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DOI: 10.1373/clinchem.2006.071696

Assay Interferences from Blood Collection Tubes: A Cautionary Note

To the Editor:

Recent publications *(1, 2)* have reported an association between the surfactant present in BD Vacutainer® blood collection tubes and interference in select immunoassays on certain instrument platforms. Blood collection tubes contain not only surfactants but multiple additives that contribute to the optimal recovery of serum or plasma for laboratory analysis. For plastic tubes, which are largely replacing glass tubes because of safety considerations, several suppliers have added silica particles to promote blood clotting *(3–5)* and polyvinylpyrrolidone to aid the adherence of silica particles to the tube walls and to facilitate rapid dissolution of the silica in the blood specimen. Moreover, silicone-based surfactants or polypropylene oxide are present as coatings for the interior tube wall *(6, 7)* to act as hemorepellent agents and improve blood flow. Stoppers of tubes are also coated with lubricant to facilitate their removal and to maintain the lower pressure inside the evacuated tubes *(4)*. Separator gels are present in some tubes to serve as a barrier between the serum (or plasma) and the clot after centrifugation of the tubes *(8)*. Plastic blood collection tubes have been widely shown to be suitable for routine clinical chemistry analytes, hormone analysis, and therapeutic drug monitoring *(9–11)*.

Surfactants are also a common component of many immunoassays. They are used to decrease or eliminate nonspecific adsorption, improve stability of the reagents, or modify the solid-phase surface to render it less hydrophobic and thus minimize loss of noncovalently bound antibody. Inclusion of surfactants in immunoassay reagents requires careful selection and optimization. High concentrations of surfactants may lead to direct loss of passively adsorbed antibody from the solid phase, among other nonspecific effects *(12–13)*.

The reports by Bowen et al. *(1, 2)* show that a high concentration of a silicone-based surfactant is a potential source of the immunoassay interference in the DPC IMMULITE® 2500 Total Triiodothyronine (TT_3) assay. The authors indicate that one of the possible mechanisms of interference is desorption of the antibodies from the solid phase by the surfactant for the TT_3 assay *(1)*, resulting in a falsely increased estimate of the TT_3 concentration. As described above, this phenomenon is not unknown in immunoassays in which the antibodies are passively adsorbed onto the solid phase *(12–13)*. Other types of assay formats with more robust antibody binding schemes do not show this problem, even at high concentrations of surfactant as demonstrated on the AxSym™ analyzer. The concentration of surfactant at which Bowen et al. demonstrated the desorption of antibody in the TT_3 assay was 2- to 24-fold higher than the concentration of surfactant per milliliter of blood present in the BD Vacutainer tubes that exhibited the interference in the TT_3 assay. The current adjusted BD Vacutainer tubes have been shown to produce no clinically significant differences for a variety of assays across many instrument platforms when compared with competitive products [see "Note added in proof" in reference *(2)*]. The concentration of the surfactant has been adjusted to decrease any known assay interferences and yield clinically equivalent results compared with glass tubes *(14)*.

Assay interferences from blood collection tubes can present challenges to clinical laboratories because they are not easily detected by the daily quality control or even by proficiency testing programs because the samples for such testing are not exposed to the additives in the blood collection tubes *(15)*. However, it is always good practice for laboratories to monitor their reference intervals and population trends and report deviations to the device manufacturers. All laboratorians should be vigilant for potential effects on laboratory assays and work together in partnership with tube manufacturers and diagnostic companies to prevent and minimize problems.

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DOI: 10.1373/clinchem.2006.069997

Correction

For the article entitled "Association of Inosine Triphosphate 94C>A and Thiopurine *S*-Methyltransferase Deficiency with Adverse Events and Study Drop-Outs under Azathioprine Therapy in a Prospective Crohn Disease Study", by N. von Ahsen, V.W. Armstrong, C. Behrens, C. von Tirpitz, A. Stallmach, H. Herfarth, J. Stein, P. Bias, G. Adler, M. Shipkova, M. Oellerich, W. Kruis, and M. Reinshagen (*Clin Chem* 2005;51:2282–8; DOI: 10.1373/clinchem.2005.057158), the authors wish it to be known that, because of his major participation in the original study design and initial analytics to compare 6-thioguanosine nucleotides concentration-guided azathioprine dosing with standard dosing according to body weight, Ekkehard Schütz should have been listed as a coauthor of the manuscript. At the time of the research, he was affiliated with the Department of Clinical Chemistry, University of Göttingen, Göttingen, Germany (current affiliation: Institute of Veterinary Medicine, University of Göttingen).

DOI: 10.1373/clinchem.2006.073601

Correction

For the Technical Brief entitled "Analytical Performance and Diagnostic Accuracy of Immunometric Assays for the Measurement of Circulating Oxidized LDL" by P. Holvoet, E. Macy, M. Landeloos, D. Jones, J.S. Nancy, F. Van de Werf, and R.P. Tracy (*Clin Chem* 2006;52:760–4; DOI: 10.1373/clinchem.2005.064337), the name of author J.S. Nancy is incorrect. The author's name should be Nancy S. Jenny.

The authors apologize for any confusion this error may have caused.

DOI: 10.1373/clinchem.2006.073619

Correction

In the article entitled "Utility of Thrombin-Generation Assay in the Screening of Factor V G1691A (Leiden) and Prothrombin G20210A Mutations and Protein S Deficiency" by N. Hézard, L. Bouaziz-Borgi, M-G. Remy, and P. Nguyen (*Clin Chem* 2006;52:665–70), in Table 2 (page 668), the ETP [endogenous thrombin potential] values (as nmol/L thrombin) for persons with no thrombophilic disorder are incorrect. The mean (SD) currently reads as 882 (317) and the range as 11196–2666. The correct mean (SD) is 1882 (317), and the correct range is 1196–2666.

The error occurred in production, and all concerned apologize.

DOI: 10.1373/clinchem.2006.073130