Q&A column

Editor: Frederick L. Kiechle, MD, PhD

Submit your pathology-related question for reply by appropriate medical consultants. CAP TODAY will make every effort to answer all relevant questions. However, those questions that are not of general interest may not receive a reply. For your question to be considered, you must include your name and address; this information will be omitted if your question is published in CAP TODAY.

Q. Which criteria should be used to interpret mixing studies, not only for lupus anticoagulants but also for other inhibitors?

A.April 2023—There are several criteria for interpreting mixing studies, and practices can vary widely among institutions and coagulation laboratories. As no standard set of guidelines for assessing a mixing effect is provided by the International Society on Thrombosis and Haemostasis scientific and standardization committee's subcommittee on lupus anticoagulant/antiphospholipid antibodies or the CAP Hemostasis and Thrombosis Committee, the most common approach is to utilize in-house reference ranges determined using normal pooled plasma or normal donor samples. Accordingly, mixing studies are interpreted against a normal range or expected mean. The Chang percent correction[1] and Rosner index of circulation anticoagulant[2] are two well-described and widely used calculations.[3,4]

As factor assays and lupus anticoagulant (LA) testing become more routine and widely available, the need for a defined set of criteria for interpreting mixing studies becomes less pressing. A mixing study is often performed as an initial workup to determine whether a prolonged clotting time is due to factor deficiency or the presence of an inhibitor. Therefore, in many cases it may be helpful to have a lower threshold for reflexing abnormal mixing study results to subsequent factor level or LA testing.

It is important that the laboratory has a clearly defined procedure for performing a mixing study; the laboratory and clinicians using the test understand the circumstances in which a mixing study is to be performed; the interpretation of the results and any generated reports are clear to the laboratory and clinician; and every mixing study is reported with an interpretation from a qualified professional.

1. Chang SH, Tillema V, Scherr D. A "percent correction" formula for evaluation of mixing studies. *Am J Clin Pathol*. 2002;117(1):62–73.
2. Rosner E, Pauzner R, Lusky A, Modan M, Many A. Detection and quantitative evaluation of lupus circulating anticoagulant activity. *Thromb Haemost*. 1987;57(2):144–147.
3. Kershaw G. Performance and interpretation of mixing tests in coagulation. In: Favaloro EJ, Lippi G, eds. *Hemostasis and Thrombosis: Methods and Protocols.* Humana Press; 2017:85–90. *Methods in Molecular Biology*, vol 1646.
4. Chen J, Phillips B, Chandler WL. Evaluation of prothrombin time and activated partial thromboplastin time mixing

studies using an estimated factor correction method. *Blood Coagul Fibrinolysis*. 2016;27(1):90–96.

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Q. How does the CAP checklist requirement COM.30840 Pipette Carryover relate to blood bank automation? Are there CAP guidelines that address pipette carryover relative to such systems?

A.The all common checklist requirement COM.30840 Pipette Carryover applies to all test systems or analyzers that use automated pipettes, including automated blood bank instruments. Carryover studies are used to evaluate the method or instrument and do not need to include every test or analyte. The laboratory may select representative analytes for the study. Carryover must be evaluated prior to initial use of the instrument and after major maintenance or repair of the instrument's pipette assembly, following the manufacturer's guidelines.

The CAP recommends that laboratories begin by reviewing information from the manufacturer, such as the operations manual, and/or by contacting the manufacturer to determine if pipette carryover has been identified as an issue for the instrument. Carryover studies may be performed by following the instrument manufacturer's guidelines or using a study designed by the laboratory. The note in COM.30840 provides a suggested method for studying carryover that involves running patient samples with a known high concentration of analyte followed by samples with a known low concentration of analyte to see if there is a clinically significant impact on the results of the low-level samples. Laboratories may also use data from carryover studies performed by the instrument manufacturer.

If carryover is identified as a potential issue, the laboratory needs to define how it will be detected in a run and what actions are appropriate (for example, repeat analysis of subsequent specimens).

Clinical and Laboratory Standards Institute. QMS23: General Laboratory Equipment Performance Qualification, Use, and Maintenance, 2nd ed.; 2019.

College of American Pathologists. COM.30840 Pipette carryover. In: All common checklist. Oct. 24, 2022.

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Q. Our laboratory is assessing criteria for determining quantity not sufficient for a microscopic urinalysis. We were using an automated instrument but have gone back to manual microscopy for

reasons beyond our control. While most textbooks state that 10 to 15 mL is the desired amount of sample for testing, it appears that many laboratories require smaller amounts. Can you provide guidance?

A.The exact volume required for a urine sample depends on the testing method used. A good rule of thumb is to require twice the volume required by an automated method to complete the chemical and microscopic portions of the urinalysis. This allows for sufficient volume to do a manual analysis or a repeat automated analysis should the initial automated analysis generate an instrument flag. So an automated instrument that requires 2 mL to complete one analysis would require a minimum volume of 4 mL.

For urine sample volumes of 2 to 4 mL, a laboratory's policy could allow for a partial manual analysis, such as a manual dipstick with manual microscopic analysis. Urinalysis sample volumes of less than 2 mL typically are not analyzed, and they are reported as quantity not sufficient.

European Confederation of Laboratory Medicine. European urinalysis guidelines. *Scand J Clin Lab Invest*. 2000;60(suppl 231):1–96.

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