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Review

Blood collection tubes as medical devices: The potential to affect assays and proposed verification and validation processes for the clinical laboratory

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ABSTRACT

Blood collection tubes (BCTs) are an often under-recognized variable in the preanalytical phase of clinical laboratory testing. Unfortunately, even the best-designed and manufactured BCTs may not work well in all clinical settings. Clinical laboratories, in collaboration with healthcare providers, should carefully evaluate BCTs prior to putting them into clinical use to determine their limitations and ensure that patients are not placed at risk because of inaccuracies due to poor tube performance. Selection of the best BCTs can be achieved through comparing advertising materials, reviewing the literature, observing the device at a scientific meeting, receiving a demonstration, evaluating the device under simulated conditions, or testing the device with patient samples. Although many publications have discussed method validations, few detail how to perform experiments for tube verification and validation. This article highlights the most common and impactful variables related to BCTs and discusses the validation studies that a typical clinical laboratory should perform when selecting BCTs. We also present a brief review of how in vitro diagnostic devices, particularly BCTs, are regulated in the United States, the European Union, and Canada. The verification and validation of BCTs will help to avoid the economic and human costs associated with incorrect test results, including poor patient care, unnecessary testing, and delays in test results. We urge laboratorians, tube manufacturers, diagnostic companies, and other researchers to take all the necessary steps to protect against the adverse effects of BCT components and their additives on clinical assays.

Contents

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1. Introduction

Laboratory testing plays a significant role in patient care and in the United States (US) >7 billion laboratory tests are performed each year [1]. Research indicates that laboratory test results impact >70% of clinical decisions related to admission, discharge, and the administration of medications [2–4]. Consequently, errors occurring in the preanalytical (specimen collection, transport, handling, and storage), analytical (testing), and postanalytical phases (reporting) affect patient safety and unnecessarily burden hospital budgets [2,5]. The majority of these laboratory errors (~46–68.2%) originate in the preanalytical phase, largely because many of the steps performed in this phase require more human involvement, and unlike other phases, may involve staff members who are not laboratory professionals [2,6]. Technological advances and quality assurance protocols have significantly decreased analytical and postanalytical phase errors [2,6]. Green [7] reported that preanalytical errors account for 0.23%–1.2% of total hospital operating costs. For a 650 bed hospital in the US, preanalytical errors are estimated to cost ~$1.2 million dollars per year [7]. These costs are attributable to the time associated with specimen recollection, processing, lab testing materials, and additional patient treatment [7].

Blood collection tubes (BCTs) are an often under-recognized or ignored variable in the preanalytical phase of clinical laboratory testing [8,9]. The components of BCTs, which include tube walls, rubber stoppers, lubricants, anticoagulants, separator gels, clot activators, and surfactants, can affect the accuracy of laboratory tests in the following ways: by adding contaminants to the blood specimen, adsorbing blood constituents, interacting with protein and cellular components, or altering the stability of analytes (Fig. 1) [8–17]. BCTs are classified as medical devices and therefore require regulatory approval before they can be marketed. Regulatory agencies and international standards and guidelines (e.g., International Organization for Standardization [ISO] 6710, 16142, 20658, EN 13485, 9001, and 14820; CLSI GP39-A6 [formerly called H1-A6], H21-A5, and GP34-A; and World Health Organization [WHO] guidelines on Drawing Blood: Best Practices in Phlebotomy) are available to ensure that specimen collection devices (including needles and sets) are safe, effective, and perform as intended prior to entry into the market [10,18–25].

The selection of a BCT type can be based on a variety of inputs, including comparing advertising materials, reviewing the literature, observing the device at a scientific meeting, receiving a demonstration, evaluating the device under simulated conditions, or testing the device with patient samples. However, even the best-designed and manufactured BCT may not work well in all clinical settings for all analytes. Furthermore, price is not necessarily an indicator of tube quality or compatibility [16]. Therefore, clinical laboratories, in collaboration with healthcare providers, should thoroughly evaluate BCTs prior to introducing them into clinical use in order to determine their limitations and ensure that patients are not placed at risk due to poor tube performance. Some countries have regulatory requirements to verify that the BCTs used in clinical laboratories perform as intended (e.g., in the US this is regulated by the College of American Pathologists [CAP]). For example, question GEN.40942 in the CAP Laboratory General checklist states: "The laboratory director or designee evaluates significant changes to specimen containers to ensure that they do not contribute to analytic interference in the assays to be performed and approves them for use." [26]. Therefore, direct testing by laboratory personnel may be needed to confirm the acceptability of a BCT's performance in an end-user setting. Although rigorous BCT evaluation takes time and money, proper planning and execution are key to cost-effective, high-value, BCT studies and are well worth the investment.

Although many publications have discussed method validations, we detail how to perform experiments for tube verification and validation. This article highlights the most common and impactful variables related to BCTs and discusses validation studies that a typical clinical laboratory should perform when any changes in the formulation of current tubes or new BCTs are being considered. We also present a brief review of how in vitro diagnostic devices, particularly BCTs, are regulated in the US, EU, and Canada. The tube validation protocols described in this article are primarily for venous-derived serum and plasma specimens; however, some of the information may be applicable to BCTs that collect whole blood or capillary specimens in microcollection devices.

2. Medical device regulations

A medical device is defined in the US as an "instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory, which is: (1) recognized in the official National Formulary, or the US Pharmacopeia, or any supplement to them, (2) intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or (3) intended

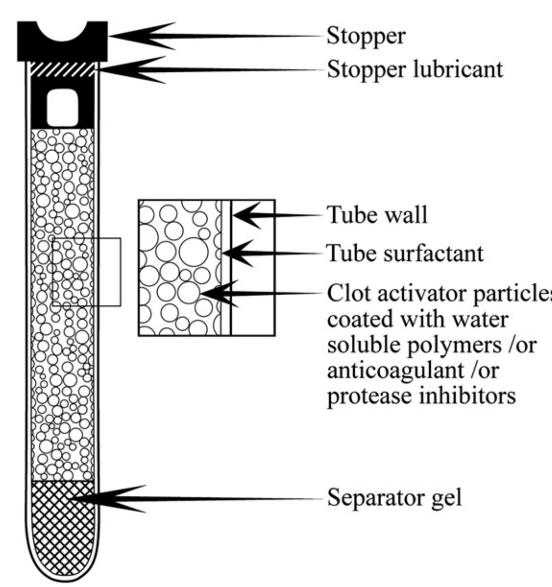

Fig. 1. Components of a blood collection tube. Adapted from Clinical Biochemistry, 43 (1–2), Bowen RAR, Hortin GL, Csako G, Otanez O, Remaley AT. Impact of blood collection devices on clinical chemistry assays, pages 4–25, 2010, with permission from Elsevier.