Coagulation laboratory tests are vital to the diagnosis, treatment, and management of bleeding and hypercoagulability disorders. Some laboratories, however, fail to follow voluntary practice guidelines for coagulation tests (1, 2), and inappropriate performance of coagulation tests, such as the prothrombin time (PT) test, may contribute to coagulation and bleeding complications (3, 4). A 2001 survey of coagulation laboratory testing practices in a randomly selected sample of US hospitals revealed substantial variability in laboratory practices (1). The lack of agreement between reported practices and recommendations (1) demonstrated a need to understand the reasons for noncompliance to better promote adherence to laboratory practice guidelines and standards. In a 2004 survey of hospital laboratories and of independent and point-of-care (POC) laboratories in the US Pacific Northwest, we evaluated PT testing practices to determine the extent to which laboratories used specific practice guidelines and standards and assessed why some testing sites did not adhere to specific recommendations and regulatory standards (2, 5). Here we compare the findings of the 2001 and 2004 surveys (1, 2, 5) and discuss the extent to which guidelines are followed for certain PT testing practices.

**International Sensitivity Index (ISI) of thromboplastin lot.** Several organizations, including the Clinical and Laboratory Standards Institute (CLSI; formerly NCCLS), College of American Pathologists (CAP), and American College of Chest Physicians, recommend using only thromboplastins with an ISI of 1.70 or less (2, 5). Several published studies have reported ISI values used by survey participants that together suggest increasing use of lower-ISI reagents. In the 2004 survey of PT testing practices, 67% reported ISIs of ≤1.70 for their current thromboplastin lots (2, 5), whereas in the 2001 survey of US hospital laboratories, 40% reported using thromboplastins with ISIs of ≤1.70 (1). The increasing use of lower-ISI reagents may have resulted from publication of guidelines advocating their use and thus contributing to their increasing availability. Although laboratorians may be in a position to choose lower-ISI reagents, some may be limited to purchasing reagents with ISI values >1.70 because lower-ISI reagents may not be available for some test systems.

**Sensitivity of PT assay to heparin.** According to consensus guidelines developed by the CAP, 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 (1). In the 2004 PT survey, 12% of respondents reported determining sensitivity of their PT assays to heparin, whereas 42% reported selecting a thromboplastin reagent that was insensitive to heparin in the therapeutic range (2). These results were quite comparable to the data obtained in the 2001 survey of US hospital laboratories, in which 16% reported determining the sensitivity of their PT assays to heparin and 45% reported selecting a thromboplastin reagent that was insensitive to heparin in the therapeutic range (1).

**Sodium citrate concentration.** The CLSI and WHO guidelines recommend use of 109 mmol/L citrate as the anticoagulant of choice for coagulation laboratory tests (1). Incomplete filling of blood collection tubes to <80% of the nominal volume produces statistically significant errors in PT assays when the tubes contain 129 mmol/L (3.8%) sodium citrate. By contrast, PT results for tubes that contain 109 mmol/L (3.2%) citrate are not affected by filled volumes of between 60% and 100% (1). In the 2004 PT survey, 93% of laboratories used 109 mmol/L sodium citrate (2). This may be compared with the results obtained in the 2001 survey of US hospital coagulation laboratories, in which 72% reported using 109 mmol/L sodium citrate (1). It appears—based on these results and those published before 2001 (1)—that with time more laboratories are purchasing and using collection tubes with the recommended 109 mmol/L sodium citrate concentration.

**Validation of new reagent lots.** Various practice standards and guidelines address issues associated with implementing new lots of test reagents (1, 2, 5). Given a list of practices associated with validation of new lots of thromboplastin reagents, respondents to the 2004 PT survey answered affirmatively at various proportions ranging from 24% for establishing ISI with calibrators and 42% for performing correlation studies with another method or site to 84% for verifying their reference intervals (2, 5). Verification of the ISI value in the product insert with every lot of reagents is a simple and effective solution to help alleviate serious calculation errors (3). In the 2004 PT survey, 81% verified that their ISI value was correct for their instrument/reagent combination.

**Measurement unit for PT.** Several practice guidelines and publications suggest that reporting of PT results for patients on oral anticoagulation therapy include the use of international normalized ratio (INR) values (1, 2, 5). This appears to be a recommendation that is almost universally followed based on the results from these two surveys: 99.6% of respondents reported PT as INR in the 2004 survey (2, 5), and 99.9% said they did so in the 2001 survey (1).

**Use of voluntary practice guidelines.** Of those responding to the 2004 PT survey, a minority (22%–46%) said they used voluntary practice guidelines to select their reagents, select citrate concentration, develop policies for specimen acceptability, and develop policies for validating new lots of reagents (2). Of those noting that they did not use a practice guideline (27%–39%), most (52%–61%) stated that they were not aware of any guidelines relating to these practices. Other reported reasons that guidelines were not used included performing own studies (15%–
24%), performing own literature review (13%–21%), following manufacturer’s recommendation (3%–8%), and not agreeing with guidelines (0%–1%). Of the respondents noting use of practice guidelines, most (57%–81%) mentioned using the CLSI guidelines, 20%–31% named the CAP guidelines, and 14%–24% mentioned both the CLSI and CAP as their source.

We compared responses of those who used traditional laboratory methods for PT with responses of those who used POC methods for PT. We looked specifically at reported use of guidelines to select reagents and reported use of guidelines to develop policies for validating new lots of reagents (2). Responses did not differ significantly between the 2 groups ($P = 0.06$ and 0.15, respectively) in this small sample, but we were interested in the results. Those using traditional methods reported using guidelines more frequently than did respondents using POC methods (25% vs 11% and 37% vs 25%, respectively, for the two guideline topics). This may suggest that those using POC methods are prime targets for efforts to increase their awareness of available guidelines.

An inherent limitation of these surveys is that responses may not consistently reflect actual practices. The findings should, however, accurately reflect the state of reported PT testing practices in various types of laboratories located in the US Pacific Northwest in 2004 and in US hospitals in 2001 because the response rates were 50% and 79%, respectively, and the responding laboratories appeared to be representative of those targeted. Like results of any survey, these are subject to framing bias. It is well known that the way a question is posed, or “framed”, may have a dramatic impact on the response (1). However, we attempted to reduce framing bias by having these questionnaires pilot-tested at different testing sites. Our results showed substantial variabilities in some PT testing practices as they relate to laboratory practice guidelines and standards. For the 2004 survey, several questions elicited significantly different responses, particularly from POC and hospital/independent laboratories as well as from laboratories using traditional and POC methods. When we found significant differences, usually a greater proportion of hospital/independent laboratories or those using traditional test methods adhered to laboratory practice guidelines and standards.

A key finding of the 2004 PT survey is that most of the respondents who were not following specific laboratory practice guidelines were not aware of them. This finding indicates that publication of guidelines is insufficient to ensure their adoption and underscores the need to identify the most effective means to raise awareness of guidelines that can improve health.

References

Shahram Shahangian1*
Kathleen M. LaBeau2
Devery A. Howerton1

1CDC
Atlanta, GA
2Washington State Department of Health
Shoreline, WA

* Address correspondence to this author at: CDC, 4770 Buford Hwy, NE, G-23, Atlanta, GA 30341-3717. E-mail sshahangian@cdc.gov.

DOI: 10.1373/clinchem.2005.065433