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Validation of Vacuum Consistency of The Internal Evacuated Blood Collection Tube (BCT)

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ABSTRACT

Evacuated blood collection tube (BCT) or also known as Vacutainer® is a device which accumulate negative pressure as a function of vacuum to collect blood as a specimen for pharmaceutical analysis. Nevertheless, BCT consist of three (3) components which is transparent tube, rubber stopper, and hemogard closure. Study of vacuum on BCT has become interest in many researchers about its consistency due to effect by its surrounding condition. In this research, impact of storage temperature will be studied to identify the effect of vacuum content within BCT, also to investigate the problem and seek proper (surrounding) placement for these BCT. At the same time, it should develop with a new benchmark vacuum volume (negative pressure) inside BCT aiming to obtain the standardise figure. This BCT should be placed under temperature condition between 4°C to 25°C as suggested by BD-Vacutainer® company and under certified humidity condition are ranged between 40% to 60%. It is to ensure the pharmaceutical device which is sterile and consist of shelf life does not deplete its properties drastically and sustain its life span as recommended based on technical data sheet. Thus, the amount of negative pressure in BCT presentively indicate as a shelf life.

1. Introduction

In the industry of medication, treatment and curing have changed their approach proportionally to illness and disease from ancient times to the present. By using blood of a patient, the medical department can diagnose the symptom and illness that is fused with the patient. Blood consists with varies of information and data content of a particular person [1]. As such, blood needs to be evacuated from the body of an organism to a container and proceeded with laboratory testing. This process is known as phlebotomy where the vein of a person is cut aiming to acquire blood or might be used for further treatment if requisite. Since the current legalization is being practised the use of glass on such medical instruments and appliance starts to be abolished due it is freely 'in contact' with human skin for blood evacuation purposes [2]. This is to overcome the case of accident or

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unwanted incident to be happened such as the transmission of HIV/viruses due to container breakage/leak which may contact the patient. As a result, polymers based being used since the 1990s to produce all the medical appliances that are only in contact with patients for medication purposes [2]. The common product for blood evacuation is known to be syringes, vials and blood collection tubes or regularly called Vacutainer®.

However, plastic tubes have hydrophobic surfaces that interfere with the coagulation process. Clots formed on the surfaces of plastic BCTs are more gelatinous when compared to those formed in glass tubes. Furthermore, blood does not flow smoothly over hydrophobic plastic surfaces [3], which can result in the adherence of platelets, fibrin, or clotted [4]. Alternatively, the interior plastic tube wall surface can be coated via spraying, dipping, filling and aspirating, brushing, wiping with surfactants (SFs), and water-soluble polymers (e.g., hydrogels), or hydrophilic–hydrophobic block copolymers [4]. SFs have the potential for desorption (leaching). Recently, Samuel Kim at all (2015) explained a chemical treatment process of the interior wall surface of plastic Polyethylene Terephthalate (PET) [5] tubes via a transesterification reaction with polyols (e.g., ethylene glycol), catalyzed by a guanidine base, to produce chemically modified PET (chemoPET) tubes and contain no problematic SFs [3].

Generally, in the production of blood collection tubes, BCT is made up of polymer with certain component are assemble, which is the Hemogard closure, Rubber stopper, and clear transparent Tube. Thus, in the scope of manufacturing and processing material are Low-Density Polyethylene (LDPE), Bromobutyl Rubber, and Polyethylene terephthalate (PET), respectively. The most common shelf life for a polymer base BCT is known to be a minimal time of more than 12 months [6, 7] compared to glass base BCT generally limited by the shelf life of the additive due to the minimal losses of vacuum and water vapour, over time [2]. In addition, the Rubber Stopper material is poor at radiation resistance pertaining to its drawback factor [8]. However, it is good at barrier properties. Blood collection tube is used to fill with blood automatically (without force required) due there is a vacuum (negative pressure) within these tubes. The vacuum within the evacuated tube is created artificially by pulling out air from the tube leaving negative pressure in these BCT. The amount of vacuum pulled by the manufacturer from the Vacutainer® is based on the size and label on the BCT [9]. The existence of a vacuum in a BCT is a part and parcel requirement for medical purposes which is mainly used for blood evacuation.

The amount of vacuum being produced is commonly referred to the size of the tube which can be categorized under its measurement with a diameter of 13mm to 16 mm alongside the height of 100mm and 75 mm. Also, there are two types of BCT which are Hemogard and Regular [10]. There is usage for adult, pediatric and fingerstick which hold 3 to 10 ml of blood, 2 to 4 ml and one-half ml, respectively [6]. Thus, this research focuses on verifying and validating the consistency of vacuum inside the Vacutainer® [11] with hemogard (plastic/polymer material)[12]. At present, there is no such benchmark to validate the vacuum pressure or vacuum volume inside BCT for purposes of standardisation. Besides, there are also a few variables which can influence the vacuum sustainability to provide the best condition to store Vacutainer® so that the shelf life will be prolonged.

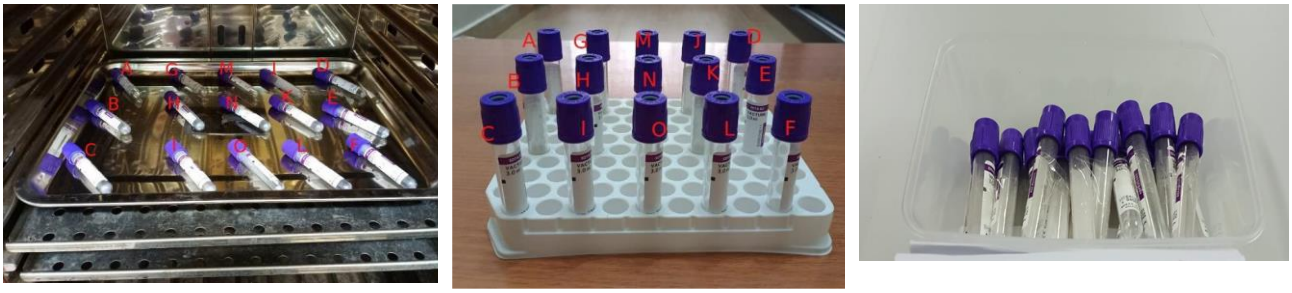
2. Methodology

2.1 List of Materials and Equipment

Evacuated blood collection tube (EDTA K2) [13] with hemogard closure, heating oven, pressure check machine, burette setup with retort stand and butterfly needle 21G with connector, wash bottle fill up with plain water 250ml.

2.2 Experiment Description

The experiment is done by preparation of BCT EDTA K2 with Hemogard closure (3mL) product which gained 45pcs for 1st experiment and 600pieces for experiment 2nd. In experiment 1, it indicated the proper location for BCT to place under qualified temperature and humidity. Thus, the test/study is to place the BCT under a temperature condition of 20°C (cleanroom condition), 30°C standard room condition, and 35°C to 38°C (heat in the oven) as shown in Figure 1. Based on experiment 1 the variable parameter for this research is the amount of plain water filled into the BCT after all the BCT are collected from all the three states of the region. From the origin condition of 3.0mL, every tube will undergo draw volume due to changes in pressure and temperature that affect the negative pressure of the internal BCT. Thus, the result will gain below the indicator that can be depicted on the label. The experiment was done for 5weeks. Thus, the BCT tube of 3 units will be collected from all the 3 regions. The collection will be done every week. From the collection, all the BCT will undergo a draw volume test to identify the vacuum affected upon each BCT according to the Temperature condition which affects the properties of BCT.



(a) (b) (c)

Fig. 1. (a) Placement of BCT within Oven with 35°C to 38°C (b) Placement of BCT at standard room condition of 30°C (c) Placement of BCT at dim area with clean room condition of 20°C

Next, the second experiment, is to determine the specification of volume vacuum (negative pressure) of internal BCT by identifying the consistency of the vacuum of the internal BCT. A product with negative pressure is considered as a vacuum mechanism. The larger the size of the BCT product the lower the negative pressure within it [14]. Thus, there are two variables used in this experiment to indicate the vacuum consistency which is the negative pressure (pressure check test) and plain water (draw volume test) for test one and test two.

However, the quantity of BCT of EDTA K2 (3mL) allocated is 600 pieces (6 trays) which are used and divided into two tests. 300 units are used for first test (Test A), while another 300 units are used for second test (Test B) which is the draw volume test and vacuum check test, respectively. Two tests have been conducted, it is to develop a benchmark pertaining to the content of the volume of vacuum inside the BCT, as prepared in Figure 2. Three trays have been tested using a burette, fill up with plain water and another three trays were tested for its pressure inside the BCT using a pressure vacuum check machine as set up in Figure 3.

Fig. 2. BCT preparation of 6 trays for 2nd experiment

2.2.1 Pressure check test

The vacuum check machine is one of the operating automation machines with help of a cartesian robot as depicted in Figure 3. This machine's functionality is to check the negative pressure of internal BCT. It is designed to find the most accurate pressure inside every 100 units of BCT tubes, as every tube consists of its pressure tolerance due to the pressure extracting process at the production line are not equal on each hole. The vacuum check machine or also known as a vacuum leak test machine is widely applied in the medical industry (pharmaceutical) for checking strips, blisters and bottles, etc [15].

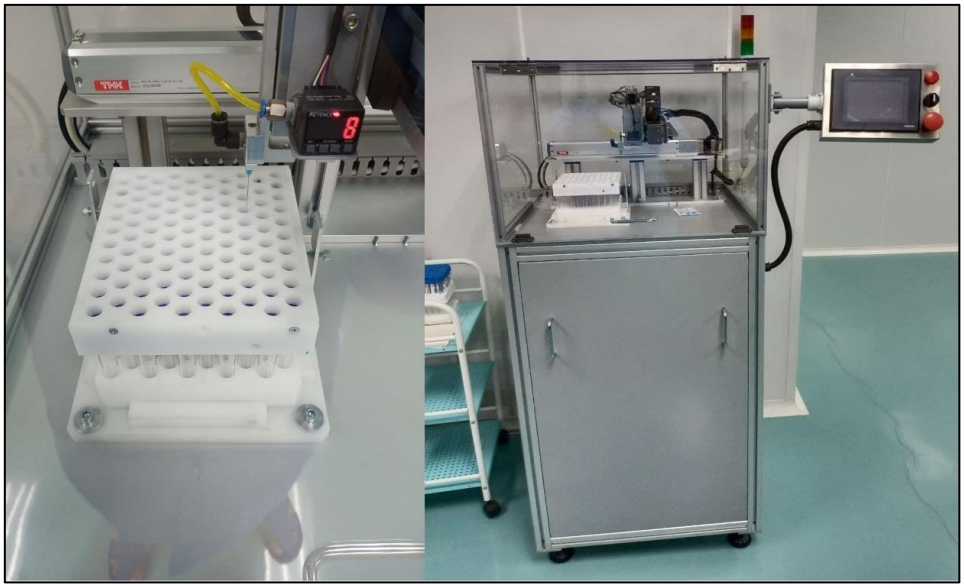
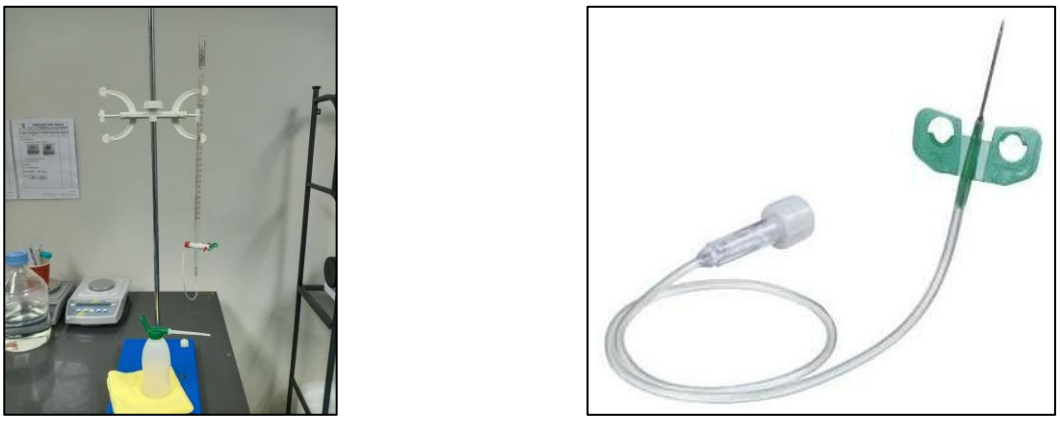


Fig. 3. Vacuum check machine

2.2.2 Draw volume test

The usage of a burette of 25ml with the scale of 1:10 and a butterfly-needle with a connecter is to fill plain water into BCT after the experiment happened for experiment 1 and experiment 2 for the 2nd test. It is to ensure the capable amount of volume collected based on the negative pressure left within it. As shown in Figure 4 the image of burette setup with retort-stand and butterfly-needle 21G with connector, respectively. Every filling of plain water into BCT, the data will be collected and tabulated into a table and will be plotted into a graph. However, from the table and graph, deduction will be made based on the analysis of the results.



(a) (b)

Fig. 4. (a) Burette setup with Butterfly-needle 21G hold on retort stand (b) Butterfly needle 21G with connector [Note: Burette setup for draw volume test for experiment 1 and experiment 2 (test2)]

3. Results

3.1 Experiment 1: Effect of Temperature on BCT (Proper Placement for BCT)

Before the experimentation is done, polymer BCT is used for the testing procedure, where water has been filled into the BCT. Thus, is to identify the zero error of volume collected in BCT, as a result, the volume gained is 3.1ml differ from the labelled attached to the tube. However, for the (1st Objective) the results shown in Table 1 are as predicted, where the draw volume of the tube from temperature condition of 38°C to 35°C starts to deplete every week as present in table one below. Meanwhile, at 30°C, all the tube undergoes a draw volume of 5% every week. However, the BCT which placed under 20°C sustain its exact/origin volume of 3.1ml.

From Figure 5, the data recorded and collected, polymer BCT that been left under a temperature condition of 25°C and above has been affected by its vacuum content inside the BCT due to the pressure changes influenced by temperature change between surrounding conditions and inside the BCT. Also, can be seen from the data collected at temperatures 35°C to 38°C vacuum starts to draw in 3rd week, saying that it is not a proper condition to place the BCT under high-temperature conditions. As stated in ideal gas law, deduction from the general equation as PV=nRT [16], as temperature increases and the pressure inside the product is lower from surrounding conditions cause the product to shrink and damage due to the particle inside the product is at far apart [17]. In addition, it prone to leachable by external factors due to an uncoated Rubber stopper [18]. Thus, simultaneously draw the volume of vacuum from the BCT to stabilize with the outside condition. As a result, the BCT is left with less amount of negative pressure for the vacuum mechanism to function properly and not conform to the technical data sheet.

Table 1
Temperature effect on vacuum content of BCT for 5 weeks

Week	Label	Temperature	Average Volume Collected (ml)
1	A1 / B1 / C1	20°C	3.10
	A2 / B2 / C2	30°C	3.10
	A3 / B3 / C3	35°C to 38°C	2.95
2	D1 / E1 / F1	20°C	3.10
	D2 / E2 / F2	30°C	3.10
	D3 / E3 / F3	35°C to 38°C	2.90
3	G1 / H1 / I1	20°C	3.10
	G2 / H2 / I2	30°C	3.05
	G3 / H3 / I3	35°C to 38°C	2.85
4	J1 / K1 / L1	20°C	3.10
	J2 / K2 /L2	30°C	3.05
	J3 / K3 / L3	35°C to 38°C	2.80
5	M1 / N1 / O1	20°C	3.10
	M2 / N2 / O2	30°C	3.00
	M3 / N3 / O3	35°C to 38°C	2.70

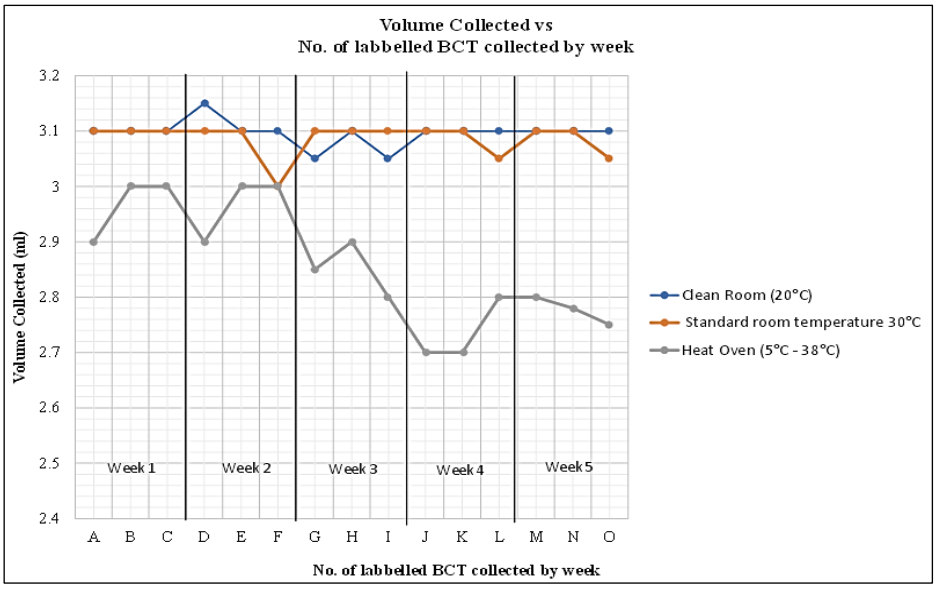


Fig. 5. Temperature effect on vacuum content of BCT

The humidity of the circumstances in which 45 pieces of BCT have been placed is not in the certified condition of 4°C-25°C in a well-ventilated environment with a relative humidity of less than 80% RH [19]. However, the precise and best condition of humidity is at 40% to 60% RH as mentioned in Carel Industries [20,21]. Moreover, we can look at the polymer (PET) structure after the moulding process, present the appearance of crystalline as shown in Figure 6 [22]. Thus, may cause defects if placed under the high humidity condition due to the content of hydrogen molecules that may affect the structure and mechanical properties of the PET. Thus, high humidity which also can be explained by high hydrogen (H2) solubility in polymers, may lead to mechanical degradation or failure upon decompression [23]. The phenomenon is known to be blistering which induces by hydrogen molecules as depicted in Figure 7.

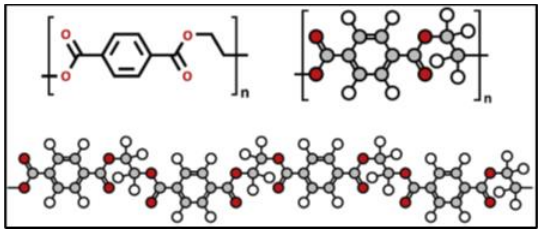


Fig. 6. Polymer structure of PET [22]

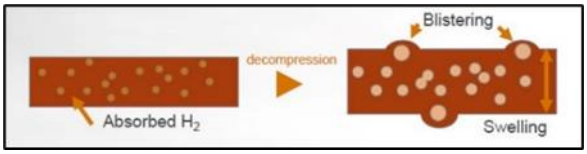
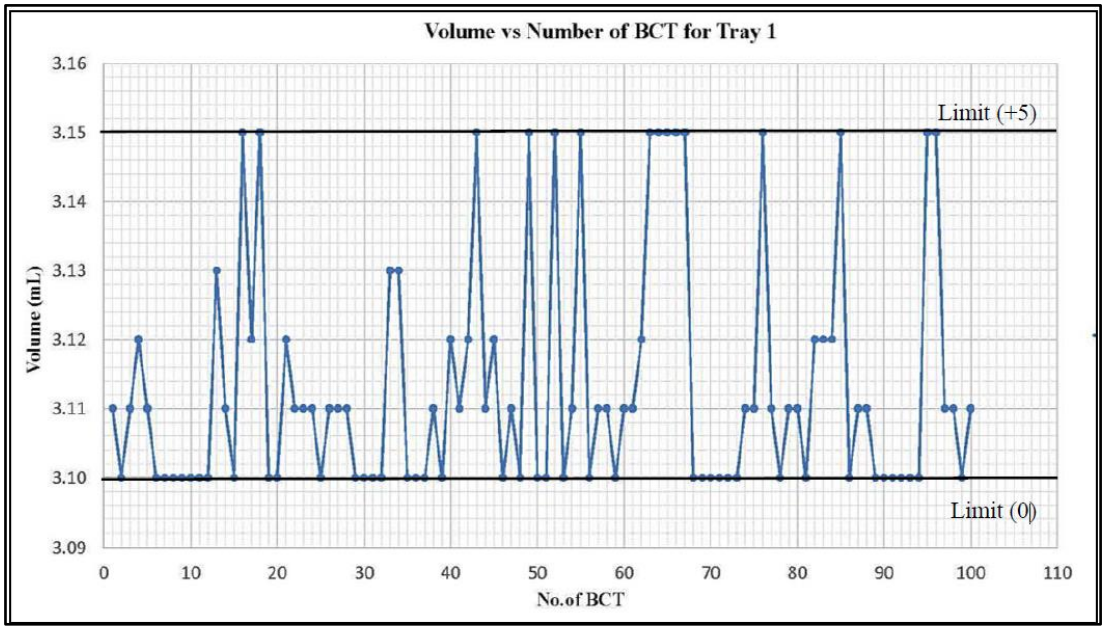


Fig. 7. Hydrogen induce Polymer Blistering [20]

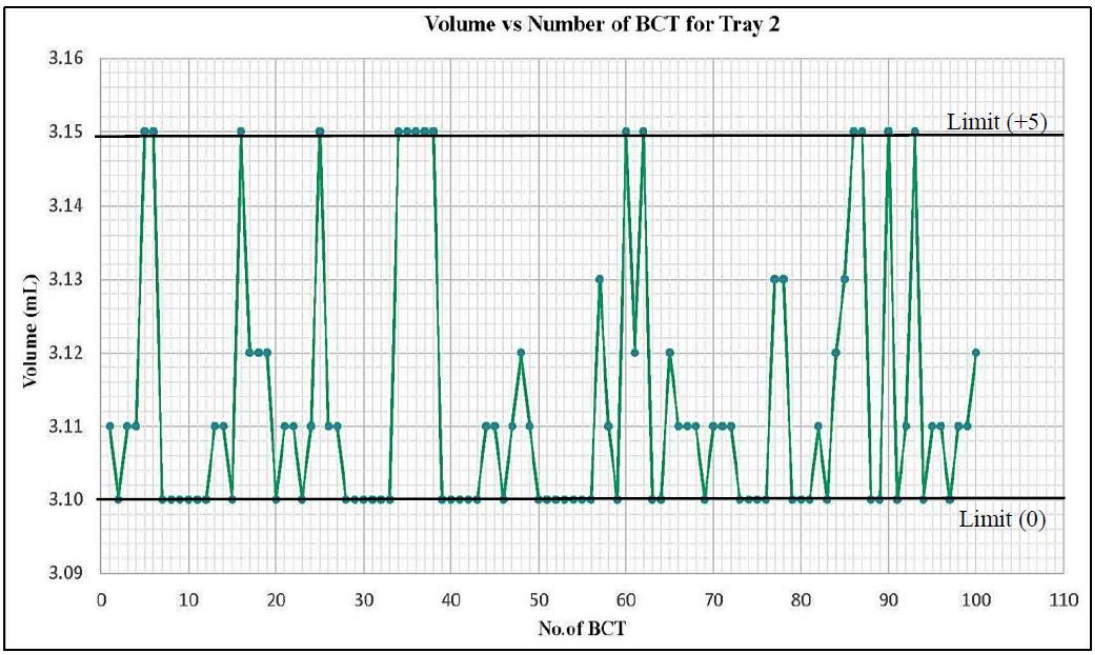
3.2 Experiment 2: Development of a New Benchmark (Specification) Vacuum Volume of BCT

Validation of Vacuum Consistency done with six trays, all together in total are 600 units of BCT tube. All these BCTs used in this 2nd experiment are prepared right away(instant) from the production line. Three trays were tested using a fluid volume test with plain water using a burette setup considered Test A. The result is presented in Figure 8. While another three trays were tested using a pressure check test machine to evaluate the (vacuum) volume of negative pressure inside the BCT presented the results in Figure 9, considered Test B.

Thus, the presented results in Figure 8 (Test A) of trays 1, 2, and 3 are consistent pertaining to the outcome gained, as the fluctuation of data for complete 100 pieces of BCT for each tray does not exceed those limits of ±0.05ml. The test was analysed in the QC laboratory room right after the BCTs had been prepared. The experiment was operated manually by complying with precaution procedure and steps to obtain the best results approach and achieve the hypothesis. All the results obtained were meticulously observed, where the eye lens was perpendicular to the meter ruler (scale) and jotted down (tabulated) on the prepared table as depicted in Figure 9 below.



(a)



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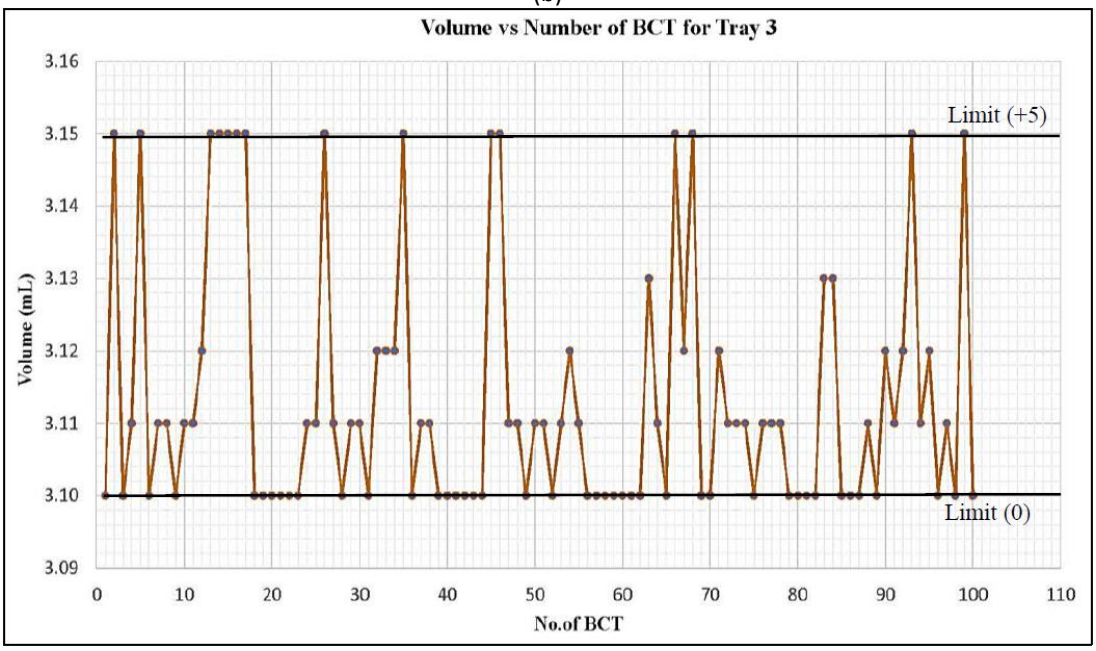

(c)

Fig. 8. (a) Graph of Fluid Volume Test for Tray 1 (b) Graph of Fluid Volume Test for 2 (c) Graph of Fluid Volume Test for 3

In Figure 9, the reading fluctuates inconsistently ranging between 304mmHg to 324mmHg for three (3) trays. The data fluctuate and exceed the limit that has been set at ±5(unit) as shown in Figure 5, known to be a random error. This happened due to the failure of the machine to run properly as mentioned by the technician from the lab of company X. From fluid test using burette, where the reading can be seen with naked eyes and clearly. On the other hand, using the vacuum check machine, as ordinary Process Inspection (PI)/Quality Control (QC) cannot be seen with the naked eyes of the checking process cause the machine runs on its own programmed and automated control.

Also, the leak test machine consists of some error in reading the results due to no calibration/diagnosis done upon the vacuum check machine (technician feasible to calibrate).

Improvement, upon the machine, must be done by servicing and re-calibrate the machine to its proper condition to gain a better outcome for the industry to use as a Quality Control (QC) tool to ease the process of inspection for mass production.

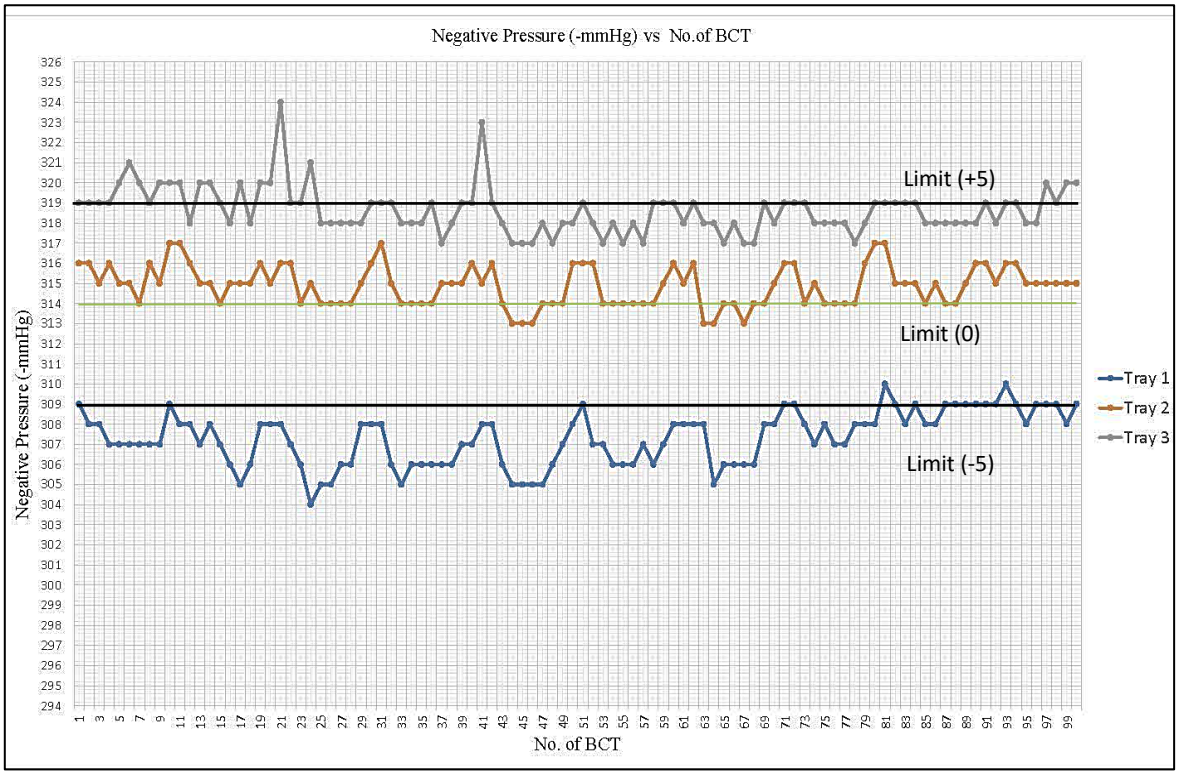

Fig. 9. Graph of Negative Pressure vs Number of BCT for Vacuum Check machine. [Note: Results of 100pcs of BCT on each tray undergo pressure check test machine. Refer appendix A for clear/high resolution]

4. Conclusions

In conclusion, BCT should be placed under temperature conditions between 4°C to 25°C as suggested by BD-Vacutainer® company, also under certified humidity conditions are ranged between 40% to 60%. Thus, can be placed in a clean room as the comply with the pharmaceutical approach. In addition, coating the rubber stopper with teflon-coated, will improvise the life expectancy of vacuum properties. This is to ensure the pharmaceutical device which is sterile and consists of shelf life does not deplete its properties drastically and sustains its life span as recommended in the technical data sheet. However, during the transportation process, the installation of a dehumidifier and cooling system on the truck is an important step to reduce or prevent from draw volume of vacuum by the BCT, since the product is delivered only by using trucks. As to reduce the cost of delivery and no installation made for such device on the truck, we may deliver the product during night-time since the temperature and humidity are at the desired state. Last but not least, this research will assist all the manufacturing sector as a fundamental guideline of vacuum properties pertaining to pharmaceutical devices.

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