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About: Factor Assays When an Inhibitor is Present
From: **Russell Higgins, MD**, colleague of **John Olson, MD**
To: **Dee McMichael**, Blood Bank Supervisor, All Children's Hospital, St. Petersburg, FL

Hello Dee,
Some experts are concerned about introducing matrix effect when diluting beyond 1:160. However, I haven't seen any literature to support or refute this cutoff. The accuracy of diluting a specimen 1:320 is another relevant concern. The decision of how many dilutions to make is ultimately up to the medical director.
It is important to write an interpretive comment for factor assays with inhibitors. This allows the pathologist to express the limitations of the factor assay when inhibitors are present, to record the dilution performed, and to result a "greater than value" when necessary.
The example of a specific factor VIII inhibitor is a difficult one. In contrast to a lupus anticoagulant where it is often possible to dilute out the inhibitor with a 1:160 dilution, it may not be possible to dilute out high titer factor VIII inhibitors without running into limitations of the assay. In the example given, my preference would be to report >12% at a 1:160 dilution along with a comment explaining the limitations of measuring factor VIII in the presence of a strong inhibitor. The >12% result may give the treating physician some useful information if the next result is >30% at a 1:160 dilution. If all of the dilutions (1:10 through 1:160) are truly below the analytical measurement range (linearity) of your regular curve, then simply reporting that the factor VIII activity could not be obtained due to a strong inhibitor pattern is sufficient. I believe <7% could potentially be misleading because it could be misinterpreted as no factor VIII activity.
I am not sure which CAP survey you referred to in your comments. There was a recent specimen, CGE-04, in the 2012 CGE-B survey that included normal plasma spiked with rivaroxaban. This was intended, as an educational exercise, to demonstrate that many clot-based assays are affected by this drug. Unlike dabigatran or unfractionated heparin, where we can do a thrombin time to screen for the drug, there are no routine screening assays for rivaroxaban. Rivaroxaban may cause laboratories to report incorrect results if the inhibitor effect is not identified. Although the true factor VIII activity was 100% (normal plasma), the all method mean of peer groups was 55% indicating that many laboratories did not recognized the inhibitor pattern. 54 labs (11%) reported a greater than value. 22% of laboratories performed more than 4 dilutions on the rivaroxiban sample (CGE-04) compared to 6% on the sample without an inhibitor (CGE-03) in the same survey.

Thank you for the discussion,
Russell Higgins, MD