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Marvelous™ (MRVLS)

Elcam Medical's New & Innovative Minimal Residual Volume Luer Activated Stopcock

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Revision 8, October 2021

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Abstract

Catheter Related Blood Stream Infections (**CRBSI**) are a well-known and increasingly disturbing problem in hospitals, especially in Intensive Care Units (ICUs) and other units utilizing catheters and their accessories for patient care.

Reducing the risk of microbial colonization and proliferation on stopcocks, a valve assembled into a catheter set enabling access to it, can contribute to reducing the rates of catheter colonization. Additionally, needle stick injuries and resulting contamination are a well-known risk for medical staff. Reducing the risk of needle sticks can increase the safety of the medical staff and patients.

Elcam Medical, the leading provider of stopcocks to the U.S. and European OEM markets, has currently designed the ***Marvelous™*** with the purpose of increasing the safety of patients and medical staff.

Elcam Medical's Marvelous™is a standard Stopcock (STP) with two additional features that were designed in order to increase patient safety relative to infection prevention: 1) the Luer- activated Valve that serves as a bacterial barrier, enables access to the line without having to open it, practically creating a closed system and allows needle free connection; and 2) the minimal residual volume feature that automatically flushes the side port along with the flow line, minimizes the STP's dead space and contributes to preventing bacterial colonization.

In order to prove the safety of the Marvelous™ for human usage in general, and the functionality of the minimal residual volume feature in particular, Elcam Medical conducted tests performed by well-established laboratories. The **Flushing study** was designed for the purpose of demonstrating that the Marvelous™ minimal dead space and minimal residual volume feature is as safe as other devices in the market with regard to blood residuals after flushing.
This was achieved by quantifying blood residuals in the Marvelous™ versus other corresponding devices at the sampling port after line and port flushing. The **Bacterial contamination of residual blood solutions study** was designed as a continuation of the Flushing study, for the purpose of characterizing the bacterial growth in saline containing low concentrations of blood at different time periods. The Marvelous™ was tested for **mechanical hemolysis** by simulating hospital procedure, and its **Biocompatibility** was evaluated in accordance with the FDA's *Memorandum* and with International Standard ISO 10993,-1.
All the test results show that the Marvelous™ is safe for its intended use and establishes the functionality of the minimal residual volume feature.

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Pathogenesis

The management of critically ill patients, often hospitalized in intensive care units (ICU), essentially involves the use of Central Venous Catheters (CVCs) for the administration of intravenous (IV) fluids, medications, blood products and parenteral nutrition. They also enable monitoring of the hemodynamic status of critical patients and blood sampling. CVC sets include one or more stopcocks (STPs). These are valves serving as ports of entry into the circulatory system of the patient and are used for different interventions. CVCs, although indispensable in the critical care setup, pose risks of serious complications, of which the most common are infections (1-4). Infections can be localized along the insertion-site of the catheter tunnel, spread systemically as they disperse into the bloodstream or metastasize to distant body sites and seed infection in specific organs (3). According to The American Center for Disease Control and Prevention (CDC), more than 80,000 catheter-related bloodstream infections are reported each year from American ICUs alone (a total of 250,000 cases per year) (5). CRBSI are associated with mortality rates of 10% to 20%, increased morbidity, prolonged hospitalization and increased medical care costs – $3700-$29,000 attributed cost per infection (5, 6).

The pathogenesis of catheter-related infections is complex and multifactorial. Two important mechanisms have been demonstrated to be involved:

1. Insertion site-related: skin microorganisms at the insertion site of the catheter migrate along the catheter tract and colonize the catheter and inner tissues, rendering development of local infection (7-8).
2. Catheter hub-related: the hub of the catheter is the part to which tubes or syringes are connected, usually through a stopcock, for administration of fluids or medications and for monitoring. Contamination of the hub by frequent manipulations may result in intraluminal colonization of the catheters (9-12) , with possible infectious complications.

The relative importance of the two mechanisms of catheter contamination depends on several factors and is subject to continuing debate (6). Three different groups (Salzman, Linares and Cicco) that studied microbial colonization of catheters found the hub to be the most common source of catheter infection and bacteremia (54%,70% and 45% respectively) (9,12,13).

The Stopcock (STP) is a multi-directional rotating valve, assembled into a catheter set (sometimes including several units in the same set) and used during diverse interventions for the administration of different medical fluids, parenteral feeding and blood sampling.

A typical stopcock is designed with a proximal (male) port and a distal port, serving as an inlet and outlet of the line, and a side(female) port, used to be accessed with a syringe for injecting or sampling as described above. Due to the design of the stopcock, there is a 'dead space' at the junction between syringe attachment point at the side port and the flow of fluids between the distal and proximal ports. This space cannot be efficiently cleared of all the fluid remnants passing through it despite standard flushing procedures, resulting in an accumulation of residue debris. During the period in which a catheter is constantly present in a blood vessel, this accumulation inside the STP encourages bacterial colonizing in the 'dead space' area triggering CRBSI (14). Recurrent manipulations expose the stopcock to increased contamination, making it a major source of nosocomial infections (15).

A CDC report from 2002 declared that stopcock contamination is common, occurring in 45%-50% of CRBSI cases (5).
Reducing the chance of microbial colonization on stopcocks can contribute to reducing the rates of catheter colonization.

The Minimal Residual Volume Luer - Activated Swabbable Stopcock (Marvelous™)

Elcam Medical is a world-class producer of medical equipment in the area of disposable flow control devices.

In light of the pronounced risks associated with hospital-acquired infections in patients who need therapy using stopcocks, the company has currently designed an innovative Stopcock, **the Marvelous™** with the purpose of increasing patients and medical staff safety, especially those patients treated in the intensive care, oncology and dialysis units, who comprise more than 50% of the total STP users. The Marvelous™ is a standard STP (as seen in *Figure A*) with two additional features.

The first component is a **Luer Activated Valve** which is attached to the product by ultrasonic welding, replacing one or both female ports (luers). This feature is depicted in *Figure B* (the text describing the new component is highlighted in yellow in the text box).
The Luer-activated valve component is purchased by Elcam from Halkey-Roberts and its design is based on Halkey-Roberts's *needleless injection site valve* that was cleared under 510(k) K002689 on March 06, 2001. The Luer-activated valve is illustrated in *Figure C*. The valve has an elastomeric "stem" that maintains the female port (luer) closed, canceling the need to close it with a cap, in order to avoid leakage and/or port's contamination.

The elastomeric stem has a slit that enables the "stem" to be in an either open or closed position. Once a male luer is introduced into the closed port through the **Luer-activated valve** component, the fluid path automatically opens to allow injection or blood sampling. Once the male luer is taken out, the female port is automatically closed (due to the valve's elastomeric stem that seals itself).
The valve actually serves as a needleless injection site integrated in the stopcock. Besides eliminating the usage of needles, thereby minimizing needle stick occurrences, the end user benefits by not having to use caps or manipulate the stopcock's handle, in order to close the port before and after injection or blood sampling. Swabbing the valve's top (injection site) with aseptic fluid such as alcohol prior to male luer insertion supports the safety requirements.

The Luer Activated Valve enables a needle free manipulation of the stopcock and therefore improves the staff's safety. The valve creates a bacterial barrier closed system that contributes to fighting infections by preventing contamination.

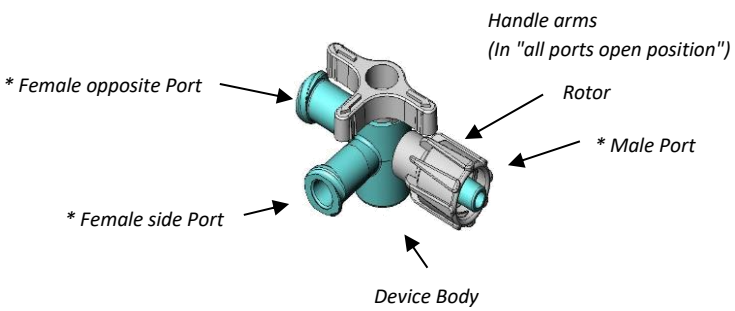

Figure A:
a model of Elcam's Standard STP

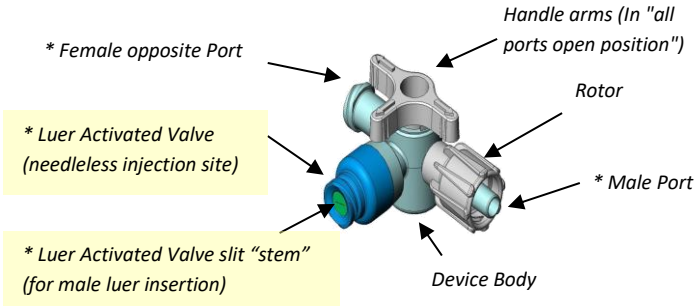

Figure B:
a model of Elcam's STP with a Luer-activated Valve

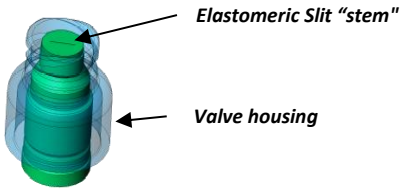

Figure C:
Luer-activated valve – illustration
*The term **Port** is also valid for the term **Luer**.*

The second additional improvement is the "**Minimal Residual Volume**" feature. Conventional stopcocks are made of a body and a handle with a linear through-bore between them, serving as flow path allowing the fluid to flow only through the handle (see in following *Figure D*). An additional side bore, perpendicular to the former, serves as a flow path for connecting the side port to the through-bore. This design leaves areas in the stopcock without ongoing flushing (namely the side bore). The **Minimal Residual Volume** feature enables fluid flow around the handle so the fluid constant flow accesses the entire stopcock handle's internal volume. In addition, a fluid flow guide is placed on the handle, directing the flow into the internal volume defined by the side port of the stopcock's housing and the valve (see following in *Figure E*).

This unique design enables the user to perform ongoing flushing during the medical procedure by the mere linear flow in the line **and therefore significantly reduces the "residual volume" in the stopcock, and further contributes to preventing bacterial colonization.**

The advantage of the ***minimal residual volume*** is in simplifying the flushing of the stopcock in a manner that besides its simplicity reduces cost and clinician's labor, while keeping the stopcock flushed, and clean during medical procedures.

The ***minimal residual volume*** feature is achieved thanks to a modification in the stopcock handle and body design, which changes the fluid path from the conventional fluid flow through the handle's bore to a "circumferential channel" with a flow guide formed therein. The Marvelous™ handle channel and the flow guide are illustrated in *Figure E*.

The Marvelous™ body partition is illustrated in *Figure G*. The Marvelous™ fluid flow path and residual volume are demonstrated in comparison to a Luer-activated valve stopcock in *Figure H*.

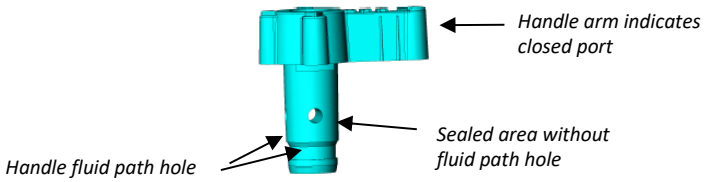

Figure D:
a model of the handle fluid path hole in Elcam's Standard Stopcock

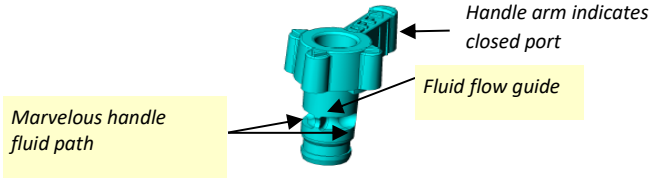

Figure E:
a model of Elcam's Marvelous handle channel and flow guide

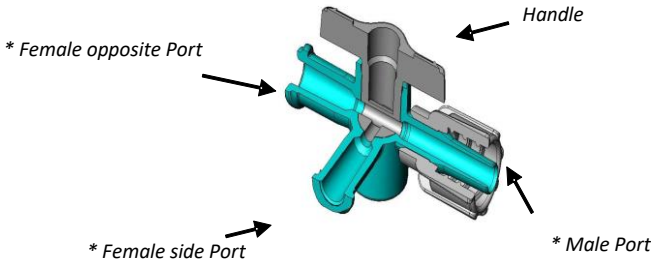

Figure F:
a model of Elcam's Standard Stopcock

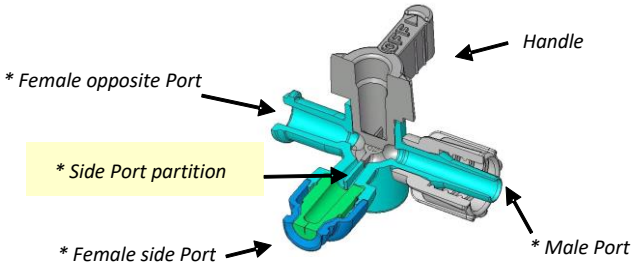

Figure G:
a model of Elcam's Marvelous with the body partition

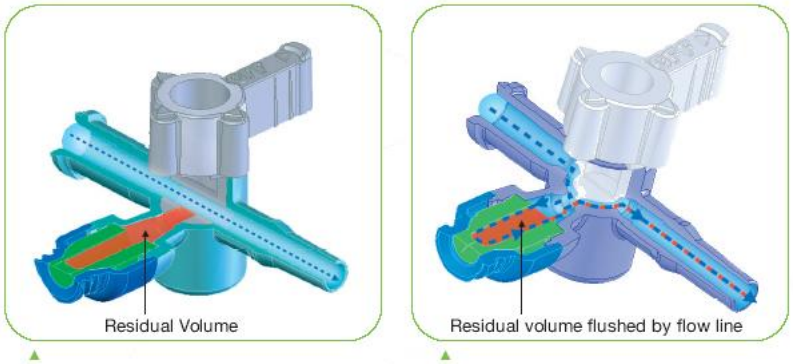

Figure H:
Illustration of the Marvelous flow path and residual volume in comparison to a Luer-Activated Valve Stopcock

The Marvelous™ is intended for both IV and monitoring applications.
For **IV applications** Elcam is offering the **Marvelous™ Large Bore (LB)** which has a 200 ml/min flow and enables administration of high volume fluids as required in IV therapy. The advantage of the Marvelous for IV applications lies primarily in the continuous flushing feature that can help prevent contamination and reduce infection rates.

For **monitoring applications**, Elcam is recommending the **Marvelous™ Economy** with a 140ml/min flow that matches the low-flow required in monitoring. The advantages of the Marvelous™ for monitoring applications are: 1) the ability to maintain the self-side port flushing performance with no excessive damping of the BP signal by the soft elastomeric valve stem, thanks to the rotating handle that can direct the flow away from the valve; 2) time and labor saving in the blood aspiration mode as a result of a single flush of the STP after blood sampling (in comparison with two boluses – of the valve and the line required with a regular stopcock); and 3) minimal blood residues that help prevent contamination and reduce infection rates.

The Large Bore and Economy versions are suitable for both IV and monitoring applications.

Safety and functionality of the Marvelous

Elcam Medical has conducted a large number of tests in order to establish the safety of the Marvelous™ for human use in general and the functionality of the minimal residual volume feature in particular. All the tests were conducted by well established certified laboratories.

A. Flushing Study

The purpose of this study was to show that the Marvelous™ minimal dead space and minimal residual volume feature is as safe as and even safer than other devices in the market with regard to blood residuals after flushing. This purpose was achieved by quantifying blood residuals in the Marvelous™ vs. other corresponding devices at the sampling port (Marvelous™ vs. another self-flushing sampling site) after line clearing; and at the sampling port (Marvelous™ vs. a regular 4way stopcock + a known Luer Activated Valve) after line and

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port clearing. The test procedure was designed to mimic real-life hospital procedures(16).

One study compared the Marvelous™ to two common sampling ports in monitoring sets with an in-line reservoir:

- An arterial line including a sampling port and a reservoir, was filled with saline and its tip was dipped in sheep blood.
- Saline mixed with blood was drawn up the line by manipulating the reservoir. The amount of blood drawn was set per medical practice to be 4 times the volume between the tip and the sampling port,
  in order to assure pure blood at the sampling port.
- Some blood was withdrawn through the port.
- The mixed blood was returned down the line by an in-line reservoir.
- The Line and port were flushed by an in-line flush device for X seconds [X= 4, 6, 8].
- The Blood residuals samples were collected through the tested sampling port.
- Blood residuals were quantified by DAS* photo spectroscopy at 234nm wavelength.
- Each tested group included 10 products.

No significant differences in Blood residues (LOQ*<0.00001 mg/L) (Alpha=0.05) were found between the three types of products after in-line flushing for 4, 6 & 8 seconds (Wash Time). Therefore we concluded that the Marvelous™ is as good as or better than the other marketed sampling ports of reservoir including monitoring sets *(Graph1).*

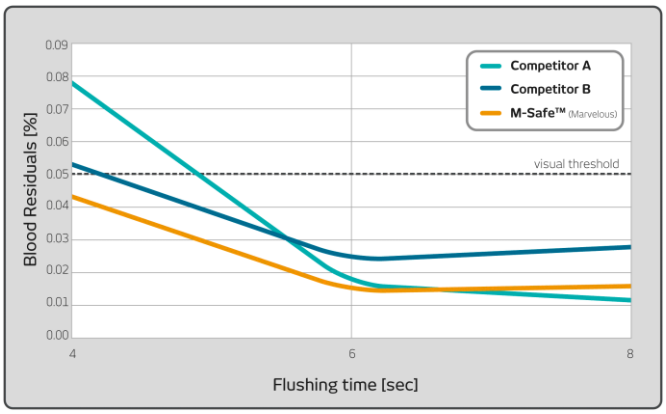
A second study compared the Marvelous™ to some common luer activated valves, attached to stopcocks in monitoring sets without an in-line reservoir:

- An arterial line including a sampling port in the form of a luer activated valve attached to a stopcock, was filled with saline and its tip was dipped in blood.
- Saline mixed with blood was drawn up the line by using a syringe at the top of the line. The amount of blood drawn was set per medical practice to be 4 times the volume between the tip and the sampling port, to assure pure blood at the sampling port.
- Blood was drawn through the tested port.
- The line and port were flushed separately by an in-line flush device for X seconds [X=1, 2, 3, 4] each.
- The blood residuals samples were collected through the tested sampling port.
  Blood residuals were quantified by DAS* photo spectroscopy at 234nm wavelength.
- Each tested group included 3-10 products.
- All of the product groups showed significant differences in blood residue concentrations (LOQ**<0.00001 mg/L) (Alpha=0.05) between 1 and 2 seconds wash times. There were no significant differences in blood residue concentrations between 2, 3 and 4 sec. wash times.
- In all wash time flushes (1,2,3,4 sec) there were significant differences in blood residues concentration between the different analyzed products (LOQ**<0.00001 mg/L) (Alpha=0.05)

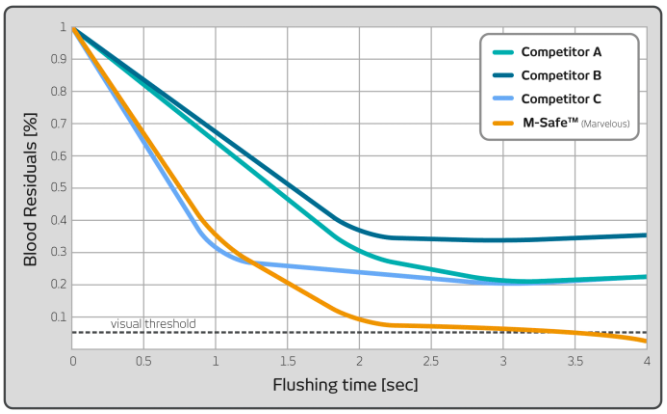
The Marvelous™ was always at the lower end of the curve (lower blood residue concentration), Therefore we concluded that the Marvelous™ is as good as or even better than the other marketed sampling ports in monitoring sets without a reservoir *(Graph 2).*

*DAS –Diode Array Spectrophotometer

** LOQ – Limit Of Quantitation –a resolution index - the lowest value detected by the photo spectrometer.



Graph 1:
Blood residuals vs. flushing time – Marvelous in comparison to competitors, monitoring set with reservoir

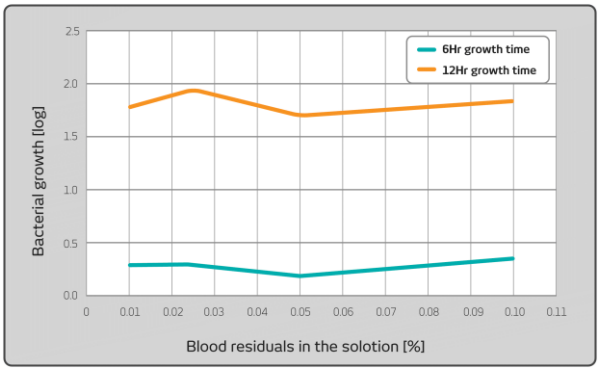


Graph 2:
Blood residuals vs. flushing time – Marvelous in comparison to competitors, monitoring set, no reservoir

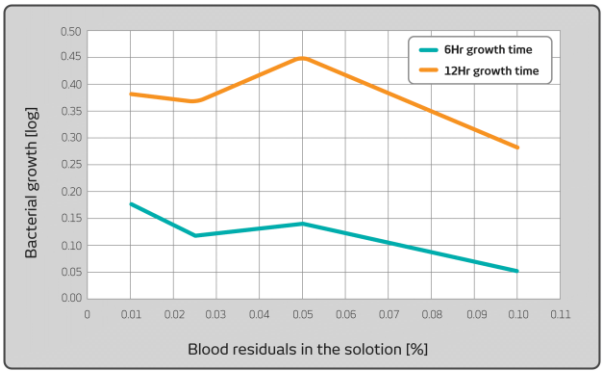
B. Bacterial contamination of residual blood solutions

This study was designed as a continuum of the Flushing study, in the purpose of characterizing the bacterial growth in saline containing low concentrations of blood at different time periods. This study was designed to simulate a real-life situation of the Marvelous™ in hospital surroundings – bacteria entering STP cavities with blood residuals in the saline solution, at room temperature (17).

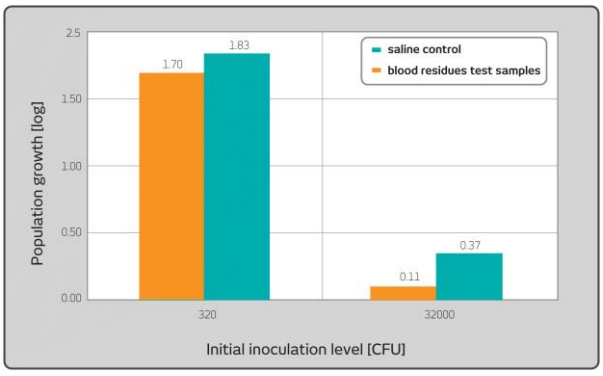
- Four degrees of blood dilutions in saline were examined (0.1%, 0.05%, 0.025%, 0.01%), and one control group (saline solution).
- According to usage characteristics of the Marvelous™ in hospital settings, the maximal time range between device manipulation (i.e. passing of solutions through the valve) is 12 hours, therefore the bacterial growth was examined after 6 and 12 hours (previous studies showed no bacterial growth 4 hours after inoculation).
- The tested microorganism was Staphylococcus aureus ATCC 6538 at 2 initial concentrations – $3.2x10^2$ and $3.2x10^4$.
- According to laboratory practice, a 0.5 log difference between the initial inoculating concentration and the final bacterial concentration is needed in order to establish growth of a bacterial population. This was calculated by the formula:
  LOG ("final contamination") – LOG ("initial inoculation") > 0.5.
- The study was conducted in test tubes.
- Results showed no correlation between the percentage of blood residues and the final bacterial count**, therefore the blood residuals differences in the evaluated concentration range, have no effect on bacterial growth** *(Graphs 3, 4). Graph 5* shows that **blood residue does not contribute to bacterial growth in comparison to a saline control group.** *Graphs 3* and *4* also show that shortening the growth time from 12 to 6 hours, dramatically decrease the final bacterial count, therefore **frequent use of the Marvelous™ prevents development of bacteria to a quantity that can risk patients.**



Graph 3:
Bacterial growth in relation to blood residual after 6 and 12 hours (initial inoculation – $3.2x10^2$)



Graph 4:
Bacterial growth in relation to blood residuals after 6 and 12 hours (initial inoculation – $3.2x10^4$)



Graph 5:
Bacterial growth- saline control vs. blood residues test samples- 12hours growth time

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C. Mechanical Hemolysis

The Marvelous™ was tested for mechanical hemolysis by simulating hospital procedure. Blood was drawn from a reservoir of cow blood using a Marvelous™ at three different flow rates - 1ml/0.5sec, 1ml/2.5sec and 1ml/5sec; Blood was also drawn at a constant flow of 1ml/5sec while the Marvelous™ handle was deviated by 10° and 25° from its intended position.

In the control group blood was drawn using either a 23G needle and a 3ml syringe or a 3ml syringe alone. A regular STP was used as the gold standard for hemolysis. The study groups included 10 products each. The current international standard for chemical hemolysis is 5%, but a recent study claimed that chemical hemolysis during contact with polyethylene is 0.7%, and the acceptance criteria was set at 0.7% in accordance with the polyethylene STP handles. The hemolysis level was determined using a DAS – Diode Array Spectrophotometer.

The results were all under 0.42% hemolysis, well below the acceptance criteria. In comparison to the gold standard no statistically significant difference was observed. **We conclude that Elcam Medical's Marvelous™ does not cause mechanical hemolysis.**

D. Biocompatibility

Biocompatibility evaluation was performed in accordance with the FDA's Memorandum – #G95, 1- May 1, 1995 and with International Standard ISO 10993,-1 under the classification of "Externally Communicating Device, Blood path-indirect, Prolonged (up to 96 hours) Contact Duration".

Based on that classification, the following types of tests were performed and successfully passed: Cytotoxicity, Systemic Toxicity, Intracutaneous Reactivity, Sensitization and Chemical Hemolysis. All tests were performed by Namsa US Laboratory.

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In accordance with all the studies and tests conducted by Elcam Medical and detailed in this document, we conclude that the minimal residual volume feature is functional as stated and that the Marvelous™ is safe for human use.

Shelf life: The Marvelous™ has been tested from both mechanical and efficacy aspects and was approved for a **shelf life of 5 years**.

Regulatory status:

The Marvelous™ is 510(k) cleared and CE approved.

Elcam Medical has been manufacturing various stopcocks for the medical market during the past 25 years in full compliance with FDA CFR 21 820 Quality System Regulations and ISO 13485:2016.

Elcam holds marketing approvals from the Israeli Ministry of Health, as well as from the US FDA and The European MDD (Medical Devices Directive) - Annex II Section 3 of the Council Directive 93/42/EEC.

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