89:1963–1967).

Algorithm for Diagnosing a Lupus Anticoagulant (LA)

Offering an LA profile. Eighteen percent of the respondents stated that they offered an LA profile.

Practices leading to mixing studies. When a PT result was prolonged, 37% of the respondents did not offer mixing studies for PT, and 56% did so only if there was an additional order for the mixing study. When an aPTT result was prolonged, 33% of the respondents did not offer mixing studies for aPTT, and 59% did so only if there was an additional order for the mixing study.

Workup to diagnose an LA. If the results of the mixing study for aPTT did not correct to normal, 17% of the respondents initiated a workup to diagnose an LA. Those routinely initiating a workup to diagnose an LA most commonly performed the following tests:

- dilute Russell viper venom time, 79%;
- hexagonal phase phospholipid (Staclot LA) assay, 51%;
- lupus sensitive aPTT, 40%; and
- platelet neutralization procedure, 35%.

Practices Relating to Monitoring for Low Molecular Weight Heparin (LMWH) Therapy

Monitoring of LMWH therapy. Fourteen percent of the respondents (19% of the large and 10% of the small hospitals, $P = 0.002$) noted that they monitored LMWH therapy.

Assays used. The CAP recommends the chromogenic anti–factor Xa method for monitoring LMWH (*Arch Pathol Lab Med*. 1998;122:799–807). In this survey, those monitoring LMWH therapy did so most commonly by using aPTT (72%) and anti-Xa (53%) assays. While 65% of the large hospital respondents used an anti-Xa assay to monitor for LMWH therapy, 18% of of the small hospital respondents did so ($P = 0.001$). Fifty-eight percent of the large hospital respondents used an aPTT assay to monitor LMWH therapy compared to 96% of the small hospital respondents ($P = 0.001$). The observation that 17% of the large hospital respondents reportedly performed in-house anti-Xa assay compared to 2% of the small hospital respondents ($P < 0.001$) may help to explain these findings.

Calibrators used. According to the CAP guideline, a hospital pharmacy should dispense heparin of a single manufacturer and lot number (*Arch Pathol Lab Med*. 1998;122:782–798). The most common calibrators for anti-Xa assay were reportedly

- LMWH supplied by pharmacy, 53%;
- internal standard LMWH, 22%;
- unfractionated heparin, 14%; and
- internal standard unfractionated heparin, 11%.

The CAP recommends that a calibrated LMWH be used to establish the standard curve for an assay to measure LMWH and that unfractionated heparin not be used to establish the standard curve for monitoring LMWH (*Arch Pathol Lab Med*. 1998;122:799–807). While 74% of the respondents used different calibration curves for LMWH and unfractionated heparin, 42% did so for each type of LMWH.

Timing of anti-Xa assay. The CAP recommends that when LMWH is monitored, the sample be obtained 4 hours after subcutaneous injection (*Arch Pathol Lab Med*. 1998;122:799–807). Forty-six percent of the respondents did not recommend a time for anti-Xa testing after subcutaneous administration of LMWH, 32% performed anti-Xa testing 4 hours after injection, and 14% did so between 2 and 4 hours after injection.

Availability of Specific Coagulation Tests

The top 8 most commonly performed coagulation tests were PT (100%), aPTT (99%), bleeding time (90%), fibrinogen (78%), D-dimer (66%), fibrin(ogen) degradation products (52%), activated clotting time (43%), and thrombin time (38%). We found no significant differences between the large and small hospital respondents in terms of the proportions performing in-house testing of the 3 most commonly assayed coagulation tests: PT, aPTT and bleeding time. Except for plasminogen antigen assay (performed by 2 large hospitals), a significantly greater proportion of the large hospital respondents performed all other tests in-house compared to the small hospital respondents ($P < 0.001$, $P = 0.035$ for vWF multimers with 5 large hospitals performing this assay).

Test Result Information, Interpretations and Recommendations

From 90% to 98% of the respondents provided measurement units and 76–87% provided needed specimen comments for PT, aPTT, vWF Ag and protein C assays. From 93 to 97% of the respondents supplied reference intervals for these assays. The following proportions of respondents provided therapeutic ranges: PT, 54%; aPTT, 38%; aWF Ag, 5%; and protein C, 5%.

From 4 to 6% of the respondents noted that they specified testing methodology/reagent on coagulation test reports for these 4 tests. One percent noted possible drug interactions for PT and aPTT assays; 7% did so for vWF Ag assay; and 21% stated drug interactions in reporting protein C results.

Two percent of the respondents suggested diagnoses for PT and aPTT assays compared to 10% and 12% for protein C and vWF Ag assays, respectively. The proportions providing written interpretations were as follows: aPTT, 4%; PT, 6%; vWF Ag, 21%; and protein C, 22%.

While 2% of the respondents provided recommendations for further testing for PT and aPTT assays, 12% and 14% did so for vWF Ag and protein C assays, respectively. The proportions providing recommendation for treatment were as follows: PT, 1%; aPTT, 1%; protein C, 3%; and vWF Ag, 5%. The proportions providing recommendation to test family members were as follows: PT, 0.2%; aPTT, 0.2%; protein C, 8%; and vWF Ag, 10%.

From 29% to 33% provided no result interpretation for any of these 4 tests, and 46–51% provided no testing/treatment recommendations.

Process of Reporting Results

Reporting of critical values. Ninety-nine percent of the respondents reported critical values. Of those noting that they reported critical values, the respondents adhered to the following practices:

- critical values telephoned to the clinician and the call documented, 99%;
- critical values repeated and documented as confirmed, 91%;
- critical values telephoned to the clinician and the call not always documented, 6%; and
- critical values indicated on the report, but no further action taken, 5%.

Repeating a coagulation test. Circumstances under which a coagulation test was usually repeated were reportedly as follows:

- control(s) out of range, 98%;
- results outside instrument technical ranges, 98%;

- results being critical values, 95%;
- results not agreeing with previous results, 73%; and
- results outside of the reference interval, 16%.

These data suggest a need for improved reporting of laboratory test results.

Quality Assurance (QA) Procedures

Respondents usually took the following QA steps:

- critical values brought to immediate attention of the clinician, 99%;
- calibration of all instruments periodically verified, 99%;
- critical values reviewed, 99%;
- new analytical methods validated, 98%;
- patient information on specimen tube and laboratory-generated labels matched, 93%;
- specimen label and requisition form matched, 90%;
- instrument printout compared to reported value, 82%;
- patient's previous results checked, 76%;
- specimens run in duplicate, 39%;
- controls run in duplicate, 38%; and
- plasma checked for platelet count after centrifugation, 23%.

According to the Clinical Laboratory Improvement Amendments of 1988 (CLIA) regulations, a laboratory report must be sent promptly to the authorized person, the individual responsible for using the test results or the laboratory that initially requested the test (*CLIA Subpart K* Sec. 493.1253 Condition: Hematology. (http://www.phppo.cdc.gov/clia/regs/subpart_k.asp#493.1253) One percent of the respondents did not adhere to this practice ($P = 0.005$). Patient and control specimens must be tested in duplicate for manual coagulation tests; duplicate testing is not required for automated coagulation tests (*CLIA Subpart K* Sec 493.1253 Condition: Hematology). Patient and control specimens were reportedly run in duplicate by 39% and 38% of the respondents, respectively. We did not ask whether this duplicate testing was performed using manual or automated methods.

Two percent of the respondents reportedly did not validate new analytical methods ($P < 0.001$); and 1% of the respondents indicated that they did not periodically verify calibration of all of their instruments ($P = 0.003$).

These data suggest a need for improvement in performing certain QA procedures.

Coagulation Laboratory Personnel and Resources

Testing location. Respondents performed coagulation tests in the following locations: core laboratory, 55%; hematology laboratory, 38%; coagulation laboratory, 16%; point of care, 11%; and stat laboratory, 5%. Two percent noted that coagulation testing was done at none of these locations.

Number of full time equivalents (FTEs). Seventy-one percent employed less than 4 FTEs to perform coagulation testing, while 17% employed 4–9 FTEs and 12% employed ≥10 FTEs.

Components of competency assessment program. The respondents included the following components in their competency assessment program for coagulation testing personnel:

- successful performance of QC with documentation of remedial actions, 92%;
- review of procedure manuals, 86%;
- analysis of unknown samples, 80%;
- direct observation of a task, 74%;
- participation in continuing education, 61% and periodic written examination, 30%.

Educational degrees of coagulation laboratory director. Ninety-one percent of the respondents noted that the laboratory director had an M.D., while 7% stated that this individual had a Ph.D. Both M.D. and Ph.D. degrees were noted by 4% of the respondents. Eight percent of the respondents noted other degrees, and 27% of this group also noted that the laboratory director possessed an M.D.

Certifications of coagulation laboratory director. The proportions of the laboratory directors with specific professional board/society certifications were as follows:

- in clinical pathology, 76%; 81% of the large versus 71% of the small hospital respondents (P = 0.002);
- in anatomical pathology, 63%; 73% of the large versus 53% of the small hospital respondents (P < 0.001);
- by the American Society of Clinical Pathologists (ASCP), 25%; 21% of the large versus 29% of the small hospital respondents (P = 0.020);
- in medicine (18%);
- in hematopathology, 8%; 14% of the large versus 1% of the small hospital respondents (P < 0.001); and
- in hematology, 5%; 9% of the large versus 1% of the small hospital respondents (P < 0.001).

Coagulation service capacities. A clinician was reportedly available for consultation having expertise in coagulation disorders in 57% of the responding hospitals (74% of the large versus 38% of the small hospitals, P < 0.001). An anticoagulation outpatient clinic specializing in the adjustment of oral anticoagulants reportedly existed at the institutions of 20% of the respondents (27% of the large versus 12% of the small hospitals, P < 0.001). Nine percent of the respondents stated that they had an outpatient clinic specializing in the diagnosis and treatment of coagulation disorders (17% of the large versus 2% of the small hospitals, P < 0.001).

Point-of-Care Testing (POCT) for PT Assay

Availability of POCT for PT assay. Nine percent of the respondents (15% of the large versus 3% of the small hospitals, P < 0.001) had POCT for PT assay.

Laboratory oversight of coagulation POCT. The laboratory reported having oversight of coagulation POCT (including certification and regulatory compliance) in 93% of cases (98% of the large versus 67% of the small hospital respondents, P = 0.001).

Location of coagulation POCT. The respondents noted the following sites for performing coagulation POCT: coagulation clinic, 64%; cardiac catheterization laboratory, 27%; satellite laboratory, 23%; operating rooms, 21%; bedside, 18%; dialysis clinic, 13%; and other sites, 2%.

Integration of POCT results. Forty percent of the respondents stated that coagulation POCT results were integrated into the laboratory's results reporting system. Of these, 95% noted that coagulation POCT results were integrated into the laboratory's reporting system in the order of collection time.

Reference interval for POCT of PT. Reference interval for the POCT PT assay was reported to be the same as the laboratory PT reference interval for 45% of the respondents. Of the remaining, 36% noted that the POCT reference interval was established by the same method used to establish the PT reference interval for the laboratory.

Type of quality control (QC) material/method. Seventy-four percent of the respondents used electronic QC, 52% employed lyophilized QC material, and 44% used liquid QC material. Sixty-seven percent used

2 or more types of QC. Those using 2 or more types of QC reported they used electronic QC methods along with liquid QC material (33%), lyophilized QC material (30%), or both (4%).

Frequency of QC runs. According to the CLIA regulations, for all non-manual and CLIA non-waived coagulation testing systems, the laboratory must include 2 levels of control each 8 hours of operation, i.e. once per an 8-hour shift, and each time a change in reagents occurs (*CLIA Subpart K*. Sec. 493.1253 Condition: Hematology. http://www.phppo.cdc.gov/clia/regs/subpart_k.asp#493.1253). Thirty-nine percent of the respondents performed QC once per shift, while 54% did so once per day. Ninety-three percent of the respondents performed QC either once per day or once per shift.

Our findings show substantial variability exists in certain coagulation laboratory practices. To our knowledge, this is currently the only report of a broad and comprehensive survey of nationally based coagulation-specific and general laboratory practices in hospitals. We believe these results present a representative and accurate snapshot of hospital coagulation laboratory practices in the United States in 2001.

INTRODUCTION

We are reporting the results of a survey of the U.S. hospital coagulation laboratory practices conducted in 2001. The Centers for Disease Control and Prevention (CDC) contracted with Research Triangle Institute (RTI), Durham, NC to conduct this survey. RTI subcontracted with the Analytical Sciences, Inc. (ASI), Durham, NC to assist the CDC in the development and administration of this survey to a sample of the U.S. hospital laboratories.

Hospital clinical laboratories play an important role in the health of Americans; and as documented in this survey, virtually all hospital laboratories performed some coagulation tests. Coagulation laboratory testing is vital to the diagnosis, treatment and management of bleeding and hypercoagulability disorders affecting millions of patients in the U.S. For example, the most commonly performed coagulation test, prothrombin time (PT) assay, is currently performed over 40 million times annually. The majority of coagulation laboratory tests are performed as screening tests for coagulation disorders or to monitor therapeutic anticoagulant therapy; these assays are also used in conjunction with other tests to increase overall diagnostic accuracy. Although variation in coagulation testing practices within individual laboratories has been documented, little is known about the extent or nature of variation across hospital laboratories. Variability in some testing processes can affect test result accuracy and result interpretation, potentially impacting patient outcomes (e.g., complications of bleeding or thrombosis). Given that the diagnosis and treatment of many patients depend, in part, on coagulation testing, such variation could have serious consequences for patient and population health care and assessment.

In response to the uncertainty surrounding coagulation testing practices, we conducted this national survey of hospital coagulation laboratories. This survey focused on testing practices involving 3 coagulation disorders potentially impacting patient outcomes. These disorders were (1) hypercoagulability or thrombophilia, (2) von Willebrand disease (vWD), and (3) heparin induced thrombocytopenia (HIT)/heparin-induced thrombocytopenia thrombotic syndrome (HITTS). We chose these disorders because, in our judgment along with that of a panel of coagulation laboratory experts,[*] (1) they had serious health consequences affecting a large number of people and (2) valid test results were critical for their diagnosis and treatment.

Our purpose here was to assess variation of coagulation laboratory practices in the U.S. hospitals by assessing

- availability of specific tests for diagnosing and treating hypercoagulability or thrombophilia, vWD and HIT/HITTS,
- pre-analytical issues such as collection methods, information provided with specimens, and processing of specimens,
- analytical issues such as instrumentation, quality control (QC), and qualifications of testing personnel,
- post-analytical issues such as result reporting, interpretations, and recommendations, and
- use of selected laboratory practices specific to each test that are subject to variation (such as availability, methodology and sensitivity) and that are critical to the diagnostic or therapeutic use of the test.

[*]The members of this panel were Michael Laposata, M.D., Ph.D. of Harvard Medical School, Boston, MA, Connie Miller, Ph.D. of the CDC, Atlanta, GA, Stephan Moll, M.D. of the University of North Carolina, Chapel Hill, NC, and John Olson, M.D., Ph.D. of the University of Texas Health Science Center, San Antonio, TX.

METHODS

Study Sample

The target population was U.S. hospital laboratories. The sampling frame was hospitals from the 1999 directory of the American Hospital Association (AHA). This database is not limited to the AHA members and includes 95% of all U.S. hospitals (personal communication, AHA, November 1999 and as verified against the Online Survey, Certification and Reporting database of CLIA-registered hospitals). This database includes the number of beds, permitting us to stratify hospitals by this variable as a surrogate measure of hospital size. We stratified hospitals into those with ≥200 beds (large hospitals) and those with <200 beds (small hospitals). The randomly selected large and small hospitals in the study sample constituted 26% and 9% of the large and small hospitals listed in the sampling frame, respectively.

Questionnaire Development

We developed this survey questionnaire based on the recommendations of an advisory panel and numerous discussions and deliberations within the CDC. We began the process to develop the survey by formulating an initial set of questions that reflected these deliberations. The initial version of the questionnaire then underwent numerous revisions to improve clarity, brevity and formatting. We also asked a survey expert at the CDC's National Center for Health Statistics to review the clarity, framing and formatting of the survey questions. After revising the survey based on the comments we received, we pretested the questionnaire by sending it to laboratory management personnel of 9 hospital coagulation laboratories. (See the Appendix for a copy of the actual survey used.)

Following the recommendation of the U.S. Office of Management and Budget (OMB), we developed an Internet based questionnaire and offered it to all the respondents as an alternative means of responding to the survey. This electronic version mirrored the printed questions, answer selections and formatting. Additionally, it incorporated logical constraints to prevent the respondents from entering conflicting or contradictory answers.

Sample Size and Number of Beds

The rationale for sample size was based on the criterion of ensuring a maximum confidence interval of ±6% for any estimated proportion within the selection strata. We used a random sample stratified by large hospitals (with ≥200 beds) and small hospitals (with <200 beds) to ensure sufficient numbers of the respondents for the 2 strata so that we could analyze data separately for each. The purpose of examining large and small hospitals as separate groups was to determine whether they had different practice profiles regarding coagulation testing:

Type of facility	Population size (1999 AHA directory)	Size of selected sample (percent)
Small Hospitals (< 200 beds)	4,245	375 (9%)
Large Hospitals (≥200 beds)	1,662	425 (26%)
Total	**5,907**	**800 (14%)**

Below is the distribution of the number of beds for the final 632 respondents that composed 79% of the study sample.

Distribution of Number of Beds		
Number of beds	**Number of hospitals**	**Proportion of total**
<50	101	16%
50–99	98	16%
100–149	71	11%
150–199	41	6%
200–249	86	14%
250–299	64	10%
300–349	45	7%
350–399	34	5%
400–499	27	4%
500–599	25	4%
600–799	23	4%
800–999	11	2%
1000–1399	6	1%
0–1399	**632**	**100%**

Survey Implementation

Upon receiving the OMB approval for the survey, the CDC directed ASI to take the following steps:

- identify and contact each laboratory director while verifying the hospital's mailing address,
- print the survey questionnaires and post it on a secure CDC website,
- mail the survey packets to the entire sample, providing each laboratory the option of responding electronically,
- mail reminder postcards to each (potential) participant 1 week after mailing the printed survey, and
- contact the non-respondents by telephone and, if needed, send additional survey packets.

Before selecting the study sample, we excluded laboratory personnel who were involved in pretesting the questionnaire. We also removed the institutions of members of the expert panel from the sampling frame.

We sent each questionnaire along with a cover letter addressed to the laboratory director by name. This letter included the identification code and the password for each hospital to enable them to respond electronically if they elected to do so. We administered this survey and collected results between June 2001 and October 2001. One week after the initial mailing of the questionnaire, the ASI sent a reminder postcard to each respondent, and telephoned the non-respondents within 2 weeks after mailing the postcard. The purpose of the call was to confirm that the respondent received the survey, to encourage the hospital laboratory to participate, and to secure a commitment from the laboratory director to complete and return the survey. We followed up with non-respondents between July 2001 and September 2001. We were not able to contact 7 non-respondents.

Data Entry and Management

Two different individuals keyed the data from each paper survey. Data management personnel had the 2 separate data entries compared, identified any discrepancies, and documented these. A data entry supervisor then performed the adjudication process. The second quality assurance (QA) system used to assess the integrity of the data entry process consisted of examining 10% of the survey booklets after the rekey and adjudication of discrepancies. The auditor compared the survey booklet answers to the database to determine if the answers were correct.

Data Exclusion

We combined the databases containing responses from the 2 modes of data collection (paper and electronic) to create the final analysis database. We found 10 instances when the participant had responded both affirmatively and negatively to a question. We excluded these responses. There were also 9 other instances when the respondent had checked more than 1 selection, despite the instructions specifying that the respondent could check only 1 selection. We excluded all such responses. We also excluded all responses to a gate question and those relating to it if the survey instruction had specified that those subsequent questions not be answered. Due to such a problematic response pattern, we excluded all responses to 1 of the survey's 43 questions (Question 31) and the 3 subsequent sub-questions involving a total of 1,300 responses. We also excluded a total of 568 other responses because, after responding negatively to a gate question, participants provided answers to 1 or more subsequent questions.

After excluding the question and sub-questions noted above, there remained 153 questions and sub-questions involving 96,696 possible responses. The following illustrates how participants responded:

Response Pattern		
Type of response	**Number of responses**	**Proportion of total responses**
Valid	62,321	64%
Blank	33,788	35%
Invalid response pattern	568	0.6%
Invalidly responding both yes and no	10	0.01%
Invalid response to more than 1 selection	9	0.01%
All	**96,696**	**100%**

Data Presentation and Statistics

Reported frequencies relate to affirmative responses we observed for yes-or-no questions and all responses checked in multiple-response questions. These frequencies did not include the excluded data noted above. Percent response in yes-or-no questions is percent of affirmative responses. Percent response in multiple-choice questions is percent of all those responding to 1 or more selection(s). For the check-all-that-apply type questions, these percentages may total >100% if 1 or more respondents checked more than 1 selection. For the choose-only-one type questions, these percentages total 100% because we excluded all multiple responses from further analysis. We compared responses from large and small hospital laboratories using 2-tailed χ^2 test. When significant ($P \leq 0.050$) differences existed, we provided response frequencies and percentages for large and small hospitals separately. We compared the number of professional certifications of the large and small hospital respondents by using 2-tailed *t*-test.

RESULTS AND DISCUSSION

Several surveys addressing specific areas in hospital coagulation laboratory practices have been conducted.[1–12] However, none has dealt with a broad cross section of this specialty in clinical laboratory medicine. Considering that no survey of coagulation laboratory practices can cover all areas of coagulation testing, we tailored the present survey to capture 2 types of information. One set of questions related to general laboratory practices that can also be posed for other areas of laboratory medicine. The other set dealt with specific tests and coagulation disorders with substantial public health significance. In doing so, we hoped to gain a better understanding of the state of coagulation laboratory practices and the extent of their variability across a random sample of hospital laboratories. Our objective was not to formulate testing recommendations. Rather, we undertook to document the extent of variability in laboratory practices so that laboratory and health systems researchers could further evaluate its impact on patient and population health outcome. The result of these outcome-based studies can then be used to formulate recommendations and guidelines for more uniform laboratory testing practices.[13–17]

Response and Sampling Rates

We received 632 responses corresponding to a response rate of 79% (including 20 responses submitted electronically). Response rates of large and small hospitals were as follow:

Survey Response		
Number (Percent) of large hospitals	**Number (Percent) of small hospitals**	***P***
321 (76%)	311 (83%)	0.010

Due to the degree of participation (79% response rate) and sampling (26% of large and 9% of small hospitals), we believe that the results of this survey accurately reflect the state of coagulation laboratory practices as viewed by the respondents in 2001. This response rate may be compared to those for written surveys obtained for other more specific (and shorter) surveys: 51% for a survey of activated partial thromboplastin (aPTT) reporting in Canadian medical laboratories,[1] 77%[5] and 70%[11] for a survey of INR reporting in Canada, and 85% for a survey of prothrombin time (PT) monitoring of anticoagulation therapy in Massachusetts.[12]

Performance of Coagulation Testing

Of those responding, 98% of the large hospitals and 97% of the small hospitals stated that they performed coagulation testing.

Test Requisition and Specimen Management

Use of test requisition forms and information items requested on them. Fifty-six percent stated that they used test requisition forms. Responses of large and small hospital laboratories were as follows:

Use of Test Requisition Forms		
Number (Percent) of large hospitals	**Number (Percent) of small hospitals**	***P***
135 (46%)	188 (67%)	< 0.001

It is conceivable that some participants negatively responding to this question may have done so because they ordered coagulation tests electronically without using a paper-based requisition form. There was a wide variation in the proportion of respondents requesting specific information items on test requisition forms:

Information item	Number (Percent) of large hospitals	Number (Percent) of small hospitals	*P*
Diagnosis	105 (78%)	156 (82%)	0.401
Coumadin use	74 (57%)	86 (51%)	0.276
Unfractionated heparin use	59 (49%)	49 (31%)	0.003
Heparinoid use	47 (39%)	43 (28%)	0.044
LMWH* use	32 (29%)	28 (18%)	0.045
Salicylate (Aspirin) use	18 (17%)	25 (16%)	0.882
Oral contraceptive use	10 (9%)	6 (4%)	0.087

*LMWH is low molecular weight heparin.

Rejection of coagulation specimens. The respondents noted the following reasons for rejecting coagulation specimens based on their policies and procedures:

Reasons for specimen rejection	Number (Percent) of large hospitals	Number (Percent) of small hospitals	*P*
Clotted specimen	312 (100%)	300 (100%)	1.000
Improperly anticoagulated specimen	308 (99%)	296 (99%)	0.961
Insufficiently labeled specimen containers	306 (99%)	297 (99%)	0.678
Excessive specimen transport time	279 (92%)	270 (92%)	0.915
Conflicting patient information	273 (91%)	274 (93%)	0.399
Hemolyzed specimen	266 (86%)	252 (85%)	0.739
Specimen stored at inappropriate temperature	251 (83%)	251 (87%)	0.282
Lack of hospital medical record number	175 (59%)	88 (31%)	< 0.001
Specimen collected via indwelling catheter	96 (33%)	90 (32%)	0.896

These findings indicate that a minority of both large and small hospital respondents noted their policy against use of indwelling catheters for specimen collection. It has been recommended that, due to the presence of anticoagulants at such collection sites, specimens used for monitoring heparin therapy should be collected from a different extremity than the one used for heparin infusion.[16]

Practices Relating to Prothrombin Time (PT) Assay

Performance of PT assay. Of the respondents that provided valid responses, 100% noted performing PT assay.

Anticoagulant concentration. The respondents used the following sodium citrate concentrations:

Concentration	Number (Percent*) of large hospitals	Number (Percent*) of small hospitals
3.2% (109 mmol/L)	244 (81%)	193 (68%)
3.8% (129 mmol/L)	60 (20%)	96 (34%)

*Percentages total >100% due to 8 respondents (4 large and 4 small hospitals) noting that they used both concentrations of sodium citrate.

The respondents reported exclusive use of 3.2% sodium citrate as follows:

Exclusive Use of 3.2% Sodium Citrate		
Number (Percent) of large hospitals	**Number (Percent) of small hospitals**	***P***
240 (80%)	189 (66%)	< 0.001

Based on the WHO recommendations and the NCCLS guidelines, 3.2% citrate is the anticoagulant of choice for coagulation testing.[14] In a recent study,[18] the recommendation to use 3.2%, as opposed to 3.8%, sodium citrate was supported by noting that the concentration of sodium citrate had a significant effect on PT and aPTT assay results. In another study,[19] underfilling of specimen tubes containing 3.8% sodium citrate prolonged PT and especially aPTT compared to 3.2% sodium citrate. When responsive PT and aPTT reagents are used, concentration of sodium citrate has a significant effect on assay results, with 19% of patients receiving intravenous heparin therapy having a greater than 7-second difference when aPTT results were compared.[20] In a survey of aPTT reporting in Canadian medical laboratories,[1] 46% of laboratories were still using 3.8% citrate. In this survey, 27% of the respondents noted that they used 3.8% citrate (5% of these respondents noted that they used both 3.2% and 3.8% citrate), potentially resulting in falsely elevated PT or aPTT results.

Reporting of PT results. Virtually all (99.8%) respondents used international normalized ratio (INR) to report PT; 97% also reported PT in seconds and/or as therapeutic PT ratio:

Results reported in	Number (Percent)
International normalized ratio (INR)	601 (100%)
Seconds	577 (97%)
Therapeutic PT ratio	77 (16%)

Reporting PT results in seconds may lead clinicians to inappropriately compare results between institutions.[5] Reliance on therapeutic PT ratio has been documented to cause errors in anticoagulant therapy.[5,21] Reporting of PT results in INR only is, therefore, the preferred method. Reporting of PT results in INR has increased over the years from 5–57% in 1992[11,12] to 98–100% in 1996[5,10] and 99.8% in the current survey. Reporting of PT results in INR only in Canada increased from 15% of all licensed medical laboratories in 1992 to 36% of these laboratories in 1996. This survey shows that 3% of the U.S. hospital laboratories reported PT results in INR only. Reporting PT results in both seconds and INR increased steadily over the years from 36% in 1992 (Canada) to 60% in 1996 (Canada) and 80% in 2001 (U.S.). Finally, the practice of reporting PT results in seconds only decreased from 36% in 1992 to <1% in 1996–2001.

Ninety-seven percent of the respondents provided PT results in seconds. This may be compared to the rates of 99% reported in 1992,[12] 95% reported in 1996,[10] 72% in a 1992 Canadian survey reported in 1995,[11] and 60% in a follow-up 1996 Canadian survey reported in 1998.[5]

Sixteen percent provided therapeutic PT ratio. This rate may be compared to a rate of 43% in a survey of anticoagulant therapy monitoring reported in 1996,[10] and rates of 13% and 2.5% in the 1992[11] and 1996[5] surveys of Canadian medical laboratories, respectively. The rate of 43% in the former survey is less generalizable since it involved only 58 U.S. health centers, which were all academic institutions. Furthermore, those conducting the survey of these centers themselves have noted that wide variation existed in the reporting of coagulation tests (seconds and INR) and of patient therapeutic status.[10]
The following table shows how PT results were reported in our survey compared to the results of the 1992 and 1996 Canadian surveys:

Format Used to Report PT Result by the U.S. Hospitals and Canadian Medical Laboratories			
Reporting format	U.S., 2001 (n = 626)	Canada, 1996 (n = 649)[5]	Canada, 1992 (n = 857)[11]
Seconds and INR	60%*	60%	36%
Seconds, INR and PT ratio	12%†	–	–
Not specified	4%	–	–
INR only	3%	36%	15%
INR and PT ratio	0.5%	1.5%	6%
Seconds only	0%	<1%	36%
PT ratio only	0%	1%	7%

*An additional 20% noted that they reported PT results in both seconds and INR but had failed to indicate whether or not they used therapeutic PT ratio.

†This proportion may be as high as 32% since an additional 20% noted that they reported PT results in seconds and INR while failing to note whether they used therapeutic PT ratio.

Reference interval for PT assay. Ninety-two percent of the respondents conducted in-house evaluations to establish reference intervals for PT assay. Responses from large and small hospitals were significantly different:

Number (Percent) of large hospitals	Number (Percent) of small hospitals	*P*
291 (97%)	277 (87%)	< 0.001

The respondents not conducting in-house evaluations to establish reference intervals for PT did so as follows:

Other method used to establish PT reference interval	Number (Percent)
Manufacturer's instructions	31 (57%)
Published values	16 (30%)
Others	10 (19%)

*Percentages total >100% due to 3 small hospital respondents noting that they used both published values and manufacturer's instruction to establish their PT reference intervals.

In-house determination of the PT reference interval was based on the following minimum number of subjects:

Minimum number of subjects used	Number (Percent*) of large hospitals	Number (Percent*) of small hospitals
20 or fewer	24 (8%)	62 (25%)
21-39	112 (38%)	123 (49%)
40-59	88 (30%)	40 (16%)
60-119	56 (19%)	18 (7%)
120-199	11 (4%)	4 (2%)
200 or more	5 (2%)	4 (2%)

*Percentages do not equal 100% because of rounding to the nearest 1%. The response patterns of the large and small hospital respondents were significantly different ($P < 0.001$).

Most respondents (46% of the large hospitals and 74% of the small hospitals, $P < 0.001$) used less than 40 subjects to establish their PT reference intervals. To establish a reference interval, the NCCLS has recommended a minimum of 120 subjects for each reference population or subclass as the smallest number allowing determination of a 90% confidence interval around reference limits.[22] In this survey, 5% of the respondents noted using at least 120 subjects to establish their reference ranges for PT assay.

Methods and reagents used to assay for PT. The respondents used the following methods to assay for PT:

Method Used to Assay for PT	
Method	**Number (Percent)**
Optical	527 (88%)
Mechanical	71 (12%)
Manual	1 (0.2%)
None of the above	1 (0.2%)

In the 1996 survey of Canadian medical laboratories, 1% used a manual method to assay for PT.[5]

The respondents used the following reagents for PT assay:

Reagents Used for PT Assay*		
Reagent	**Large hospital (percent) response**	**Small hospital (percent) response**
Dade Behring Thromboplastin C Plus	76 (25%)	106 (36%)
Innovin	72 (23%)	46 (16%)
Hemoliance Brain Thromboplastin	37 (12%)	23 (8%)
OTC Simplastin L	26 (8%)	11 (4%)
Pacific Hemostasis D	4 (1%)	10 (3%)
Others	98 (32%)	97 (33%)

*The use of trade names is for identification purposes only and does not constitute endorsement by the CDC or the U.S. Department of Health and Human Services. There were 4 large hospitals that responded by stating that they used 2 different reagents–resulting in percentages totaling >100%.

Among thromboplastins listed, Innovin is the only recombinant protein (human tissue factor or factor VIIa).[23] Results obtained with recombinant thromboplastin on an optical analyzer even after prolonged storage of the plasma samples at room temperature were considered suitable for oral anticoagulation control.[24] Advantages of recombinant reagents such as Innovin and Recombiplastin are purity and consistency of reagents. Innovin and Recombiplastin have been shown to yield different INR values when compared to traditional reagents purified from tissue extracts.[23,25,26] Of all the respondents, 20% used Innovin. Of the large hospital respondents, 23% reported using Innovin compared to 16% of the small hospital laboratory respondents ($P = 0.019$). Although use of Recombiplastin as the other major recombinant thromboplastin was not assessed, larger facilities may use this and other recombinant reagents in preference to traditional reagents prepared from tissue extracts with their inherent variability from lot to lot or from reagent to reagent.

Sensitivity of PT assay to heparin

Determining sensitivity of PT assay to heparin. Seventeen percent of the respondents determined the sensitivity of their PT assays to heparin.

Selecting a PT-thromoboplastin reagent insensitive to heparin in the therapeutic range. Fifty percent of the respondents selected a PT-thromboplastin reagent that was insensitive to heparin in the heparin therapeutic range. Significantly different proportions of the large and small hospitals selected an insensitive PT-thromboplastin reagent:

Number (Percent) of large hospitals	Number (Percent) of small hospitals	*P*
170 (59%)	101 (40%)	< 0.001

According to consensus guidelines developed at the 1997 CAP conference, laboratories should determine the sensitivity of their PT assay to heparin and, where possible, select a thromboplastin that is insensitive to heparin in the therapeutic range.[14]

International sensitivity index (ISI) of thromboplastin lot currently used. The ISI of the respondents' current thromboplastin lot was 0.89–2.63 (average, 1.60; median, 1.81). The large hospital respondents reported an average ISI of 1.52 (median, 1.56), while the small hospitals reported an average of 1.70 (median, 1.89).

Due to increased variability in INR resulting from ISI values deviating significantly from unity, various professional organizations have recommended using thromboplastin reagents with ISI values closer to 1. The CAP recommends thromboplastins with a manual ISI between 0.9 and 1.7 and toward the lower end of this scale.[14] The ISI of the respondents' current reagent lots ranged between 0.89 and 2.63. Forty-four percent reported ISI values of ≤1.70. Of the large hospital respondents, 50% reported ISI values of ≤1.70 compared to 36% of the small hospital respondents ($P = 0.001$).

Two published articles have reported ISI values of survey participants. A 1992 report involving 88 acute care hospitals in Massachusetts reported ISI values of 1.89–2.74.[10] The second involved a survey of all licensed Canadian medical laboratories in 1996 and 1992.[5] This latter report noted that average ISI value had decreased from 2.07 in 1992 to 1.63 in 1996.[11] Of the respondents to the 1996 survey of Canadian medical laboratories, 35% had reported ISI values of ≤1.2 as recommended by the American College of Chest Physicians.[27] In this survey, 34% of the respondents used an ISI of ≤1.20. Forty-two percent of the large hospital respondents reported ISI values of ≤1.20 compared to 24% of the small hospital respondents ($P < 0.001$).

In a survey of 58 academic institution in the U.S., 79% of the hospitals did not confirm accuracy of the ISI for their own analyzers.[10] Coagulation instruments may affect ISI, which can differ from the assigned value by a clinically significant degree.[14,28] We did not capture in this survey the proportion of the respondents confirming accuracy of the ISI value for their own analyzers.

Practices Relating to Activated Partial Thromboplastin Time (aPTT) Assay

Performance of aPTT assay. Ninety-nine percent of the respondents performed aPTT assay.

Therapeutic range. The respondents noted having an aPTT therapeutic range for heparin as follows:

Number (Percent) of large hospitals	Number (Percent) of small hospitals	*P*
213 (73%)	142 (53%)	< 0.001

While 64% of the respondents stated they reported the aPTT therapeutic range for heparin when monitoring heparin therapy, 9% included the corresponding heparin concentration with aPTT results.

It has been recommended that each laboratory establish an individual therapeutic range for heparin specific to its own reagent and instrument system.[29,30] Significant variations between heparin sensitivity of aPTT reagents produced under the same name by the same supplier have been observed.[29] Variations were such that, using the recommended aPTT ratio or prolongation of aPTT for monitoring heparin therapy, one would have achieved significantly different degree of heparinization from year to year. Also, the latest CAP consensus guideline notes that therapeutic range of unfractionated heparin for the aPTT reagent-instrument system should be determined with each change in reagent (lot number or manufacturer) or instrument.[16]

In a 1998–1999 survey of aPTT reporting in Canadian medical laboratories,[1] 66% of institutions had established an individual therapeutic range for aPTT testing. The current 2001 U.S. survey of hospital coagulation laboratories produced similar results (64%).

How the aPTT therapeutic range for heparin was determined. The respondents did the following to determine the aPTT therapeutic range for heparin:

Practices to determine the aPTT therapeutic range for heparin	Large hospitals	Small hospitals	*P*
Using samples from patients on heparin therapy to compare a new reagent lot to an old reagent lot	116 (66%)	57 (50%)	0.007
Using heparin spiked samples to compare a new reagent lot to an old reagent lot	80 (47%)	50 (46%)	0.881
Performing anti-Xa assay	76 (47%)	17 (18%)	< 0.001
Using heparin spiked samples to compare a new heparin lot to an old heparin lot	19 (12%)	22 (21%)	0.038
Using samples from patients on heparin therapy to compare a new heparin lot to an old heparin lot	19 (11%)	14 (14%)	0.602
Performing protamine sulfate titration	17 (11%)	5 (5%)	0.134

The number of practices used to determine the aPTT therapeutic range for heparin was as follows:

Number of practices[*]	Number (Percent) of large hospitals	Number (Percent[†]) of small hospitals
0	121 (38%)	192 (62%)
1	103 (32%)	74 (24%)
2	65 (20%)	33 (11%)
3	25 (8%)	9 (3%)
4	5 (2%)	2 (0.6%)
5	1 (0.3%)	1 (0.3%)
6	1 (0.3%)	0

[*]The number of practices were significantly different for the large and small hospital respondents ($P < 0.001$).
[†]Percentages do not total 100% due to rounding to the nearest 1%.

Reagent sensitivity in *ex vivo* samples has been reported to be substantially different to that in *in vitro* samples.[30] Specific therapeutic ranges may be necessary. Samples prepared by adding heparin to normal plasma *in vitro* can be misleading and should not be used. *In vitro* sensitivity curves using different reagents are varied at therapeutic heparin levels.[25] In contrast, aPTT reagents reportedly did not differ *ex vivo*. Studies have shown that *in vitro* curves demonstrate poor performance. In one study,[31] 60% of patients did not adequately compare by aPTT estimation of plasma heparin levels. The aPTT therapeutic range for heparin should be determined by comparing (1) *ex vivo* specimens with an appropriately validated heparin assay (preferably) or (2) *ex vivo* specimens to a previously calibrated aPTT using a method to control for reagent drift.[16] Equivalence should be determined by using *ex vivo* plasma samples obtained from patients treated with unfractionated heparin rather than spiked *in vitro* heparinized plasma samples.[30,31] Forty-six percent of all respondents reported using heparin-spiked samples to determine their aPTT therapeutic range for heparin, while 59% used *ex vivo* specimens from heparinized patients. These may be compared to the rates of 67% and 33% for heparin spiked and *ex vivo* specimens, respectively, obtained in the 1998–1999 Canadian survey.[1] As part of a 1995 CAP comprehensive coagulation survey, 23% of laboratories reported using in vitro heparin spiking to establish an aPTT therapeutic range for heparin.[32]

In this survey, 9% (n = 22) used protamine sulfate titration to assay for heparin in *ex vivo* specimens, while 37% (n = 93) used anti-Xa assay for heparin assay. Other methods were used by 27 respondents. Sixty-five percent of the respondents assaying for heparin did so using an anti-Xa assay, 15% used protamine sulfate titration and 19% used other methods. In the 1998–1999 Canadian survey, 90% used an anti-Xa assay and 10% used protamine sulfate titration. In this Canadian survey, however, no option was provided for other methods.[1]

<u>When the aPTT therapeutic range for heparin was reconfirmed</u>. The respondents reconfirmed the aPTT therapeutic range for heparin under the following circumstances:

Circumstances to reconfirm the aPTT therapeutic range for heparin	Number (Percent) of hospitals
When new instrumentation is used	282 (79%)
When new reagent lots are used	269 (75%)
When new reagents are used	181 (51%)
After a specified time period	77 (22%)
None of the above	29 (8%)

Current consensus maintains that therapeutic ranges should be recalculated after the introduction of a new reagent or a new lot of the same reagent or a change in instrument.[1,16,33] Ninety percent of the respondents reconfirmed the aPTT therapeutic range for heparin when either new reagents, new reagent lots or new instrumentation was implemented; and 47% did so in all 3 circumstances. The response patterns obtained from large and small hospitals were significantly different. Fifty-two percent of the large hospitals noting adherence to at least 1 of the 3 practices adhered to all of the 3 practices compared to 39% of the small hospitals (P = 0.021).

<u>Specimen management for aPTT assay</u>. The respondents indicated they adhered to the following practices to manage specimens before aPTT analysis:

Practices used for the aPTT assay specimen management	Large hospitals	Small hospitals	*P*
Specimens were assayed within 4 hours after phlebotomy	276 (96%)	259 (97%)	0.490
Specimens were centrifuged within 1 hour of collection	229 (84%)	238 (92%)	0.007
Specimens were kept at room temperature prior to testing	223 (84%)	196 (80%)	0.188
Specimens were kept at 4 °C prior to testing	47 (20%)	54 (24%)	0.335

Specimens for aPTT assay are stable for up to 8 hours at room temperature except for patients receiving unfractionated heparin therapy.[34] Heparinized samples, when stored uncentrifuged at room temperature, demonstrate a clinically significant shortening of aPTT and individual samples demonstrate a more than 50% decrease in *ex vivo* heparin levels at 4 hours. According to an approved NCCLS guideline,[35] samples can be assayed up to 4 hours after phlebotomy if centrifuged within 1 hour of collection.

Ninety-six percent of all respondents stated that specimens were assayed within 4 hours after phlebotomy, and 88% noted that specimens were centrifuged within 1 hour of collection. Also, 22% of the respondents noted that specimens were kept at 4 °C prior to testing, and 82% of the respondents stated that specimens were kept at room temperature before testing. In the 1998–1999 survey of Canadian medical laboratories,[1] 90% of responding laboratories reported analyzing specimens within 4 hours of specimen collection. Of the participants responding to 1 or both questions relating to aPTT assay within 4 hours after collection and tube centrifugation within 1 hour of specimen collection, 99% adhered to at least 1 practice and 74% adhered to both. In this survey, of the large hospital respondents, 69% assayed for aPTT within 4 hours of phlebotomy and centrifuged specimens within 1 hour of collection compared to 79% of the small hospital respondents (P = 0.005).

Practices Relating to Assays for von Willebrand Disease (vWD)

Performance of von Willebrand factor antigen (vWF Ag) assay. Six percent of the respondents performed vWF Ag assay. Responses from large and small hospitals were significantly different:

Number (Percent) of large hospitals	Number (Percent) of small hospitals	*P*
35 (12%)	1 (0.4%)	< 0.001

Reporting of ABO specific reference interval for vWF Ag assay. Nineteen percent of the respondents that performed vWF Ag assay, reported an ABO specific reference interval for this assay.

Significantly higher vWF Ag levels have been found in individuals homozygous for the Se allele than in those heterozygous for this allele,[36] and lower levels of factor VIII and vWF Ag have been reported in individuals with blood type O compared to individuals with other ABO blood types.[37] Data clearly show significant linkage between the ABO locus and vWF Ag, with levels of vWF Ag exhibiting significant differences between O heterozygotes and non-OO homozygotes. However, use of ABO adjusted ranges for vWF Ag levels might not be essential for the diagnosis of this disorder; bleeding symptoms may depend on vWF Ag regardless of the ABO type.[38]

Methodology used for vWF Ag assay. The respondents used the following methodologies to assay for vWF Ag:

Methodology used for vWF Ag assay	Number (Percent)
Latex immunoassay (LIA)	13 (37%)
ELISA	10 (29%)
Electrophoresis	6 (17%)
Others*	6 (17%)

*Five of the respondents used immunoturbidimetric assays and 1 used Laurel rocket immunoassay. No respondent reported using more than 1 methodology for vWF Ag assay.

The electroimmunodiffusion (EID) method, also known as Laurel rocket immunoassay is associated with the greatest variability in vWF Ag test results, and both the EID and LIA methods show poorer sensitivity at low vWF Ag levels compared to ELISA methods.[4] Forty percent of the respondents used LIA or EID methods.

Performance of assay for von Willebrand factor (Ristocetin cofactor) activity. Seven percent of the respondents performed assay for Ristocetin cofactor activity. Responses from the large and small hospital respondents were significantly different:

Number (Percent) of large hospitals	Number (Percent) of small hospitals	*P*
41 (14%)	1 (0.4%)	< 0.001

Methodology used for assay of Ristocetin cofactor activity. The respondents used the following methodologies to assay for Ristocetin cofactor activity:

Methodology for assay of Ristocetin cofactor activity	Number (Percent)
Platelet aggregometry	31 (76%)
ELISA	2 (5%)
Collagen binding assays	1 (2%)
Others*	7 (17%)

*One respondent stated using a platelet function analyzer while the other 6 noted using platelet agglutination/aggregation methods–which is the same as platelet aggregometry–with 2 of these specifying use of the Dade Behring method. No respondent reported using more than 1 methodology for Ristocetin cofactor activity assay.

Collagen binding assays for vWF activity (Ristocetin cofactor activity) have been shown to perform better than other assays in terms of their ability to detect functional von Willebrand factor (vWF) discordance, i.e., Type 2 vWD.[4] However, these assays are less sensitive than vWF Ag assay in terms of their ability to measure overall level of vWF since they detect only highly adhesive vWF. For assays of vWF activity, the greatest variability in results and the poorest sensitivity to low vWF Ag levels was obtained using the platelet agglutination/aggregation methods; however, these methods showed better performance in identifying Type 2 vWD.[4] In our survey, 5% performed ELISA to assay for vWF activity and 2% used a collagen binding assay. The remaining 93% used platelet function tests based on platelet agglutination/aggregation as functional tests for vWF activity. Of the respondents noting that they performed 1 or more vWF assays (antigen, activity or multimers assays), 38% performed both vWF Ag assay and a vWF activity assay, 25% performed only vWF activity assays, 15% performed only vWF Ag assays, 15% performed all 3 vWF assays, and 6% provided results for vWF multimers.

Sixty-nine percent of the respondents performed vWF Ag test. In a 1999 Australasian multi-laboratory survey of diagnostic practice and efficacy of laboratory tests for vWD, all 25 laboratories performed tests for vWF Ag, 60% of the respondents performed both vWF Ag assay and a vWF activity assay, and 40% performed all 3 vWF assays.[4] In our 2001 U.S. survey, 46% performed a single vWF test (vWF activity, 25%; vWF Ag, 15%; vWF multimers, 6%) to evaluate vWD, while no respondents in the 1999 Australasian survey did so. Assaying for vWF Ag will not detect many qualitative defects; so, use of this assay alone will lead to many Type 2 vWD patients being missed by the laboratory.[4] A survey conducted in Australasia pointed to considerable variation among laboratories in the tests and methods as well as the composite test panels used to diagnose vWD.[3] What we have observed here implies a laboratory practice pattern not consonant with an adequate assessment of vWD.[39] Performance of vWF Ag assay by only 69% of the respondents and performance/use of only a single test by 46%, including 15% using vWF Ag alone, were somewhat surprising. Caution is indicated against diagnosis of vWD made based on single vWF assay results.[40] In our survey, 79% of the respondents assayed for vWF activity; and they did so either alone (25%), in combination with vWF Ag assay only (38%), and in combination with both vWF Ag and vWF multimers assays (15%). These results should be viewed in light of the fact that the questions on vWF Ag and vWF activity dealt with actual performance of these assays; some participants responding negatively to these questions may provide results for vWF Ag and vWF activity tests by sending their specimens to outside laboratories.

Provision of vWF multimers results. Two percent of the respondents provided results for vWF multimers. The responses from large and small hospitals were significantly different:

Number (Percent) of large hospitals	Number (Percent) of small hospitals	*P*
10 (3%)	1 (0.4%)	0.007

The respondents noted the following circumstances for the assay of vWF multimers:

Circumstance for the assay of vWF multimers	Number (Percent)
Only when ordered by a clinician	9 (82%)
When Ristocetin cofactor is decreased	3 (38%)
When Ristocetin cofactor is disproportionately decreased relative to vWF Ag	2 (29%)
When antigen and activity are both low	2 (25%)
Only if Ristocetin induced platelet aggregation indicates a Type II B vWD	1 (13%)

This assay is used to confirm or subtype vWD that has been previously diagnosed.[40] It has been suggested that it would not be appropriate to assay for vWF multimers during initial vWD investigation process. Although 8 of the 11 the respondents assayed for vWF multimers in combination with assays for vWF Ag and vWF activity, 3 respondents assayed for vWF multimers without noting that they assayed for either vWF Ag or vWF activity. In 2 recent Australasian surveys of vWF testing laboratories, 12–16% of the respondents assayed for vWF multimers.[3,4] This may be compared to 21% of the U.S. hospital laboratory respondents doing the same as reported in this survey. The result of this survey should be considered in light of the observation that the value of vWF multimers assay is diminishing in the face of better test systems and diagnostic processes.[40] Assays for vWF multimers are used to imply probable Type II A or Type II M vWD and not Type II B vWD.[40] Interestingly, 9 of the 11 respondents stated that they performed vWF multimers assays only when ordered by a clinician.

The following shows vWF testing patterns in this 2001 U.S. survey and a 1999 Australasian survey:

Test Patterns Used by the U.S. Hospitals and the Australasian Medical Laboratories for Diagnosis of vWD		
Test(s)	U.S., 2001 (n = 52)	Australasia, 1992 (n = 25)[4]
vWF Ag and vWF activity	20 (38%)	15 (60%)
vWF Ag, vWF activity and vWF multimers	8 (15%)	10 (40%)
vWF activity only	13 (25%)	–
vWF Ag only	8 (15%)	–
vWF multimers only	3 (6%)	–

Practices Relating to Thrombosis/Hypercoagulability Workup

Protein S assays. Five percent of the respondents usually performed the assay for protein S activity (functional test) before the antigenic assay. The responses from large and small hospitals were significantly different:

Number (Percent) of large hospitals	Number (Percent) of small hospitals	*P*
31 (10%)	1 (0.3%)	< 0.001

If the results of the functional test were decreased, 17% performed antigenic assay to differentiate Type I deficiency from Type II while 20% performed free and total protein S antigen assay.

Performance of activated protein C (APC) resistance and factor V mutation assays. Six percent of the respondents performed activated protein C (APC) resistance assay. The responses from large and small hospitals were significantly different:

Number (Percent) of large hospitals	Number (Percent) of small hospitals	*P*
32 (11%)	3 (1%)	< 0.001

If after performing the APC resistance assay, results indicated resistance to APC, 61% obtained results for factor V Leiden mutation.

More than 11 million Americans are factor V Leiden carriers, and 143,000 are homozygous for this mutation.[41] Homozygosity or heterozygosity for factor V Leiden in the absence of symptoms does not necessarily indicate that preventive treatment is required.[42] Furthermore, there is no established intervention to reduce thrombotic risk. Thrombotic risk can be modified by various acquired and environmental conditions such as pregnancy, oral contraceptives, estrogen therapy, malignancy, stroke with extremity paresis, trauma, surgery or immobility.[43]

Depending on the APC resistance functional assay used and the cut-off values for defining an abnormal result, factor V Leiden mutation may account for 85–95% of patients with APC resistance.[43] Factor V Leiden mutation is believed to produce a relative risk of venous thrombosis of 7-fold in the heterozygous state and 80-fold in the homozygous state. Even in the homozygous state, however, this mutation does not appear to cause disease early in life, as seen with protein S and protein C homozygosity. Activated protein C resistance with normal factor V genotype is a risk factor for venous thrombosis.[44] However, there is no major effect of APC resistance on life expectancy.[45] Consequently, long-term anticoagulation in carriers of factor V Leiden, on the basis of the carrier state alone, is not indicated. In view of all these, it was interesting to note that 61% of the respondents obtained results for factor V Leiden mutation if results indicated resistance to APC.

Algorithm for Diagnosing a Lupus Anticoagulant (LA)

Offering an LA profile. Eighteen percent of the respondents offered an LA profile. The responses from large and small hospitals were significantly different:

Number (Percent) of large hospitals	Number (Percent) of small hospitals	*P*
92 (30%)	18 (6%)	< 0.001

Our obtained rate of 18% for offering an LA profile may be compared to the rate of 34% obtained in the 1998–1999 Canadian survey.[1]

Practices leading to mixing studies. Participants noted the following circumstances for performing a mixing study when PT result was prolonged:

When mixing studies are performed with prolonged PT*	Number (Percent†) of large hospitals	Number (Percent†) of small hospitals
Only if there is an additional order for the mixing study	227 (78%)	98 (34%)
Our laboratory does not offer mixing studies for PT	36 (12%)	175 (61%)
Always when PT is prolonged	10 (3%)	5 (2%)
Only if PT was ordered as part of the LA Profile	10 (3%)	0
Others	9 (3%)	7 (2%)

*The response patterns from large and small hospitals were significantly different ($P < 0.001$).
†Percentages do not total 100% due to rounding to the nearest 1%.

Participants noted the following circumstances for performing a mixing study when aPTT result was prolonged:

When mixing studies are performed with prolonged aPTT*	Number (Percent†) of large hospitals	Number (Percent) of small hospitals
Only if there is an additional order for the mixing study	228 (78%)	98 (37%)
Our laboratory does not offer mixing studies for aPTT	30 (10%)	153 (58%)
Always when aPTT is prolonged	12 (4%)	5 (2%)
Only if aPTT was ordered as part of the LA Profile	13 (4%)	0
Others	8 (3%)	8 (3%)

*The response patterns from large and small hospitals were significantly different ($P < 0.001$).
†Percentages do not total 100% due to rounding to the nearest 1%.

Workup to diagnose an LA. Seventeen percent of the respondents routinely initiated a workup to diagnose an LA if results of the mixing study for aPTT did not correct to normal. The responses from large and small hospitals were significantly different:

Number (Percent) of large hospitals	Number (Percent) of small hospitals	*P*
54 (21%)	9 (8%)	0.004

If results of the mixing study for aPTT did not correct to normal, the respondents indicated routinely performing the following assays to diagnose an LA:

Tests performed	Number (Percent)
Dilute Russell viper venom time (1)	46 (79%)
Hexagonal phase phospholipid assay (Staclot LA) (2)	24 (51%)
Lupus sensitive aPTT (3)	19 (40%)
Platelet neutralization procedure (4)	17 (35%)
Tissue thromboplastin inhibition test (5)	4 (9%)
Kaolin clotting time (6)	2 (5%)

Of those using 1 or more of the above tests, 58% used more than 1 test. The respondents noted the following test combinations more than once:

Test combinations performed*	Number (Percent†)
1 and 2	8 (23%)
1 and 4	6 (17%)
1, 2 and 3	6 (17%)
3 and 4	3 (9%)
1 and 3	2 (6%)
2 and 3	2 (6%)
1, 2, 3 and 4	2 (6%)

*There were a total of 13 test combinations. The above combinations constituted 83% of all those using more than 1 test. The numbers refer to the designated tests noted in the previous table.
†Percentages refer to the proportion of respondents noting the use of more than 1 test.

Practices Relating to Monitoring of Low Molecular Weight Heparin (LMWH) Therapy

Fourteen percent of the respondents monitored LMWH therapy. The responses from large and small hospitals were significantly different:

Number (Percent) of large hospitals	Number (Percent) of small hospitals	*P*
55 (19%)	27 (10%)	0.002

Since we did not ask whether their institutions used LMWH therapy, we do not know what proportion of the respondents using LMWH actually monitored for it. In the 1998–1999 survey of Canadian medical laboratories, 71% of institutions used LMWH, thus obviating many of the issues surrounding aPTT testing.[1] Some form of monitoring for LMWH therapy was used by 25% of all Canadian medical laboratories (35% of those using LMWH therapy). This rate of 25% may be compared to the overall rate of 14% in our survey.

Assays used. Those monitoring LMWH therapy used the following assays:

Assay used to monitor LMWH therapy	Number (Percent) of large hospitals	Number (Percent) of small hospitals	*P*
aPTT	23 (58%)	24 (96%)	0.001
Anti-Xa	32 (65%)	3 (18%)	0.001
Factor Xa (inhibitor assay)	3 (8%)	1 (6%)	0.795
Thrombin inhibitor assay (HEP test)	0	0	–

The chromogenic anti–factor Xa method is recommended for monitoring LMWH, while aPTT is not.[15] Of all the respondents, 53% used an anti-Xa assay to monitor LMWH therapy, while 72% used aPTT assay to do so. While a significantly smaller proportion of the large hospital respondents used aPTT assay to monitor LMWH therapy compared to the small hospital respondents ($P = 0.001$), a significantly greater proportion of the large hospitals respondents used anti-Xa assay to do so ($P = 0.001$). In the 1998–1999 Canadian survey, 71% of those monitoring LMWH did so by a chromogenic anti-Xa assay, and the remaining 29% used an anti-Xa clotting assay. In agreement with our findings, none of the Canadian respondents used thrombin inhibitor assay (HEP test).

Calibrators used. The respondents indicated they used the following calibrators for anti-Xa assay:

Calibrator	Number (Percent)
LMWH supplied by pharmacy	19 (53%)
Internal standard LMWH	8 (22%)
Unfractionated heparin	5 (14%)
Internal standard unfractionated heparin	4 (11%)
Heparinoid	1 (3%)
Others	8 (22%)

Seventy-four percent of the respondents used different calibration curves for LMWH and unfractionated heparin, while 42% used different calibration curves for each type of LMWH. The CAP has recommended that laboratories use different calibrations for LMWH and unfractionated heparin,[15] and establish calibration curves with each lot and type of LMWH.[16] The CAP has also recommended that pharmaceutical heparin be calibrated against an international (preferably the WHO) standard using an anti-factor Xa assay.[16]

Four of the 19 the respondents reporting use of a LMWH supplied by pharmacy also stated that they used unfractionated heparin as a calibrator for the anti-Xa assay. One of these 4 respondents also used heparinoid as a calibrator. Finally, 1 of the 8 respondents using an internal LMWH standard also used an internal standard for unfractionated heparin. A calibrated LMWH has been recommended for establishing the standard curve for assay of LMWH, and unfractionated heparin cannot be used for this purpose.[15]

Nevertheless, 28% of the respondents reported using reagents other than LMWH as a calibrator for the anti-Xa assay. Nine of these 10 respondents used unfractionated heparin while 1 used heparinoid.

Timing of anti-Xa assay. We obtained the following responses regarding how long after subcutaneous administration of LMWH the laboratory recommended specimen collection for anti-Xa testing:

Time of specimen collection after subcutaneous administration of LMWH	Number (Percent)
Our coagulation laboratory does not recommend a time for testing	17 (46%)
4 hours after injection	12 (32%)
Between 2 and 4 hours after injection	5 (14%)
Do not know	2 (5%)
5 hours or more after injection	1 (3%)
Others	0

When LMWH is monitored, the sample should be obtained 4 hours after subcutaneous injection.[15]

Availability of Specific Coagulation Tests

The respondents performed the 29 tests examined in this survey as follows:

Test	Number (Percent) of large hospitals	Number (Percent) of small hospitals	*P*
PT	310 (100%)	295 (100%)	1.000
aPTT	309 (99%)	292 (98%)	0.229
Bleeding time	277 (89%)	270 (90%)	0.699
Fibrinogen	295 (95%)	163 (59%)	< 0.001
D-dimer	252 (83%)	124 (46%)	< 0.001
Fibrin(ogen) degredation products	200 (67%)	92 (35%)	< 0.001
Activated clotting time	170 (58%)	70 (27%)	< 0.001
Thrombin time	159 (54%)	50 (19%)	< 0.001
Factor VIII activity	105 (36%)	5 (2%)	< 0.001
Factor IX activity	92 (32%)	3 (1%)	< 0.001
Factor VII activity	70 (25%)	3 (1%)	< 0.001
Platelet aggregation study	70 (24%)	2 (0.8%)	< 0.001
Factor V activity	67 (24%)	2 (0.8%)	< 0.001
Factor X activity	64 (23%)	2 (0.8%)	< 0.001
Factor II activity	54 (19%)	2 (0.8%)	< 0.001
Heparin assay (Anti-Xa)	48 (17%)	4 (2%)	< 0.001
vWF (Ristocetin cofactor) activity	41 (14%)	1 (0.3%)	< 0.001
Bethesda assay-inhibitor titer	40 (14%)	0	< 0.001
Ristocetin titration of platelet aggregation	36 (13%)	1 (0.4%)	< 0.001
vWF Ag	35 (12%)	1 (0.4%)	< 0.001
Factor VIII antigen	33 (12%)	2 (0.8%)	< 0.001
Activated protein C resistance	32 (11%)	3 (1%)	< 0.001
Euglobulin clot lysis time	25 (9%)	2 (0.8%)	< 0.001
Factor V Leiden	27 (10%)	0	< 0.001
Plasminogen (functional) assay	23 (8.2%)	1 (0.4%)	< 0.001
Factor X antigen	17 (6.0%)	0	< 0.001
Platelet antibody	14 (5.0%)	0	< 0.001
vWF multimers	5 (1.8%)	0	0.035
Plasminogen antigen	2 (0.7%)	0	0.184

Except for the hospitals performing tests for PT, aPTT and bleeding time, and the 2 large hospitals assaying for plasminogen antigen, a significantly greater proportion of large hospitals performed any of the above tests in-house compared to small hospitals ($P = 0.035$ for 5 large hospitals performing vWF multimers and $P < 0.001$ for all other tests.). Only 4 small hospitals performed an in-house anti-Xa assay for heparin. This is in agreement with our finding (previously discussed) noting a significantly lower uptake of anti-Xa assay for LMWH therapy compared to the large hospital respondents ($P = 0.001$). It also shows that the apparent reason the small hospitals mostly use aPTT assay in lieu of anti-Xa assay to monitor LMWH therapy may be that few of them even perform an in-house anti-Xa assay.

Test Result Information, Interpretations and Recommendations

The respondents provided the following test result information, interpretations and recommendations for 4 selected coagulation tests:

Item noted on test reports	PT	aPTT	Protein C	vWF Ag
Measurement units	592 (97%)	589 (98%)	58 (92%)	38 (90%)
Reference (Normal) interval	591 (97%)	585 (97%)	60 (95%)	39 (93%)
Specimen comments (if needed)	535 (87%)	528 (87%)	48 (76%)	33 (79%)
Therapeutic ranges	331 (54%)	229 (38%)	3 (5%)	2 (5%)
Written interpretation	38 (6%)	24 (4%)	14 (22%)	9 (21%)
Testing methodology/reagent	26 (4%)	23 (4%)	4 (6%)	2 (5%)
Suggested diagnoses	13 (2%)	10 (2%)	6 (10%)	5 (12%)
Possible drug interactions	5 (1%)	7 (1%)	13 (21%)	3 (7%)
No test result interpretation	179 (29%)	182 (30%)	19 (30%)	14 (33%)
Recommendations for further testing	11 (2%)	14 (2%)	9 (14%)	5 (12%)
Recommendations for treatment	5 (1%)	4 (1%)	2 (3%)	2 (5%)
Recommendations to test family members	1 (0.2%)	1 (0.2%)	5 (8%)	4 (10%)
No recommendation	312 (51%)	302 (50%)	29 (46%)	20 (48%)

The reporting of coagulation tests and patient therapeutic status varies widely.[6] This survey shows that the information items most frequently provided on coagulation laboratory test reports were measurement units (90–98% of the respondents), reference intervals (93–97% of the respondents) and specimen comments (76–87% of the respondents). Ninety-seven percent provided a reference range on PT test reports, compared to the rate of 93% in a survey of 58 academic hospital clinical laboratories.[10] Adjusted dose and therapeutic heparin require anticoagulant monitoring within a defined therapeutic range.[16] Sixty-six percent of institutions in the 1998–1999 survey of Canadian medical laboratories established therapeutic ranges for aPTT testing, and 64% routinely reported therapeutic ranges for oral anticoagulation control.[1] In our survey, 54% reported providing therapeutic ranges for PT and 38% did so for aPTT.

Items least often provided by the respondents on coagulation reports for PT, aPTT, vWF Ag and protein C were possible drug interactions, suggested diagnosis, testing methodology/reagent, and recommendations for (1) further testing, (2) treatment, and (3) testing of family members. Considering the laboratory results are likely to be method-dependent, 4–6% of the respondents noted the testing methodology/reagent for PT, aPTT, vWF Ag and protein C assays.

Two percent of the respondents recommended further testing when reporting PT and aPTT results, while 12% and 14% did so for vWF Ag and protein C tests, respectively. Abnormal results obtained with these tests should require further laboratory investigation. Results of PT and aPTT are known to influence anticoagulant dose and are closely used in their monitoring. This survey shows that 99% of the respondents provided no recommendation for treatment using either PT or aPTT tests. Eight percent and

10% of the respondents recommended testing family members when reporting test results for protein C and vWF Ag tests, respectively, even though these tests are related to genetic coagulopathy and bleeding disorders. These results suggest a need for further research to determine how coagulation laboratories are providing relevant information, interpretations and recommendations to those involved in patient care.

Process of Reporting Results

Reporting of critical values. One percent of the respondents did not report critical values for coagulation tests (*P* = 0.025). Of those stating that they did, they noted the following practices in reporting critical values:

Laboratory practice	Number (Percent) of large hospitals	Number (Percent) of small hospitals	*P*
Critical values telephoned to clinician and call documented	301 (99%)	284 (99%)	0.610
Critical values repeated and documented as confirmed	253 (88%)	258 (94%)	0.019
Critical values telephoned to clinician and call not always documented	7 (3%)	22 (10%)	0.002
Critical values indicated on report and no further action taken	12 (5%)	12 (5%)	0.842

The CAP and several Canadian provincial accreditation bodies require laboratories to have critical (panic) values and, when critical values are obtained, to inform medical staff immediately so that appropriate action can be taken.[5] In our survey, 99% stated that they reported critical values for coagulation tests. In a 1996 survey of Canadian medical laboratories,[5] 75% of laboratories reported critical results by telephone.

Repeating a coagulation test. Circumstances under which a coagulation test is usually repeated were

Circumstance to repeat a coagulation test	Number (Percent) of large hospitals	Number (Percent) of small hospitals	*P*
Control(s) is (are) out of range	296 (98%)	288 (99%)	0.226
Results are outside instrument technical ranges	297 (97%)	285 (99%)	0.194
Results are critical (panic) values	280 (91%)	291 (99%)	< 0.001
Results do not agree with previous results (using Delta check)	226 (75%)	198 (71%)	0.236
Results are outside of the reference interval	35 (13%)	52 (20%)	0.017

Two percent of the respondents noted that a coagulation test would usually not be repeated when the control(s) is (are) out of range (*P* = 0.001) or when results are outside instrument technical ranges (*P* < 0.001).

Quality Assurance (QA) Procedures

The respondents usually took the following QA steps in their laboratories:

QA procedure used	Number (Percent) of large hospitals	Number (Percent) of small hospitals	*P*
Match specimen label and requisition form	265 (88%)	267 (91%)	0.322
Match patient information and laboratory generated labels	297 (97%)	261 (89%)	< 0.001
Compare instrument printout to reported value	249 (82%)	238 (83%)	0.816
Check patient's previous results (Delta check)	263 (86%)	193 (66%)	< 0.001
Review critical (panic) values	300 (97%)	296 (100%)	0.022
Bring critical values to immediate attention of the clinician	302 (98%)	296 (99%)	0.169
Validate new analytical methods	304 (99%)	283 (97%)	0.041

QA procedure used (continued)	Number (Percent) of large hospitals	Number (Percent) of small hospitals	*P*
Periodically verify calibration of all instruments	307 (99%)	290 (98%)	0.082
Check plasma for platelet count after centrifugation	105 (34%)	32 (11%)	< 0.001
Run specimens in duplicate	99 (33%)	136 (46%)	0.001
Run controls in duplicate	97 (32%)	132 (45%)	0.001

Information on specimen tube. Ninety percent of the respondents usually matched specimen label and requisition form. Consistent with this finding, we noted in a previous part of the survey that 92% of the respondents included conflicting patient information on the requisition form and specimen label as reasons for rejecting coagulation specimens in their policies and procedures. Of those who did not usually match specimen label to requisition form, 73% did include conflicting patient information on the requisition form and specimen label as a reason for rejecting coagulation specimens in their policies and procedures. However, of those not having in their policies and procedures conflicting patient information on the requisition form and specimen label as a reason for rejecting coagulation specimens, 81% did not usually match the information on the specimen label and requisition form.

Procedures relating to laboratory test results. The CAP and several Canadian provincial accreditation bodies require laboratories to inform medical staff immediately when a critical value is obtained so that appropriate action can be taken.[5] According to the CLIA regulations, a laboratory report must be sent promptly to the authorized person, the individual responsible for using the test results or the laboratory that initially requested the test.[46] One percent of the respondents did not adhere to this practice (P = 0.005).

Procedures relating to methodology and instrumentation. Two percent of the respondents reported not validating new analytical methods ($P < 0.001$). One percent of the respondents indicated that they did not periodically verify calibration of all of their instruments ($P = 0.003$).

Procedures relating to testing of specimens and controls. In a 1998–1999 survey of Canadian medical laboratories, 59% of the respondents routinely performed testing to verify the platelet-poor status of plasma used for aPTT testing. In the current 2001 survey of the U.S. hospital coagulation laboratories, 23% of the respondents stated that they checked plasma for a platelet count after centrifugation.

There are conflicting reports relating to the need to perform replicate analyses in coagulation. Replicate analyses reportedly enhanced neither the precision nor the accuracy of coagulation studies.[47] Another report, however, indicated that the frequency of errors produced by single estimations was too great for satisfactory clinical practice.[48] CLIA requires that patient and control specimens be tested in duplicate for manual coagulation tests; duplicate testing is not required for automated coagulation tests.[49] In a 1996 survey of licensed Canadian medical laboratories, 62% of laboratories ran specimens in duplicate.[5] In the followup 1998–1999 survey of Canadian medical laboratories, 71% ran specimens in duplicate.[1] These may be compared to the rate of 39% reported in this survey.

Coagulation Laboratory Personnel and Resources

To our knowledge, this is the only survey of laboratory practices that has covered coagulation laboratory personnel and resources at a national level in the U.S. or elsewhere.

Testing location. The respondents performed coagulation tests in the following locations:

Hospital location	Number (Percent) of large hospitals	Number (Percent) of small hospitals
Core laboratory	125 (40%)	209 (70%)
Hematology laboratory	167 (54%)	64 (21%)
Coagulation laboratory	69 (22%)	26 (9%)
Point of care	56 (18%)	8 (3%)
Rapid response (Stat) laboratory	28 (9%)	3 (1%)
None of the above	2 (1%)	8 (3%)

The response patterns of large and small hospital were different in that a greater proportion of the small hospital respondents noted the core laboratory and other unlisted location(s) as a place coagulation testing was performed, while a greater proportion of the large hospital respondents noted hematology, coagulation, point of care and stat laboratories for coagulation testing.

<u>Number of full time equivalents (FTEs)</u>. The respondents indicated that the following number of FTEs performed coagulation laboratory testing:

Number of FTEs*	Number (Percent) of large hospitals	Number (Percent) of small hospitals
Less than 4	215 (70%)	212 (72%)
4–9	44 (14%)	57 (19%)
10 or more	49 (16%)	26 (9%)

*The response patterns of large and small hospitals were significantly different (P = 0.014).

We consider the FTE calculations to be based on the annual hours worked. However, we did not define this term on the survey, possibly subjecting it to different interpretations. Also, reporting of FTE may become subject to substantial variability when staff are shared with other laboratory areas.

<u>Components of competency assessment program</u>. The respondents included the following components in their competency assessment program for coagulation testing personnel:

Component of competency assessment program	Number (Percent) of large hospitals	Number (Percent) of small hospitals
Performance of QC and documentation of remedial actions (1)	287 (92%)	274 (91%)
Review of procedure manuals (2)	279 (90%)	246 (82%)
Analysis of unknown samples (3)	240 (77%)	251 (84%)
Direct observation of a task (4)	238 (77%)	217 (72%)
Participation in continuing education (5)	209 (67%)	161 (54%)
Periodic written examination (6)	119 (38%)	66 (22%)
None of the above	1 (0.3%)	0

Aside from the analysis of unknown samples, a greater proportion of the large hospital respondents used the other 5 assessment components of personnel competence compared to the small hospital respondents.

The numbers of responses received for each total number of competency tools used were as follows:

Number of competency tools used*	Number of responses	Proportion of all responses†
1	13	2%
2	44	7%
3	101	17%
4	174	28%
5	186	30%
6	93	15%
Total	**611**	**100%**

*On average, the respondents used 4.2 competency assessment tools (median, 4; mode, 4).
†Percentages do not total 100% due to rounding to the nearest 1%.

The 6 most common multiple response patterns, comprising 68% of all such responses, were as follows:

Personnel competency programs (as numbered in a preceding table)	Number (Percent) using the programs
1,2,3,4,5	147 (25%)
1,2,3,4,5,6	93 (16%)
1,2,3,4	77 (13%)
1,2,3,5	34 (6%)
1,2,3	30 (5%)
1,2,4,5	26 (4%)

Educational degrees of coagulation laboratory director. Educational degrees of the laboratory director were as follows:

Degree*	Number (Percent†) of large hospitals	Number (Percent†) of small hospitals
M.D.	298 (95%)	263 (88%)
Ph.D.	24 (8%)	19 (6%)
Other	14 (4%)	35 (12%)

*There were 40 participants who responded that the laboratory director had an M.D. and a Ph.D. (27 hospitals) or an M.D. and another degree (13 hospitals).
†Percentages total >100% due to multiple responses.

The 49 participants (14 large and 35 small hospitals) checking "other" for the educational degree of the laboratory director specified the following as their highest educational degree:

Highest Educational Degree Stated in the Other Category	
Degree	**Number (Percent*)**
MT(ASCP)†	19 (39%)
D.O.§	8 (16%)
B.S.§	6 (12%)
M.B.A.‡	5 (10%)
Unspecified§	4 (8%)
MLT§	3 (6%)
M.S.§	3 (6%)
Associate degree	1 (2%)
All degrees in the other category	**49 (100%)**

*Percentages do not total 100% due to rounding to the nearest 1%.
†Six respondents also noted possession of an M.D. degree by the laboratory director.
§One respondent also noted possession of an M.D. degree by the laboratory director.
‡Two respondents also noted possession of an M.D. degree by the laboratory director.

Of the respondents noting an educational degree other than an M.D. or a Ph.D, 27% also had an M.D. degree.

<u>Certifications of coagulation laboratory director</u>. The laboratory directors were reported to be certified as follows:

Laboratory Directors' Professional Certification		
Certification	**Large hospital**	**Small hospital**
Board certified in clinical pathology (CP)	250 (81%)	206 (71%)
Board certified in anatomical pathology (AP)	223 (73%)	155 (53%)
Certified by the American Society for Clinical Pathology (ASCP)	65 (21%)	86 (29%)
Board certified in medicine (M)	49 (16%)	60 (21%)
Board certified in hematopathology (HP)	44 (14%)	4 (1%)
Board certified in hematology (H)	29 (9%)	3 (1%)
Certified by the National Certifying Agency (for Clinical Laboratory Sciences) (NCA)	3 (1%)	4 (1%)
Certified by the American Association of Bioanalysts (AAB)	1 (0.3%)	3 (1%)
Certified by the American Board of Clinical Chemistry (ABCC)	3 (1%)	1 (0.3%)
Certified by the National Registry of Clinical Chemistry (NRCC)	1 (0.3%)	0
None of the above	4 (1%)	2 (0.7%)

Aside from certification by the ASCP with significantly greater proportion of the small hospital laboratory directors reported being certified compared to the large hospital directors ($P = 0.020$), a greater proportion of the large hospital laboratory directors were reported being certified in clinical pathology ($P = 0.002$), anatomical pathology ($P < 0.001$), hematopathology ($P < 0.001$) and hematology ($P < 0.001$).

The distribution of the number of the laboratory directors' certifications were as follow:

Number of Professional Certificates Possessed by Coagulation Laboratory Directors		
	Number (Percent*) of responses	
Number of Certificates	**Large hospitals**	**Small hospitals**
1	81 (26%)	127 (43%)
2	126 (41%)	112 (38%)
3	75 (24%)	41 (14%)
4	15 (5%)	10 (3%)
5	7 (2%)	2 (1%)
6	2 (0.7%)	0
7	1 (0.3%)	0
All	**307 (100%)**	**292 (100%)**

*Percentages do not total 100% due to rounding to the nearest 1%.

Sixty-five percent of the respondents noted that the laboratory director held multiple certifications. Responses from the large and small hospital respondents were significantly different; 74% of the large hospitals' laboratory directors held multiple certifications compared to 57% of small hospitals' laboratory directors ($P < 0.001$). Also, the number of certifications of directors of the large and small hospital laboratories were significantly different ($P < 0.001$). On average, the laboratory directors had 2.0 certifications (median, 2; mode, 2).

The following were the 6 most common responses for multiple certifications:

Most Common Multiple Certifications for Coagulation Laboratory Directors*	
Certification	**Number (Percent) of multiple certificates**
CP, AP	187 (48%)
CP, AP, ASCP	42 (11%)
CP, AP, M	32 (8%)
CP, AP, HP	21 (5%)
CP, ASCP	20 (5%)
CP, AP, M, ASCP	17 (4%)

*Abbreviations refer to those of certifications noted in a previous table. There were a total of 40 combinations for certification of the laboratory director including the 6 combinations above. The combinations above constituted 82% of all multiple certification responses. The next most common multiple certificate responses were those from 14 respondents noting either AP and ASCP certifications (7 respondents) or CP, AP and H certifications (7 respondents).

Coagulation service capacities. The following coagulation service capacities were available:

Capacity	Number (Percent) of large hospitals	Number (Percent) of small hospitals	*P*
Clinician available for consultation with expertise in coagulation disorders	233 (74%)	113 (38%)	< 0.001
Anticoagulation outpatient clinic specializing in adjustment of oral anticoagulants	84 (27%)	37 (12%)	< 0.001
Outpatient clinic specializing in diagnosis and treatment of coagulation disorders	52 (17%)	6 (2%)	< 0.001

Systematic outpatient anticoagulation clinic (AC) services are systems of care designed to coordinate and optimize delivery of anticoagulation therapy by (1) evaluating patient-specific risks and benefits to determine the appropriateness of therapy, (2) facilitating the management of anticoagulation dosages and prescription pick up or delivery, (3) providing ongoing education of the patient and other care givers about warfarin and the importance of self-care behavior leading to optimal outcomes, (4) providing continuous systematic monitoring of patients, INR results, diet, concomitant drug therapy, and disease states, and (5) communicating with other healthcare practitioners involved in the care of the patient.[17] Patients treated at an AC who received lower-range anticoagulation had fewer INRs >5.0, spent more time in range, and spent less time at an INR >5.[50] Patients treated at an AC who received higher-range anticoagulation had more INRs within range, had fewer INRs <2.0, and spent more time within range. The AC group also demonstrated a trend toward a lower mortality rate.[50] In our survey, 20% had an AC that specialized in the adjustment of oral anticoagulants. Nine percent of the respondents had an AC that specialized in the diagnosis and treatment of coagulation disorders.

Point-of-Care Testing (POCT) for PT Assay

Further study of point-of-care devices to test for PT is needed to fully evaluate their safety and efficacy for home self-monitoring of oral anticoagulation therapy.[51] There is a widespread use of POCT within primary care but a haphazard approach to specific test performance issues.[7] There is generally a poor understanding of QC issues, providing a clear indication for future training and educational priorities if POCT is to develop in primary care settings. There appears to be no consensus regarding frequency of QC testing nor methods for dealing with abnormal results.[8] This survey focused on the most commonly performed POCT for a coagulation test–i.e., the PT test.

Availability of POCT for PT assay. Nine percent of the respondents performed POCT for PT assays. The responses from large and small hospitals were significantly different:

POCT	Number (Percent) of large hospitals	Number (Percent) of small hospitals	*P*
Availability	46 (15%)	9 (3%)	< 0.001

Laboratory oversight of coagulation POCT. Of those performing POCT for PT, the laboratory had oversight of testing (including certification and regulatory compliance) in 93% of cases. The responses from large and small hospitals were significantly different:

POCT	Number (Percent) of large hospitals	Number (Percent) of small hospitals	*P*
Laboratory oversight	45 (98%)	6 (67%)	0.001

Location of coagulation POCT. The respondents noted the following sites for performance of coagulation POCT:

Hospital location	Number (Percent)
Coagulation clinic	36 (64%)
Cardiac catheterization laboratory	15 (27%)
Satellite laboratory	13 (23%)
Operating rooms	12 (21%)
Bedside	10 (18%)
Dialysis clinic	7 (13%)
None of the above	1 (2%)

Of those responding to the question dealing with the location of coagulation POCT, 36% noted more than 1 location. Of the 9 small hospitals, none noted more than 1 site for coagulation POCT compared to 20 of the 47 large hospital respondents ($P = 0.015$). The number of POCT locations for these 20 respondents were as follows:

Number of Hospital Locations Performing POCT of PT	
Number of locations	**Number (Percent) of multiple POCT locations**
2	11 (55%)
3	3 (15%)
4	3 (15%)
5	3 (15%)
All	**20 (100%)**

The following were the 4 most common multiple location responses:

Most Common Multiple Location Responses for POCT of PT*	
Hospital locations	**Number (Percent) of multiple locations**
Coagulation clinic and satellite laboratory	3 (15%)
Coagulation clinic, cardiac catheterization laboratory and operating rooms	3 (15%)
Bedside and coagulation clinic	2 (10%)
Coagulation clinic and cardiac catheterization laboratory	2 (10%)

*There were a total of 14 combinations for the location of POCT of PT including the 4 combinations above. These 4 combinations constituted 50% of all multiple POCT location responses.

<u>Integration of POCT results</u>. Forty percent of the respondents stated that coagulation POCT results were integrated into the laboratory's results reporting system. Of these, 95% stated that coagulation POCT results were integrated in the order of collection time.

<u>Reference interval for POCT of PT</u>. Forty-five percent of the respondents indicated that the reference interval for the POCT PT assay was the same as the PT reference interval for the central laboratory. Of the remaining, 36% noted that the POCT reference interval was established by the same method used to establish the PT reference interval for the laboratory. Those noting that they followed a method different from the laboratory to establish the POCT reference interval stated that they used the following methods:

Method used	Number (Percent*)
In-house testing	11 (61%)
Manufacturer's instruction	4 (22%)
Published values	4 (22%)
Others	1 (6%)

*Percentages total >100% since 1 large hospital used both in-house testing and manufacturer's instruction and 1 small hospital used both manufacturer's instruction and published values to establish the POCT PT reference interval.

We further examined all responses noting the use of a method different from the laboratory to establish the POCT reference interval. All 11 respondents that had noted using in-house testing (including 1 respondent using both in-house testing and manufacturer's instruction) to establish the reference interval for their POCT PT assay also noted that they used in-house testing only to establish the PT reference interval in their laboratories. These are paradoxical response patterns in that all of these respondents had specified that they used a different method to establish the POCT reference interval for their PT assay. Of the 8 respondents not using in-house testing to establish the POCT reference interval for their PT assay, all but 1 used in-house testing only to establish the PT reference interval in their laboratories. One respondent noted using the manufacturer's instruction to establish both the laboratory and POCT reference interval for their PT assay. This was another paradoxical response pattern since this institution had noted using different methods to establish the laboratory and POCT reference intervals for their PT assay.

<u>Type of quality control (QC) material/method</u>. The respondents used the following types of QC materials/methods for their POCT coagulation instruments:

Type of QC Material/Method Used for POCT Coagulation Instrument	
QC material/method	**Number (Percent)**
Electronic QC method and liquid QC material	18 (33%)
Electronic QC method and lyophilized QC material	16 (30%)
Lyophilized QC material only	10 (19%)
Electronic QC method only	4 (7%)
Liquid QC material only	4 (7%)
Electronic QC method, liquid QC material and lyophilized QC material	2 (4%)
All	**54 (100%)**

Seventy-four percent of the respondents used electronic QC methods for their coagulation POCT, while 52% utilized lyophilized QC materials and 44% used liquid QC materials. Sixty-seven percent used electronic QC methods along with liquid QC materials (33%), lyophilized QC materials (30%), or both (4%).

<u>Frequency of QC runs</u>. The respondents noted the following frequencies for their QC runs:

Frequency of QC Performed for Coagulation POCT Instrument*	
QC frequency	Number (Percent)
Once per day	29 (54%)
Once per shift	21 (39%)
Other frequencies	12 (22%)

*Percentages total >100% because of the 54 answering this question, 8 (15%) noted that they performed more than 1 QC frequency for their coagulation POCT instrument. All multiple responses included use of other frequencies in addition to once per day (7 responses) or once per shift (1 response).

The respondents noted the following as other frequencies for performing QC:

Other QC Frequencies
Electronic, daily; liquid, weekly*
Liquid QC used when new box of reagents are opened*
Lyophilized, biweekly†
Monthly*
On clinic days*
Once a week
Once per week for lyophilized controls*
Once/box, once/operator/week*
Once/each day used
QC not performed if clinic is closed– i.e., done only on days of use*
When testing is performed
With each sample

*and once per day
†and once per shift

According to the CLIA regulations, for all non-manual and CLIA non-waived coagulation testing systems, the laboratory must include 2 levels of control each 8 hours of operation, i.e. once per an 8-hour shift and each time a change in reagents occurs.[49] For manual coagulation tests, each individual performing tests must use 2 levels of control material before testing samples from patients and each time a change in reagents occurs, and patient and control specimens must be tested in duplicate. Thirty-nine percent of the respondents noted they ran QC once per shift. It is not known how many of these respondents were using POCT instruments waived under CLIA. We also did not collect data on the duration of the work shift.

Other Results and Comments

Request for a copy of the CDC findings. Eighty percent of the respondents indicated an interest to receive a copy of the report detailing the CDC findings. The following number and proportion of the large and small hospital respondents made this request:

Request for Copy of the CDC Findings		
Number (Percent) of large hospitals	Number (Percent) of small hospitals	*P*
272 (85%)	233 (75%)	0.002

Survey comments. Nine percent of the respondents provided comments regarding the questionnaire. These comments could be grouped into 4 broad categories: (1) comments based on 1 or more survey questions, (2) general comments, (3) specific comments, and (4) comments relating to survey quality and thanking for the opportunity to participate. Below is a breakdown:

Type of comment	Number (Percent*)
Specific comments, questions and suggestions (1)	19 (33%)
Survey question-based comments (2)	12 (21%)
General comments and questions (3)	9 (16%)
Comments on survey quality and appreciation (4)	5 (9%)
1 and 3	5 (9%)
1 and 4	5 (9%)
2 and 3	1 (2%)
3 and 4	1 (2%)

*Percentages do not total 100% due to rounding to the nearest 1%.

Below are selected comments grouped by type:

Selected Comments on the Survey
Specific comments, questions and suggestions
Additional surveys focused on LA, mixing studies and interpretation would be useful.
I would like to see your survey include laboratory practices and recommendations for screening of prothrombotic disorders.
There should be further explanation of why the CDC in particular is undertaking this survey.
There was (were) no question(s) regarding computer (LIS) autoverification of coagulation results.
There is variability in opinion as to how long a specimen can sit before assaying for PT or aPTT and whether unspun, room temperature, refrigerated, or spun and separated are best.
We would like a heparin curve protocol associated with pharmacy adjustment to therapy.
Include POCT for aPTT.
Would any recommendation be given as to adequate testing, reporting and QC?
Surveys should be done periodically. Following the survey should be a summary of national recommendations and guidelines.
We are one of the few laboratories in our area that reject coagulation samples if the tube is less than 90% full.
I would like to see recommendations developed for standardization of aPTT reporting.
There needs to be answers provided that deal with the receipt and processing of coagulation specimens from outreach facilities.
We do not feel that POCT for PT is appropriate for nursing.
The survey did not mention if one is a stand alone laboratory or if one is part of a greater hospital system.
Questions about requisition requirements do not take into account that 2 requisitions may be involved.
Personnel requirements are lenient; education is needed for ...
Question-based comments
#36 ambiguous (question dealing with the number of FTEs).
#39- Board certified in blood banking (transfusion medicine).
Question #36 is open to interpretation- FTE's doing coagulation on any 1 shift or FTEs on all shifts doing coagulation testing?
General comments and questions
This survey will help standardize coagulation practices, set guidelines and recommendations.
I look forward to summary and recommendation.
The use of test algorithms and test panels are helpful for most physicians and residents who lack coagulation expertise.
We follow guidelines set by the (CAP's) Anticoagulation Committee Conference ... and are very frustrated!
I believe this survey information can be very helpful to our physicians.
We would welcome recommendations as to which coagulation tests are appropriate to offer at different health care facilities.
Coagulation is important to this laboratory since we have a population composed of at least 35% senior citizens.
There were so many choices for answering the questions.
This is an area that most clinical laboratories need to improve upon.

Selected Comments on the Survey (Continued)
Comments on survey quality and appreciation
Thank you for including us in the survey.
The survey is fine.
Very educational survey.
Good job.
Very helpful–Fruit for thought.
Very informative.
Interesting survey. Thanks for letting us participate.
This is an excellent survey, especially for a small hospital.

Response rate. This survey was 14 pages long and contained a total of 157 question and sub-questions. In pilot testing of the survey by 9 hospital laboratories, average time for completion of this survey was 30 minutes. Considering the length of this survey and the associated time commitment for completing it, we were pleased to realize a response rate of 79%. The following probably contributed to the response rate we observed– hence, enhancing the generalizability of our findings:

Follow-up procedures. This involved sending reminder postcards, performing telephone follow-up of all but 7 of the non-responders, and providing replacement questionnaires for those requesting them.

Manner of contacting the respondents. In a cover letter signed by then Chief of Laboratory Practice Assessment Branch, Division of Laboratory Systems and addressed to each laboratory director by name, the CDC noted the importance of these data collections and their relevance to improve quality of laboratory practice and consequently enhance public's health.

Incentive for participation. At the end of the survey, we asked each participant to indicate whether they wanted to receive a copy of the CDC findings. We believe that this option, also noted in the cover letter, provided an incentive to the respondents to learn about nationally reported practices in hospital coagulation laboratories and how their laboratories' practices related to (1) an aggregate nationally based practice data and (2) evidence-based recommendations and guideline.

Mode of data collection. This survey was unique in that we employed 2 different modes for data collection: paper-based and electronic. Three percent of the respondents used our secure CDC Internet site to respond. We had not initially planned to administer this survey via the Internet and were concerned about the validity of pooling the results of paper-based and electronic surveys. However, other considerations prompted us to additionally collect data via the Internet. The major drivers for this decision were (1) potential increase in response rate, (2) ease of data transmission, collection and management, and (3) the OMB recommendation to allow for electronic data collection. The following probably gave rise to the relatively low electronic response rate of 3% compared to the paper-based response rate of 76%:

Logic introduced in the web-based survey. Although the respondents could return to a partially completed survey at any time, they could not submit a survey unless they addressed conflicting responses. We detected contradictory responses by programming logical operations that would flag these responses for the respondents' further actions. It is conceivable that some respondents became frustrated and did not complete the survey due to 1 or more such unsuccessful uploading attempts.

Provision of the URL. We provided each respondent with the URL of the CDC website in the letter accompanying the paper survey. This entailed (1) noting the URL in the body of the cover letter, (2) typing the URL in a browser window, and (3) entering an identification code and a password. It is conceivable that we could have achieved greater electronic response rates had we noted the URL in the form of a hyperlink along with the identification code and password in an e mail addressed to each laboratory director. However, this would have entailed knowing e mail addresses of the respondents which we did not collect during our telephone contacts due to the fact that this entailed a change in the study protocol and an OMB re-application process.

Internet access and use. Although Internet is readily available in most hospitals, it is used less frequently. For example, in a survey of 28 hospital laboratories in Northwest U.S. (involving laboratories in the States of Washington, Oregon, Idaho and Alaska), 85% had access to the Internet but 72% regularly used Internet at work.[52] This finding may partly explain the preferential use of paper survey over its electronic counterpart.

Format of questions. With many questions, we had the respondents choose between affirmative and negative responses. We did this because one could not conclude that not checking a response is equivalent to a negative response. We further limited the use of check-all-that-apply type questions. Since respondents may select any number out of possible responses, statistical tests based on contingency tables assuming independent responses cannot be used.[53] To address this, we preferentially had each respondent check either a yes or no for series of inter-related sub-questions as opposed to having them respond to a question with a check-all-that-apply format. This effort, as an attempt to enhance response accuracy, may have had a negative impact on the survey completion time; and it is conceivable that a few more from the study sample would have completed this survey if there were fewer yes-or-no type sub-questions.

Limitations. The findings from this survey are subject to several limitations:

Reporting laboratory practices. The various laboratory practices noted in this survey are those respondents reported; and like any other questionnaire survey, it may not reflect actual practices. We did not capture any data on the individual(s) who completed these surveys. It is conceivable that some responses would have been different if other individuals from the same institutions had completed these surveys. More than 1 individual may have completed some of the returned surveys. Nevertheless, we did not have any mechanism in place to capture data to evaluate the intra-respondent and inter-respondent reliabilities within the same institution.

Drawing inferences. We designed this survey principally to assess the current state of hospital coagulation laboratory practices nationwide. By design, we stratified hospitals into 2 groups based on their number of beds. We did this because we envisioned that certain laboratory practice variables were likely to be affected by hospital size as reflected in the AHA-reported number of beds. Differences in the data collected from the large (≥200 beds) and small (<200 bed) hospitals were actually borne out for many variables; these were the only instances we have drawn statistical inferences by noting the probabilities of Type I error (*P* values).

It is anticipated that many laboratory practice variables would be correlated. Based on accepted and evidence-based recommendations and guidelines, a logistic regression model may be developed that can serve as a predictor of laboratory quality. Although we do not report on such analyses in this report, collected data can be used to generate such predictive models and to note independent determinants of laboratory quality. We did not report on any such analyses here since the primary objective of this report was descriptive as opposed to being analytical.

Representativeness of findings. Due to the degree of participation (79% response rate) and sampling (26% of the large and 9% of the small hospitals listed in the 1999 AHA directory of hospitals comprising ~95% of all US hospitals), we are confident that the results of this survey accurately reflects the state of hospital coagulation laboratory practices in 2001 as reported by the participants.

CONCLUDING REMARKS

Findings from this survey show that there is substantial variability in certain coagulation laboratory practices. Although in most cases the response patterns from the large and small hospital respondents were not significantly ($P > 0.050$) different, several questions solicited significantly different responses from these 2 groups.

To our knowledge, this is currently the only report of a broad and comprehensive survey of nationally based coagulation-specific and general laboratory practices. This survey used 2 different modes of data collection: paper-based and electronic. An inherent limitation of our survey instrument is that responses may not consistently reflect actual practices. Surveys are subject to framing biases which can be reduced (e.g., by pilot testing) but not totally avoided. We believe our results present a representative and accurate snapshot of reported hospital coagulation laboratory practices in 2001.

This report is a descriptive characterization of coagulation-specific and general laboratory practices and makes no attempt to relate specific laboratory practices we have observed to other laboratory- and hospital-specific variables or to clinical and health outcomes of patients and populations. Explorations of such inter-relationships using these survey results and those that have been or may be collected in specific outcome studies will be avenues for further investigation.

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NATIONAL SURVEY OF HOSPITAL COAGULATION LABORATORIES

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Public Health Service
Centers for Disease Control and Prevention
Atlanta, GA 30333

CDC
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National Survey of Hospital Coagulation Laboratories

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Please check the box at the end of the survey questionnaire if you would like a report of the survey findings.

If you have any questions or comments about this survey, please contact Dr. Jack Leiss at ASI at 800-451-3930 or by email at jleiss@asciences.com.

It takes about 30 minutes to complete the questionnaire. Please mark either a check or X in the indicated response boxes, i.e. [✓] or [**X**]. Your participation is greatly appreciated.

A note to respondents concerning confidentiality:

This survey is being conducted under the authority of Section 301 of the Public Health Service Act. The purpose of this survey is to provide CDC with information it needs to assess the state of coagulation testing in US hospital laboratories. Advanced measures are in place to protect your privacy. Questionnaires will be numbered, and the files linking these numbers to your responses will be available only to authorized ASI personnel directly involved with the survey. Individually identified data will not be sent to CDC; the data files sent to CDC will have a record number that is different from the questionnaire number, and the file linking the record number to the questionnaire number will be available only to authorized ASI personnel. If you have any questions about the confidentiality of your responses, please call Dr. Jack Leiss at ASI at 800-451-3930.

A note to respondents concerning respondent burden:

Public reporting burden of this collection of information is estimated to average 30 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. An agency may not conduct or sponsor, and a person is not required to respond to a collection of information unless it displays a currently valid OMB control number. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to CDC/ATSDR Reports Clearance Officer; 1600 Clifton Road, NE, MS D-24, Atlanta, GA 30333, ATTN: PRA (0920-0505).

1. Does your laboratory perform any coagulation testing?

1 ❑ Yes
2 ❑ No → *The rest of the questionnaire is not applicable to your laboratory, and you have completed the survey. Please return the questionnaire in the enclosed envelope. Your participation is greatly appreciated.*

This first set of questions relates to the collection of coagulation specimens.

2. Does your laboratory use coagulation test requisition forms?

1 ❑ No → *Go to Question 3.*
2 ❑ Yes → Please indicate what diagnostic and/or medication information is requested on the requisition form for a coagulation test in your laboratory.

Information	Requested	Not Requested
Diagnosis	1 ❑	2 ❑
ICD-9 Code	1 ❑	2 ❑
CPT Code	1 ❑	2 ❑
Oral Contraceptive use	1 ❑	2 ❑
Aspirin use	1 ❑	2 ❑
Coumadin use	1 ❑	2 ❑
Heparinoid use	1 ❑	2 ❑
Heparin (unfractionated) use	1 ❑	2 ❑
Low Molecular Weight Heparin (LMWH) use	1 ❑	2 ❑

3. Which of the following are included in your policies and procedures as reasons for rejecting coagulation specimens in your laboratory?

Insufficiently labeled specimen containers .... 1 ❑ Yes 2 ❑ No
Improperly anti-coagulated specimen .... 1 ❑ Yes 2 ❑ No
Requisition and specimen have conflicting patient information........ 1 ❑ Yes 2 ❑ No
Label does not have hospital Medical Record Number (ID number) .... 1 ❑ Yes 2 ❑ No
Specimen collected via indwelling catheter .... 1 ❑ Yes 2 ❑ No
Specimen stored at an inappropriate temperature........ 1 ❑ Yes 2 ❑ No
Specimen transport time exceeds recommended time frame........ 1 ❑ Yes 2 ❑ No
Specimen is clotted .... 1 ❑ Yes 2 ❑ No
Specimen is hemolyzed........ 1 ❑ Yes 2 ❑ No

The following questions ask about the Prothrombin Time (PT) assay.

4. Does your coagulation laboratory perform the PT assay?

   1 ❑ No → *Go to Question 13.*
   2 ❑ Yes → *Please answer Questions 5 - 12.*

5. What is the concentration of sodium citrate that is used in your laboratory for samples tested for the PT assay? *(Check all that apply.)*

   1 ❑ 3.2%
   2 ❑ 3.8%

6. How does your coagulation laboratory report the PT results? *(Check all that apply.)*

Seconds..............................	1 ❑ Yes	2 ❑ No
INR......................................	1 ❑ Yes	2 ❑ No
Therapeutic PT Ratio...........	1 ❑ Yes	2 ❑ No

7. Does your laboratory conduct in-house evaluations to establish reference ranges for the PT assay?

   1 ❑ No → How does your laboratory establish the PT reference range?

   1 ❑ Using published values
   2 ❑ Using manufacturer's insert
   3 ❑ Other (*Please specify*.) ___________________________

   2 ❑ Yes → Please indicate the minimum number of participants used in the in-house evaluation for the establishment of the PT assay reference range in your laboratory. *(Check only one.)*

   1 ❑ 20 or fewer
   2 ❑ 21 - 39
   3 ❑ 40 - 59
   4 ❑ 60 - 119
   5 ❑ 120 - 199
   6 ❑ 200 or more

8. Does your laboratory determine sensitivity of the PT assay to heparin?

   1 ❑ Yes 2 ❑ No

9. What is the primary PT method used in your coagulation laboratory? *(Choose only one.)*

   1 ❑ Manual
   2 ❑ Mechanical
   3 ❑ Optical
   4 ❑ None of the above

10. Please indicate which reagent(s) is/are used for the PT assay in your coagulation laboratory. *(Check all that apply.)*

- 1 ❑ Hemoliance Brain Thromboplastin
- 2 ❑ Dade Behring Thromboplastin C Plus
- 3 ❑ Innovin
- 4 ❑ Pacific Hemostasis D
- 5 ❑ OTC Simplastin L
- 6 ❑ Other

The use of trade names is for identification purposes only and does not constitute endorsement by CDC or HHS.

11. Does your laboratory select a PT-thromboplastin reagent that is insensitive to heparin in the heparin therapeutic range? .... 1 ❑ Yes 2 ❑ No

12. What is the international sensitivity index (ISI) value for the thromboplastin lot currently being used for PT testing? *(Please fill in the blank.)* .... _______________

The following questions ask about the Activated Partial Thromboplastin Time (aPTT) assay.

13. Does your coagulation laboratory perform the aPTT assay?

- 1 ❑ No → *Go to Question 16.*
- 2 ❑ Yes → *Please answer Questions 14 and 15.*

14. Does your coagulation laboratory have an aPTT therapeutic range for heparin?

- 1 ❑ No → *Go to Question 15.*
- 2 ❑ Yes → *Please answer Questions A - D.*

A. Does your laboratory report the aPTT therapeutic range for heparin when the assay is used to monitor heparin therapy?....... 1 ❑ Yes 2 ❑ No

B. Does your laboratory indicate the corresponding heparin concentration with the aPTT results? .... 1 ❑ Yes 2 ❑ No

C. Please indicate which of the following practices your laboratory performs to determine the aPTT therapeutic range for heparin.

Uses samples <u>from patients on heparin therapy</u> to compare a new ***heparin lot*** to an old ***heparin lot*** .... 1 ❑ Yes 2 ❑ No
Uses samples <u>from patients on heparin therapy</u> to compare a new ***reagent lot*** to an old ***reagent lot*** .... 1 ❑ Yes 2 ❑ No
Uses <u>heparin "spiked"</u> samples to compare a new ***heparin lot*** to an old ***heparin lot*** .... 1 ❑ Yes 2 ❑ No
Uses <u>heparin "spiked"</u> samples to compare a new ***reagent lot*** to an old ***reagent lot*** .... 1 ❑ Yes 2 ❑ No
Protamine sulfate titration .... 1 ❑ Yes 2 ❑ No
Anti-Xa Assay .... 1 ❑ Yes 2 ❑ No
Other (*Please specify*.) ________________________________

D. Please indicate when your laboratory would reconfirm the aPTT therapeutic range for heparin. *(Check all that apply.)*

1 ❑ When new ***reagents*** are implemented
2 ❑ When new ***reagent lots*** are implemented
3 ❑ When new ***instrumentation*** is implemented
4 ❑ After a specified time period (e.g., yearly)
5 ❑ None of the above

15. What practices does your laboratory adhere to in relation to the duration of time between specimen collection and performance of aPTT for patients treated with unfractionated heparin?

Specimens are kept at room temperature prior to testing.................... 1 ❑ Yes 2 ❑ No
Specimens are kept at 4°C prior to testing .... 1 ❑ Yes 2 ❑ No
Specimens are assayed within 4 hours after phlebotomy .... 1 ❑ Yes 2 ❑ No
Specimens are centrifuged within 1 hour of collection........................ 1 ❑ Yes 2 ❑ No

The following questions ask about assays for von Willebrand's disease.

16. Does your coagulation laboratory perform von Willebrand Factor Antigen (vWF Ag)?

1 ❑ No → *Go to Question 19.*
2 ❑ Yes → *Please answer Questions 17 and 18.*

17. Does your laboratory report an ABO specific reference range for the vWF Ag assay?

1 ❑ Yes 2 ❑ No

18. Which methodology for vWF Ag is used in your coagulation laboratory? *(Check all that apply.)*

- 1 ❑ ELISA
- 2 ❑ Electrophoresis
- 3 ❑ LIA (Latex Immunoassay)
- 4 ❑ Other *(Please specify.)* ____

19. Does your laboratory perform von Willebrand Factor Activity (Ristocetin CoFactor Activity)?

- 1 ❑ No → *Go to Question 20.*
- 2 ❑ Yes → Which methodology for Ristocetin CoFactor Activity is used in your coagulation laboratory? *(Check all that apply.)*
  - 1 ❑ Platelet Aggregometry
  - 2 ❑ ELISA
  - 3 ❑ Collagen Binding Assays
  - 4 ❑ Other (*Please specify.*) ____________________________

20. Does your laboratory provide results for von Willebrand Factor Multimers?

- 1 ❑ No → *Go to Question 21.*
- 2 ❑ Yes → Under what circumstances does your laboratory perform vWF Multimers?

When the Ristocetin CoFactor is decreased......................	1 ❑ Yes	2 ❑ No
When the Ristocetin CoFactor is disproportionately decreased relative to the vWF Ag.............................	1 ❑ Yes	2 ❑ No
When the Antigen and Activity are both low	1 ❑ Yes	2 ❑ No
Only if the Ristocetin Induced Platelet Aggregation indicates a Type II B von Willebrand's disease	1 ❑ Yes	2 ❑ No
Only when ordered by a clinician	1 ❑ Yes	2 ❑ No

The following questions concern practices and/or test menu selections for a Thrombosis or Hypercoagulability Workup.

21. Does your laboratory usually perform the functional test (activity) for Protein S before the antigenic assay?

- 1 ❑ No → *Go to Question 22.*
- 2 ❑ Yes → If the results of the functional test (activity) for Protein S are decreased, does your laboratory routinely perform:

The antigenic assay to differentiate Type I deficiency from Type II?...	1 ❑ Yes	2 ❑ No
The Protein S Antigen, Free and Total?	1 ❑ Yes	2 ❑ No

22. Does your laboratory perform the Activated Protein C (APC) Resistance assay?

- 1 ❑ No → *Go to Question 23.*
- 2 ❑ Yes → If the results of the APC indicate resistance to APC, do you obtain results for the Factor V Leiden Mutation? .... 1 ❑ Yes 2 ❑ No

The following questions concern an algorithm for diagnosing a Lupus Anticoagulant.

23. Does your laboratory offer a Lupus Anticoagulant Profile (LAC Profile)? .... 1 ❑ Yes 2 ❑ No

24. If a PT result is prolonged, when would your laboratory routinely perform a mixing study on the specimen? *(Check only one.)*

- 1 ❑ Our laboratory does not offer mixing studies for PT
- 2 ❑ Only if there is an additional order for the mixing study
- 3 ❑ Always when PT is prolonged
- 4 ❑ Only if PT was ordered as part of the LAC Profile
- 5 ❑ Other

25. If an aPTT result is prolonged, when would your laboratory routinely perform a mixing study on the specimen? *(Check only one.)*

- 1 ❑ Our laboratory does not offer mixing studies for aPTT → *Go to Question 27.*
- 2 ❑ Only if there is an additional order for the mixing study
- 3 ❑ Always when aPTT is prolonged
- 4 ❑ Only if aPTT was ordered as part of the LAC Profile
- 5 ❑ Other

26. If the results of the mixing study for aPTT do not correct to normal, would your laboratory routinely initiate a workup to diagnose a Lupus Anticoagulant?

- 1 ❑ No → *Go to Question 27.*
- 2 ❑ Yes → Please indicate which of the following are routinely performed for diagnosing a Lupus Anticoagulant.

Dilute Russell Viper Venom Time (DRVVT)	1 ❑ Yes	2 ❑ No
Lupus Sensitive aPTT	1 ❑ Yes	2 ❑ No
Kaolin Clotting Time (KCT)	1 ❑ Yes	2 ❑ No
Hexagonal (II) Phase Phospholipid Assay (Staclot LA)	1 ❑ Yes	2 ❑ No
Platelet Neutralization Procedure (PNP)	1 ❑ Yes	2 ❑ No
Tissue Thromboplastin Inhibition Test (TTIT)	1 ❑ Yes	2 ❑ No

The next questions relate to the monitoring of Low Molecular Weight Heparin (LMWH) therapy.

27. Does your laboratory monitor LMWH therapy?

1 ❑ No → *Go to Question 29.*
2 ❑ Yes → *Please answer Question 28.*

28. Please indicate which of the following assays your coagulation laboratory uses to monitor LMWH.

aPTT	1 ❑ Yes	2 ❑ No	
Factor Xa (Inhibitor Assay)	1 ❑ Yes	2 ❑ No	
Thrombin Inhibitor Assay (HEP Test)	1 ❑ Yes	2 ❑ No	
Anti-Xa	1 ❑ Yes	2 ❑ No	→ *If "No", Go to Question 29.*

→ *If "Yes" for Anti-Xa, please answer Questions A – D.*

A. What calibrator is used for the Anti-Xa assay in your coagulation laboratory? *(Check all that apply.)*

1 ❑ LMWH supplied by pharmacy
2 ❑ Internal Standard LMWH
3 ❑ Internal Standard Unfractionated Heparin
4 ❑ Unfractionated Heparin
5 ❑ Heparinoid
6 ❑ Other

B. Does your laboratory use different calibration curves for ***LMWH and unfractionated heparin***? .... 1 ❑ Yes 2 ❑ No

C. Does your laboratory use different calibration curves for ***each type of LMWH***? .... 1 ❑ Yes 2 ❑ No

D. How long after subcutaneous administration of LMWH does your laboratory recommend that the specimen be collected for optimal testing of Anti-Xa? *(Check only one.)*

1 ❑ Our coagulation laboratory does not recommend a time for testing
2 ❑ Immediately after injection
3 ❑ 2 hours after injection
4 ❑ Between 2 and 4 hours after injection
5 ❑ 4 hours after injection
6 ❑ 5 hours or more after injection
7 ❑ Before the next dose is administered
8 ❑ Do not know
9 ❑ None of the above

The following question asks about the availability of specific coagulation tests in your laboratory.

29. Please indicate which of the following coagulation tests are performed **in-house** for clinical purposes (e.g., diagnosis, monitoring, screening, or treatment). Exclude assays performed for research purposes only.

Bleeding Time	1 ❑ Yes	2 ❑ No
Activated Clotting Time	1 ❑ Yes	2 ❑ No
Thrombin Time	1 ❑ Yes	2 ❑ No
Fibrinogen	1 ❑ Yes	2 ❑ No
Fibrin(ogen) Degradation Products	1 ❑ Yes	2 ❑ No
D-Dimer	1 ❑ Yes	2 ❑ No
Euglobulin Clot Lysis Time	1 ❑ Yes	2 ❑ No
Factor II Activity	1 ❑ Yes	2 ❑ No
Factor V Activity	1 ❑ Yes	2 ❑ No
Factor V Leiden	1 ❑ Yes	2 ❑ No
Factor VII Activity	1 ❑ Yes	2 ❑ No
Factor VIII Activity	1 ❑ Yes	2 ❑ No
Factor VIII Antigen	1 ❑ Yes	2 ❑ No
Bethesda Assay-Inhibitor Titer	1 ❑ Yes	2 ❑ No
Factor IX Activity	1 ❑ Yes	2 ❑ No
Factor X Activity	1 ❑ Yes	2 ❑ No
Factor X Antigen	1 ❑ Yes	2 ❑ No
Plasminogen (functional) Assay	1 ❑ Yes	2 ❑ No
Plasminogen Antigen	1 ❑ Yes	2 ❑ No
Heparin Assay (Anti-Xa)	1 ❑ Yes	2 ❑ No
Platelet Aggregation Study	1 ❑ Yes	2 ❑ No
Platelet Antibody	1 ❑ Yes	2 ❑ No
Ristocetin Titration of Platelet Aggregation	1 ❑ Yes	2 ❑ No
von Willebrand Factor Multimers	1 ❑ Yes	2 ❑ No

The following questions refer to certain aspects of reporting coagulation test results.

30. Using a check mark, please indicate what test result information, interpretations, and recommendations are provided on your coagulation test report for PT, aPTT, vWF Antigen, and Protein C assays. *(Check all that apply.)*

	PT	aPTT	vWF Antigen	Protein C
Test Not Performed	1	1	1	1
Measurement Units (e.g., seconds, %)	2	2	2	2
Specimen comments (if needed)	3	3	3	3
Reference ("Normal") ranges	4	4	4	4
Therapeutic ranges	5	5	5	5
Testing methodology/reagent	6	6	6	6
Possible drug interactions	7	7	7	7
Suggested diagnoses	8	8	8	8
Written interpretation	9	9	9	9
No test result interpretation	10	10	10	10
Recommendations for further testing	11	11	11	11
Recommendations for treatment	12	12	12	12
Recommendations to test family members	13	13	13	13
No recommendation	14	14	14	14

31. Does your laboratory offer consultation services for coagulation testing?

1 ❑ No → *Go to Question 32.*
2 ❑ Yes → *Please answer Questions A - C.*

A. Please indicate when coagulation test reports are reviewed. *(Check all that apply.)*

1 ❑ This service is not offered
2 ❑ Upon request by clinician
3 ❑ Upon request by testing personnel
4 ❑ For all specialized tests
5 ❑ None of the above

B. Please indicate who reviews coagulation test reports.
(Check all that apply.)

1 ❑ This service is not offered
2 ❑ Laboratory Director
3 ❑ Pathologist (excluding residents)
4 ❑ Laboratory Supervisor
5 ❑ Physicians in training (residents, interns, medical students)
6 ❑ None of the above

C. Please indicate who provides comments on the coagulation test reports.
(Check all that apply.)

1 ❑ This service is not offered
2 ❑ Laboratory Director
3 ❑ Pathologist (excluding residents)
4 ❑ Laboratory Supervisor
5 ❑ Physicians in training (residents, interns, medical students)
6 ❑ None of the above

The next section relates to the process of reporting results.

32. Does your laboratory report critical values (panic values) for coagulation tests?

1 ❑ No → *Go to Question 33.*
2 ❑ Yes → *Please respond to the following:*

Critical values are repeated and documented as "confirmed" .... 1 ❑ Yes 2 ❑ No
Critical values are indicated on the report and no further action is taken .... 1 ❑ Yes 2 ❑ No
Critical values are telephoned to the clinician and the call is not always documented .... 1 ❑ Yes 2 ❑ No
Critical values are telephoned to the clinician and the call is documented .... 1 ❑ Yes 2 ❑ No

33. Under what circumstances would a coagulation test usually be repeated in your laboratory?

Control(s) is/are out of range .... 1 ❑ Yes 2 ❑ No
Results are outside instrument technical ranges .... 1 ❑ Yes 2 ❑ No
Results are outside of the reference ("normal") range .... 1 ❑ Yes 2 ❑ No
Results are critical values (panic values) .... 1 ❑ Yes 2 ❑ No
Results do not agree with previous results (using a predetermined Delta Check range) .... 1 ❑ Yes 2 ❑ No

The next question asks about Quality Assurance (QA) procedures.

34. Please indicate if any of the following QA steps are usually taken in your laboratory.

Specimen label and requisition form are matched	1 ❑ Yes	2 ❑ No
Patient information on specimen tube and laboratory generated labels are matched	1 ❑ Yes	2 ❑ No
Instrument printout is compared to reported value	1 ❑ Yes	2 ❑ No
Patient's previous results are checked (Delta Check)	1 ❑ Yes	2 ❑ No
Critical (Panic) values are reviewed	1 ❑ Yes	2 ❑ No
Critical (Panic) values are brought to the immediate attention of the clinician	1 ❑ Yes	2 ❑ No
New analytical methods are validated	1 ❑ Yes	2 ❑ No
Calibration of all instruments (analyzers, centrifuges, refrigerators, etc.) is periodically verified	1 ❑ Yes	2 ❑ No
Plasma is checked for a platelet count after centrifugation	1 ❑ Yes	2 ❑ No
Specimens are run in duplicate	1 ❑ Yes	2 ❑ No
Controls are run in duplicate	1 ❑ Yes	2 ❑ No

The next section asks about your coagulation laboratory's personnel and resources.

35. Where in your facility is coagulation testing performed? *(Check all that apply.)*

1 ❑ Core Laboratory
2 ❑ Coagulation Laboratory
3 ❑ Hematology Laboratory
4 ❑ Point-of-Care Testing
5 ❑ Rapid response (Stat) Laboratory
6 ❑ None of the above

36. How many FTEs (Full Time Equivalents) does your laboratory have for performing coagulation testing? *(Check only one.)*

1 ❑ Less than 4
2 ❑ 4 - 9
3 ❑ 10 or more

37. Please indicate which of the following components are included in your competency assessment program for coagulation testing personnel. *(Check all that apply.)*

1 ❑ Periodic written exam
2 ❑ Analysis of unknown samples
3 ❑ Review of procedure manuals
4 ❑ Direct observation of a task
5 ❑ Participation in Continuing Education (CE)
6 ❑ Successful performance of quality control (QC) with documentation of remedial actions
7 ❑ None of the above

38. Please indicate the educational degree of the laboratory director who is responsible for coagulation testing. *(Check all that apply.)*

- 1 ❑ M.D.
- 2 ❑ Ph.D.
- 3 ❑ Other *(Please specify.)* ___________________________

39. Please indicate the certifications of the laboratory director who is responsible for coagulation testing. *(Check all that apply.)*

- 1 ❑ Board Certified in Clinical Pathology (CP)
- 2 ❑ Board Certified in Anatomical Pathology (AP)
- 3 ❑ Board Certified in Medicine
- 4 ❑ Board Certified in Subspecialty of Hematology
- 5 ❑ Board Certified in Hematopathology
- 6 ❑ Certified by American Association of Bioanalysts (AAB)
- 7 ❑ Certified by American Board of Clinical Chemistry (ABCC)
- 8 ❑ Certified by National Registry of Clinical Chemistry (NRCC)
- 9 ❑ Certified by National Certifying Agency (for Clinical Laboratory Sciences) (NCA)
- 10 ❑ Certified by American Society of Clinical Pathologists (ASCP)
- 11 ❑ None of the above

40. In your hospital, is there a clinician available for consultation who has expertise in coagulation disorders? .... 1 ❑ Yes 2 ❑ No

41. Does your hospital have an anticoagulation outpatient clinic that specializes in the adjustment of oral anticoagulants? .... 1 ❑ Yes 2 ❑ No

42. Does your hospital have an outpatient clinic that specializes in the diagnosis and treatment of coagulation disorders? .... 1 ❑ Yes 2 ❑ No

The next section addresses Point-of-Care Testing (POCT) for the PT assay.

43. Is POCT currently available for the Prothrombin Time (PT) assay within your hospital?

1 ❑ No → *Go to Page 15.*
2 ❑ Yes → *Please answer Questions A - F.*

A. Does the laboratory have oversight of coagulation POCT including certification and regulatory compliance?... 1 ❑ Yes 2 ❑ No

B. Where is coagulation POCT performed in your hospital? *(Check all that apply.)*

1 ❑ At the bedside
2 ❑ At a coagulation clinic
3 ❑ In a satellite laboratory
4 ❑ In a cardiac catheterization laboratory
5 ❑ In a dialysis clinic
6 ❑ In operating rooms
7 ❑ None of the above

C. Are coagulation POCT results integrated into the laboratory's results reporting system?

1 ❑ No → *Go to Question D.*
2 ❑ Yes → Are coagulation POCT results integrated into the laboratory's reporting system in the order of collection times?............................... 1 ❑ Yes 2 ❑ No

D. Is the reference range for the POCT PT assay the same as the PT assay reference ("normal") range used by your coagulation laboratory?

1 ❑ Yes → *Go to Question E.*
2 ❑ No → Was the POCT reference ("normal") range established by the same method used to establish the Prothrombin Time reference range for your laboratory?

1 ❑ Yes → *Go to Question E.*
2 ❑ No → How was the POCT reference ("normal") range established? *(Check all that apply.)*

1 ❑ In-house testing
2 ❑ Manufacturer's insert
3 ❑ Published values
4 ❑ Other *(Please specify.)*

____

E. Which type of QC material is used on the POCT coagulation instrument? *(Check all that apply.)*

1 ❑ Liquid
2 ❑ Lyophilized
3 ❑ Electronic
4 ❑ None of the above

F. How often is QC performed on each coagulation POCT instrument? *(Check all that apply.)*

1 ❑ Once per shift
2 ❑ Once per day
3 ❑ Other *(Please specify.)* ________________________________

❑ ***Please check this box if you would like to receive a copy of the report of CDC findings.***

We would appreciate your comments on this survey and on the subject of coagulation laboratory practices.

Please return this questionnaire to ASI in the enclosed reply envelope. If this envelope has been misplaced, please mail the survey to the following address:

Jack K. Leiss, PhD
Director, National Survey of Hospital Coagulation Laboratories
Analytical Sciences, Inc.
2605 Meridian Parkway, Suite 200
Durham, NC 27713

Thank you for taking the time to complete this survey. Your participation is greatly appreciated.