

# The evolution of evacuated blood collection tubes



The introduction of evacuated tubes greatly enhanced the precision and accuracy of test results by reducing errors in collection, (eg, blood-to-additive ratios or contamination). This article reviews the history of evacuated tubes, the regulations and manufacturing of evacuated tubes, the additives used in evacuated tubes, and some environmental factors influencing product performance.

“ A laboratory test is no better than the specimen, and the specimen no better than the manner in which it was collected. So stated the advertising language of BD (Becton Dickinson and Company) to promote the first evacuated blood collection tubes, back in the late 1940s and early 1950s. <sup>1</sup> This technology for blood collection, patented in 1949, is substantially similar to the technology pervasive in clinical practice today. Consider what it was like to draw blood without an evacuated tube system. Even before collecting blood, the laboratory had to prepare solutions for the additive tubes (eg, EDTA, citrate) and dispense them into test tubes for blood anticoagulation.

Then, to identify the proper draw volume, the laboratory had to etch lines in the borosilicate glass tubes. The phlebotomist collected blood specimens with needles and glass syringes. For patients who required many tests, the phlebotomist might have to stick the patient multiple times, at least once for chemistry, once for hematology, and once for coagulation. After collection, the phlebotomist would transfer the blood into a series of test tubes. They sealed the tubes with black rubber stoppers for transportation of the specimens to the laboratory.

For electrolyte measurements, they added mineral oil to the tubes to prevent loss of CO<sub>2</sub>. For serum specimens, the technologist would use wooden applicator sticks to loosen the clot from the tube walls. Before drawing blood from the next patient, the laboratory would wash the syringes and tubes. This required many rinse cycles to remove all of the soap residue. Needles were resterilized and occasionally resharpended using a grinding wheel. The shortcomings of these techniques are numerous. First, the patient is subjected to the pain of multiple needle entries to the vein.

Secondly, the possibilities for errors to occur during the collection and transfer process and the safety risks are apparent. Also, time is consumed with the multiple punctures and transfers. History of Evacuated Tubes The introduction of evacuated blood collection systems provided greater safety, while offering ease-of-use, speed, and accuracy in blood-to-additive ratios. Many advancements in blood collection techniques and devices have been made in recent years. <sup>2</sup> However, the technique of blood collection with the first evacuated tubes was not quite the same as the process used today.

During blood collection with evacuated tubes, as one end of the needle enters the patient's vein, the other end can penetrate through the rubber stopper as the tube is pushed into the open end of the holder. The vacuum enables the tube to fill with the appropriate volume of blood. Additional tubes may be inserted into the holders after completion of the previous draw, when multiple specimens are required. History of Evacuated Tubes The introduction of evacuated blood collection systems provided greater safety, while offering ease-of-use, speed, and accuracy in blood-to-additive ratios.

Many advancements in blood collection techniques and devices have been made in recent years. <sup>2</sup> However, the technique of blood collection with the first evacuated tubes was not quite the same as the process used today. During blood collection with evacuated tubes, as one end of the needle enters the patient's vein, the other end can penetrate through the rubber stopper as the tube is pushed into the open end of the holder. The vacuum enables the tube to fill with the appropriate volume of blood.

Additional tubes may be inserted into the holders after completion of the previous draw, when multiple specimens are required. The first evacuated tube patent, Evacutainer, was invented by Joseph Kleiner and assigned to BD in 1949. <sup>3</sup> Prior to the issuance of the patent, Kleiner approached BD with the Evacutainer. BD subsequently hired Kleiner as a consultant for the product and changed the name of his tube to Vacutainer®. Shortly thereafter, it became one of the company's largest selling items. BD Vacutainer® tubes were packaged and shipped in vacuum tins similar to coffee cans.

This was a breakthrough at the time because previously, a heavy clamp was used to prevent the stoppers from popping off during autoclaving. Initially, BD made only 1 kind of Vacutainer® tube, but now it makes hundreds of styles and sizes. The current evacuated tube system utilizes color-coded stoppered tubes containing the vacuum and a holder that supports a double-ended needle. The color-coded closures differentiate tube types. BD was the only evacuated tube manufacturer in the United States until the early 1970s when other manufacturers entered the market.

Today, there are regulatory agencies and guidelines that ensure the consistency in the design and manufacture of blood collection systems [eg, Food and Drug Administration (FDA); International Standardization Organization (ISO); and Clinical Laboratory Standards Institute (CLSI)]. 4-6 Federal requirements governing investigations involving medical devices were enacted as part of the Medical Device Amendment (1976) and the Safe Medical Devices Act (1990). 7 These amendments to the Federal Food, Drug and Cosmetic Act define the regulatory framework for medical device development, testing, approval, and marketing.

Additionally, the Federal Quality System Regulation (QSR) and ISO define quality system requirements for the manufacture of medical devices. 8, 9 Any class I or II products on the market prior to 1976 were grandfathered from the premarket notification (to the FDA) requirement. The Needle Stick Safety and Prevention Act revises and builds upon the Bloodborne Pathogen Directive promulgated by the federal Occupational Safety and Health Administration (OSHA). 10 Provisions of the new law require changes to an institution's current exposure control plan to include ' safety-engineered' products for blood collection.

The definition of safety-engineered medical devices includes plastic evacuated tubes with shielded caps. Manufacturing Evacuated Tubes At least 2 standards organizations, CLSI and ISO, have promulgated standards for the manufacturer of evacuated tubes. 5, 6 These standards define the tube dimensions for compatibility with centrifuges and automated instruments, draw and fill accuracy, types of additives and additive tolerances, sterility,

and labeling criteria. Manufacturers are encouraged to follow these guidelines to obtain CE mark\*.

Furthermore, all class I and II medical devices sold in the United States must receive clearance from the FDA and Center for Device and Radiologic Health (CDRH) prior to sale. Included in the FDA's review of the 510k (premarket notification) are the physical description of the product and contents, as well as product performance for safety and effectiveness. General manufacturing practices are described below. Glass evacuated blood collection tubes can be made from glass canes cut to predetermined lengths and fired at one end to close the bottom. Plastic blood collection tubes may be manufactured by an injection-molding process. 1 A mold is made to the specific size of tube desired. Typically, in the molding process, a hot, molten material is injected into a cold mold for the tube. After the tube material cools and solidifies, the mold is opened, and the tube is ejected. Once the tube is formed, additives may be topically applied and dispersed along the inner wall of the tube. 12 Most of these additives are considered to be "dry." Tubes are spray coated with additive formulations onto the inner wall using a series of nozzles.

Dispensing is achieved by either pressure activation or volume displacement. The coating is dried by forced air or vacuum.

Alternatively, additives that are dispensed into the tube as a fluid and remain as a liquid are considered "wet." A gel barrier may also be dispensed into the formed tube for gel separator tubes. After any additive or gel is inserted, the tubes are then evacuated and stoppered. An evacuating-closure device evacuates the interior of the tube and applies a stopper to the opening of the tube. 12 The tubes are subsequently labeled appropriately. In

<https://assignbuster.com/the-evolution-of-evacuated-blood-collection-tubes/>

the early days, evacuated tubes were hand assembled and not sterilized, but now manufacturers in the United States run automated machine lines and sterilize their tubes.

Sterilization is typically accomplished by irradiation after evacuation and is now only rarely achieved through autoclaving. 13 After sterilization the tubes are wrapped and boxed for shipping. Additives Although there are evacuated glass blood collection tubes without additives used to yield serum [or used as discard tubes], all other evacuated tubes contain at least some type of additive. Many of these additives are the same as those used in transfer tubes before evacuated tubes were introduced.

The additives range from those that promote faster clotting of the blood, to those that enable anticoagulation, and to those that preserve or stabilize certain analytes or cells. The inclusion of additives at the proper concentration in evacuated tubes greatly enhances the accuracy and consistency of test results and facilitates faster turnaround times in the laboratory. Additives may exist as either dry or liquid (“wet”) in evacuated tubes depending on whether the tube is glass or plastic, and depending on the stability of the solution.

The CLSI and ISO define the concentrations of these additives dispensed into tubes per milliliter of blood. Inorganic Additives There are several different types of inorganic additives in blood collection tubes. These include those that are completely inorganic in composition, (eg, silica and sodium fluoride), and those that are alkaline metal salts of organic acids, [(eg, disodium ethylenediaminetetraacetic acid (Na<sub>2</sub>EDTA), K<sub>3</sub> or K<sub>2</sub>EDTA, trisodium citrate,

and potassium oxalate]. Most dry additives tend not to be a limiting factor in determining the shelf life of the evacuated tube.

For hematology applications, EDTA is available in three forms, including dry additives (K<sub>2</sub>EDTA or Na<sub>2</sub>EDTA) and a liquid additive (K<sub>3</sub>EDTA). EDTA is combined with a metal cation to enhance its solubility and maintain pH. K<sub>2</sub>EDTA is slightly more soluble than Na<sub>2</sub>EDTA and is the anticoagulant recommended by the International Council for Standards in Hematology. 15 EDTA is an efficient anticoagulant which does not affect cell counts and minimally affects cell size. EDTA prevents clotting by chelating calcium, an important cofactor in coagulation reactions.

The amount of EDTA per milliliter of blood is essentially the same for all 3 forms of EDTA (1. 5- 2. 2 mg/mL). 6 However, slight differences in hemoglobin may be observed between K<sub>2</sub>EDTA and K<sub>3</sub>EDTA due to dilutional effects from K<sub>3</sub>EDTA. 15 For coagulation testing, only liquid additives are currently available. This is to preserve the 9: 1 ratio (blood: citrate) recommended for coagulation testing. 16 To maintain this ratio, coagulation tubes are typically available in glass (to reduce water loss).

Evacuated plastic coagulation tubes consisting solely of PET have special packaging to prevent water vapor from escaping over the shelf life of the tube. Also available are plastic evacuated tubes containing liquid additives with a polypropylene insert tube within the PET outer tube. In such configurations, the inner polypropylene tube prevents the loss of water vapor, while the outer PET tube preserves the vacuum. Trisodium citrate



( $\text{Na}_3\text{C}_6\text{H}_5\text{O}_7 \cdot 2\text{H}_2\text{O}$ ), buffered or unbuffered, is the current standard anticoagulant for coagulation testing.

Some manufacturers buffer with citric acid to maintain the pH and minimize damage to the glass tube wall. Some manufacturers may also coat the glass tube wall. Before coagulation testing became automated, several citrate concentrations in evacuated tubes were available. Today, it is available as either a 3.2% or 3.8% concentration. Different citrate concentrations can have significant effects on aPTT and PT results so interchanging these within a laboratory is not recommended. 16 The different citrate concentrations affect different patient populations and reagent responsiveness.