Validating Reusability: Assessing the Cleanability of the Vela Vacuum Extractor

A Study to Enhance Sustainability and Accessibility of the Vacuum Extractor Before Final Material Production

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MSc Biomedical Engineering
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by

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Preface

This thesis marks the final chapter of my MSc degree in Biomedical Engineering. It was truly exciting to actively contribute to the development of a new reusable medical device. Contributing to its creation added to my knowledge and aligned with the trend of transitioning towards reusable devices, which is expected to grow in the coming years. This project felt like a culmination of the insights I've gathered throughout my academic journey. It was a significant learning experience, and I'm grateful to everyone who played a role in it.

I want to extend my appreciation to my TU Delft supervisor, Jenny Dankelman, for not only facilitating my connection with LAYCO Medical Devices but also for providing excellent guidance and constructive feedback throughout the project. Additionally, I would like to express gratitude to my daily supervisor and co-founder of LAYCO Medical Devices, Dieuwertje. Her invaluable assistance has been instrumental throughout this project. I could always engage in productive discussions with her, receive feedback, and overcome challenges. On a personal note, her encouragement occasionally extended beyond the academic realm, resulting in the surprising outcome that my running shoes have seen more action than ever before. Furthermore, I want to thank Harry Leeuw from the St. Antonius Hospital. Without his enthusiasm to help me and LAYCO Medical Devices move forward, this project would never have been so successful. I enjoyed spending several days under his supervision in the central sterile services department at St. Antonius Hospital, an experience I will never forget.

Moreover, my sincere thanks go to the wonderful team at LAYCO Medical Devices. Working with you was a pleasure, and the office's friendly atmosphere made the entire project truly enjoyable. The positive vibes and warmth that characterize our interactions are greatly appreciated. Lastly, a special note of appreciation goes to my friends and family for their support throughout this journey. I could not have done this without all of you!

Cato van Leeuwen
Delft, December 2023

Abstract

INTRODUCTION: The importance of reusable medical devices is increasingly evident due to their sustainability and accessibility advantages in high- and low- & middle-income countries. In response, LAYCO Medical Devices is developing a reusable vacuum extractor, vela®, as an alternative to the commonly used disposable vacuum extractor. This study aims to validate vela®'s reusability, focusing on reprocessing and explicitly on cleaning. The design of vela® is nearing completion; however, the device has not been manufactured in the final material. Ultimately, the plan is to produce vela® through injection molding of polyphenylsulfone. However, given the current stage of vela®, both in terms of time and cost, it is not advantageous to apply this production method now. Therefore, the research is divided into two parts: material validation and design validation. The material validation involves examining the suitability of polyphenylsulfone, the proposed final material, and identifying a suitable prototype material for testing the cleanability of the vela® design. For the design validation, the vela® design is examined to determine its effectiveness in cleaning within both high- and low- & middle-income countries, as different reprocessing methods are used in these settings.
METHODS: Clinical simulation tests were performed in the material and design validations to assess contamination at predefined hard-to-clean locations after cleaning. The locations were first soiled with Browne washer-disinfector soil, then cleaned and tested with the adenosine triphosphate and protein tests, each with predetermined thresholds. For material validation, an object made of polyphenylsulfone was selected. Through 3D printing, the polyphenylsulfone object was replicated in five potential prototyping materials to facilitate a comprehensive comparison. These six test objects were subjected to clinical simulation tests. Then, the test objects underwent in-depth material analysis to understand the material better and make a more reasoned selection for the prototype material. For the design validation, the design of vela® is printed in the material obtained through the material validation. These vela®'s undergo clinical simulation tests in both high- and low- & middle-income country settings. Given the manual nature of the low- & middle-income country cleaning procedure, additional layman's tests are conducted to minimize user bias.
RESULTS: For the clinical simulation tests of the material validation, the results obtained from the polyphenylsulfone test object remained below the predetermined threshold. For the prototype material, only the test objects made of polycarbonate and tough 2000 resin withstood the cleaning procedure, and the tests stayed below the predetermined threshold value. Subsequently, the material analysis revealed that polyphenylsulfone and tough 2000 resin have the least surface irregularities and absorb the least water. Therefore, the vela® prototype was printed in tough 2000 resin. For the clinical simulation tests of the design validation, contamination was observed at specific locations of vela® in both test settings. In the high-income country setting, test results above the threshold value are observed in the space between the diaphragm. The results are more varied in the low- & middle-income country setting; hence, layman's tests were added to minimize user bias and obtain a more concrete result. Ultimately, test results above the threshold value are observed in the space between the diaphragm and the connection between the tube and handle.
CONCLUSION: For the material validation, polyphenylsulfone is identified as a suitable material for the final vela®. Tough 2000 resin is deemed appropriate as a prototype material to validate cleaning. For the design validation, it is concluded that design improvements are needed for two specific locations on the vela® to improve cleaning. The connection requires a redesign to facilitate easy disassembly. The diaphragm with stem is composed of silicone and hard plastic, and it is advisable to employ two-component injection molding to produce this part. When incorporating these suggestions into the design, it can be concluded that vela® can be safely reused in both high- and low- & middle-income countries, contributing to the sustainability and accessibility of medical devices.

Contents

List of Abbreviations

ABS acrylonitrile-butadiene-styrene

ATP adenosine triphosphate

CPE+ co-polyester+

CSSD central sterile service department

FDM fused deposition modeling

HIC high-income country

IFU instructions for use

LMIC low- & middle-income country

PC polycarbonate

PPSU polyphenylsulfone

RLU relative light unit

SLA stereolithography

TPU 95A thermoplastic polyurethane 95A

T2R tough 2000 resin

VE vacuum extractor

2k two-component

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1 Introduction

In this chapter, Section 1.1 explains the basic principles of vacuum extraction. Section 1.2 discusses the rationale for the study, and Section 1.3 addresses the research question.

1.1 Background

The following section provides background information related to the thesis. First, an explanation of what vacuum extraction entails and its application is discussed. Then, the importance of a reusable vacuum extractor is discussed.

1.1.1 Vacuum extractor

In 2021, assisted vaginal birth deliveries accounted for 7% of all births in the Netherlands [1]. Assisted vaginal delivery is a delivery method using forceps, a vacuum extractor (VE), or another instrument to facilitate vaginal delivery, with or without assistance from the mother in pushing [2]. A clear trend can be observed in the transition from using forceps to a preference for using a VE [3, 4]. During vacuum extraction, a cup is placed on the fetus's head, followed by the application of suction to the cup. Subsequently, the vacuum pressure is adjusted to the desired level, and downward traction is exerted. When the fetal head is crowning, the suction is disengaged, and the cup is detached [4]. Figure 1.1 illustrates a vacuum extraction.

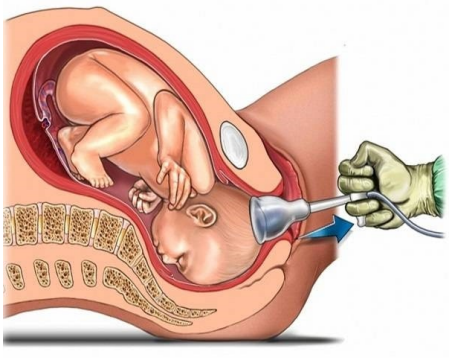


Fig. 1.1.: Illustration of a vacuum extraction, image from [5].

In a low- & middle-income country (LMIC), the use of a VE is notably less frequent than in a high-income country (HIC). In Sub-Saharan Africa, the utilization of a VE is usually less than 1% [6]. In addition, far too many birth-related maternal and perinatal deaths still occur in LMICs [7]. If a vacuum extraction is conducted under appropriate supervision and care, this method can

substantially benefit pregnant women, reducing maternal and neonatal morbidity and mortality [8]. This implies the necessity of reintroducing vacuum extraction in LMICs.

1.1.2 Reusable medical devices

A popular VE is the disposable Kiwi® OmniCup, illustrated in Figure 1.2. However, the Kiwi® OmniCup has several drawbacks due to the disposable character, making it worth exploring the benefits of switching to a reusable device.

Fig. 1.2.: The disposable Kiwi® OmniCup, image from [9].

First, reusable medical devices will reduce waste and lower the environmental burden, provided that the design for reusability has been properly considered [10]. Reusing medical devices is a more environmentally friendly practice that has recently gained attention [11]. Transitioning from disposable to reusable devices benefits the environment, leading to decreased ecological impacts across all categories except water consumption [12].

Secondly, reusable medical devices can increase accessibility for LMICs. The trajectory of medical devices has evolved from reusable to disposable, driven by concerns related to safety and costs. However, disposable devices have become progressively sophisticated, resulting in higher expenses. Hence, this necessitates the consideration of a transition back to reusable devices [13]. Thus, using a reusable VE will enhance accessibility in LMICs as it becomes more cost-effective and reduces the supply chain costs [10, 14, 15]. Research has shown that vacuum extractions increased as appropriate equipment and facilities were available in a Tanzanian hospital [8].

1.2 Rationale

In 2020, LAYCO Medical Devices was founded in response to an urgent problem: the inadequate integration and lack of medical equipment accessibility in LMICs. A reason for this is that the

development of medical devices has been predominantly centered in HICs, even though there is a pressing demand to extend healthcare services in LMICs [16]. Hence, LAYCO Medical Devices started with the development of vela®, a reusable vacuum extractor, to ensure that vacuum extraction is more accessible, which is greatly needed in LMICs [4, 8]. Simultaneously, this presents a more sustainable solution compared to disposable alternatives [12]. Vela® is in the prototype phase, but since the design is nearly complete, it is essential to perform validations whether vela® is indeed reusable.

1.3 The scope and the research question

This thesis aims to validate the reusability of the vela®. To determine the reusability of a medical device, evaluating its reprocessing efficiency is imperative [17]. Reprocessing can include the subsequent procedures: cleaning, disinfection, and sterilization [18]. The thorough cleaning of medical devices before disinfection and sterilization is often neglected. In contrast, it is widely recognized that the effectiveness of disinfection and sterilization procedures depends on adequately executing the cleaning phase [10, 19, 20]. For this reason, and to narrow the project's scope, it was decided to focus on the cleaning step of the reprocessing cycle. Therefore, the research question of this project is: *Can vela® function as a reusable vacuum extractor, focusing on its cleanability?*

The design of vela® is nearly completed; however, the device has not yet been fabricated in the final material. A proposed material for vela® is the thermoplastic material polyphenylsulfone (PPSU), which will be fabricated through injection molding. Given that this research aims to demonstrate whether possible design modifications are needed, it is premature in this phase to create an injection-molded vela® due to the time and costs of producing the molds for this process [21]. Therefore, this research is divided into two distinct validations: a material validation and a design validation. The suitability of the material PPSU is validated in the material validation. Furthermore, a prototype material is identified to produce vela® for the design validation since vela® cannot be manufactured from PPSU at this stage. In the design validation, an assessment is made regarding the safe reuse of the vela® design. Considering the rationale of LAYCO, this is tested in both HIC and LMIC settings. This resulted in the following research questions.

Can vela® function as a reusable vacuum extractor, focusing on its cleanability?

- Material validation
    1. Is PPSU a suitable material for the final production of vela®?
    2. What prototyping material best resembles the final material of vela®?
- Design validation
    1. To what extent is the vela® design cleanable in a HIC setting?
    2. To what extent is the vela® design cleanable in a LMIC setting?

2 Reprocessing of reusable medical devices

This chapter delves into the reuse of medical equipment. Section 2.1 details the reprocessing process, followed by an exploration of official reprocessing validations in Section 2.2. Section 2.3 delves into the validation approach specific to this study.

2.1 Reprocessing process

Reusable medical devices are any devices reused on multiple patients; therefore, the devices must be adequately reprocessed in between [17]. Reprocessing refers to the decontamination of a medical device [18]. "Decontamination" encompasses applying physical or chemical methods to eliminate nonfunctional pathogenic microorganisms on surfaces or items. By ensuring that microorganisms can no longer transmit infectious particles, the surface is safe for use, handling, or disposal [22]. This process may include the following procedures: cleaning, disinfection, and sterilization. These are briefly explained below [23]:

- Cleaning eliminates physically infectious substances and the organic matter supporting their growth but not necessarily destroying them.
- Disinfection involves the inactivation of pathogenic organisms, except for bacterial spores.
- Sterilization entails eliminating the viable microorganisms.

Specific reprocessing steps are performed depending on the risk category assigned to the medical device, as shown in Table 2.1 [24].

Tab. 2.1.: Reprocessing level of reusable medical devices, adapted table from [22].

Risk category	**Reprocessing level**	**Medical device example**
Non-critical	Cleaning	Blood pressure cuffs
Semi-critical	Disinfection	Non-invasive flexible endoscopes
Critical	Sterilization	Surgical instruments

Figure 2.1 shows the decontamination cycle of a medical device. For critical devices, this complete cycle is followed. Cleaning plays a crucial role, given the dependence of successful disinfection and sterilization on cleaning; therefore, the focus is on the cleaning step of the reprocessing process [10, 19, 20].

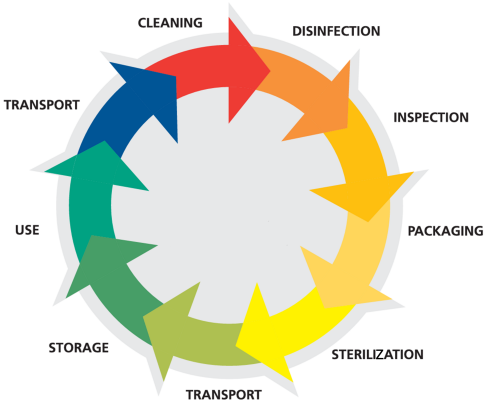


Fig. 2.1.: Decontamination cycle of a medical device. By assessing the level of risk associated with a product, the appropriate cleaning method is determined, adapted image from [22].

Reprocessing of medical devices must be conducted exclusively within the sterile services department, which should either be a distinct, delineated department or situated within a specified decontamination area. Numerous nations maintain centralized decontamination facilities, often referred to as the central sterile service department (CSSD), offering services to operating rooms, wards, and clinical areas [22].

A Dutch CSSD organizes this process into three distinct zones. A unidirectional flow of medical devices categorized as soiled, clean, and sterile is maintained to ensure appropriate airflow direction. The process begins in the "dirty room," where the device enters soiled, undergoes initial cleaning, and is further processed in a washer-disinfector. The equipment then moves to the "clean room," where the device is clean and prepared for sterilization. Upon completion, it is then taken to the sterilizer and stored in the "sterile room," where the device remains sterile until its designated use [25].

2.2 Official validation standards

Official reprocessing validation for semi-critical and critical medical devices requires the involvement of a notified body or other authorized testing body. A notified body is an organization appointed by a European Union member state to assess the conformity of specific products before they are placed on the market. There are established criteria that a medical product must meet for cleaning, disinfection, and sterilization validations.

Below, more details regarding cleaning validations are discussed. Standard washer-disinfectors are employed for cleaning and disinfection processes. Consequently, the cleaning validation is conducted after the medical device has completed a cycle in the washer-disinfector [26]. Many standard washers utilize thermal disinfection methods, involving temperatures of up to 93°C, in combination with detergents and other chemicals integrated into the washer-disinfector [27].

The testing should include medical devices representing the worst-case scenario, which is the most contaminated and challenging to reprocess. The validation studies should incorporate multiple full-use cycles and be designed to assess the accumulation of soil over time [28]. Moreover, at least two analytes related directly to clinically relevant soil should be tested for critical medical devices. Protein is a mandatory analyte, while others may be selected [29]. Each analyte has specific acceptance criteria for allowable levels encountered on the device, and this is tested. Various accepted extraction techniques, including sonication, flushing, and swabbing, can be employed. Additionally, at least three devices should be tested [26].

2.3 Validation approach for this study

Reprocessing is often given minimal consideration in the design of medical devices, making many reusable devices challenging to clean, disinfect, and sterilize. Consequently, this oversight results in inefficiencies, decreased productivity, and, tragically, contributes to hospital-acquired infections and avoidable fatalities [17]. Therefore, it is recommended to incorporate validation considerations early in the design process [19]. This validation is called the first *Clinical simulation test* in this research project. It is a straightforward method to assess the cleaning adequacy of the prototype materials and the vela® design. Ultimately, it determines whether modifications to the design are necessary and prevents the premature, costly production of the molds.

Official validation tests are reviewed to choose tests that can effectively validate the cleanliness of a device. As a result, two specific analytes were selected to capture contamination present on the devices after cleaning, resulting in the implementation of two tests. The Browne washer-disinfector test soil, which is a commonly used soil, was chosen for soiling the devices. The vivid red color of the soil makes identifying inadequately cleaned areas easy, providing a visual assessment of the cleaning equipment's efficacy. Furthermore, the soil presents the cleaning equipment with a challenge similar to the cleaning efficacy tests described in ISO/TS 15883-5, and it includes contaminants such as protein [30]. Therefore, this washer-disinfector soil from Browne is chosen. In official tests, sonication is often chosen as an extraction method, where the entire product is examined for any residual dirt. However, this study focuses on specific locations of the vela® design to identify potential design bottlenecks. Thus, a swapping technique is chosen as the extraction method. This swapping technique allows for precisely identifying areas where contamination may be present, facilitating concrete locations for redesigns based on the findings.

A literature review was conducted to get an inside into what tests could be performed for this validation. This literature review, 'Exploring Validation Tests for Assessing the Cleanliness of Reprocessed Medical Devices', is presented in Appendix A.

Following the literature review, the decision was made to conduct an adenosine triphosphate (ATP) test and a protein test. In both tests, the swab is removed from the tube, swabbed over the specific

surface, and then put back into the tube. Subsequently, the snap-valve at the top of the tube must be pressed, releasing a liquid that triggers a reaction [31, 32]. Both tests are discussed below.

2.3.1 ATP test

This first test is the UltraSnap Surface ATP test, which was purchased at Gullimex. This test should be used in combination with an ATP monitor (luminometer). Together, they establish a system for monitoring surface hygiene on reprocessed equipment and various environments across different industries [31]. ATP tests are frequently used for monitoring medical devices because they provide real-time and quantitative measurements [33].

ATP, an analyte also used in official validations, is the universal energy molecule in all animal, plant, bacterial, yeast, and fungal cells [29]. Residues of organic matter left on surfaces contain ATP. Thus, it is a good indicator of the cleanliness of a service. When a sample is collected, and ATP comes into contact with the liquid-stable Luciferase/Luciferin reagent provided within the test, light is emitted directly related to the amount of ATP in the sample. The luminometer measures this light and reports the results in relative light unit (RLU), equivalent to fmoles of ATP/cm^2 [31]. In official cleaning standards, 10 fmoles of ATP/cm^2 is considered an alert level. Therefore, this research has chosen a threshold value of 10 RLU. Anything above this threshold is classified as contaminated, while anything below it is considered clean [26].

2.3.2 Protein test

Regulatory agencies often mandate the assessment of protein levels, establishing it as the primary analyte for research as a standard practice [29]. This emphasis on protein analysis is driven by the likelihood of medical devices coming into contact with proteins during their utilization [34]. Therefore, the second test was a protein test, the PRO-clean test purchased at Gullimex.

PRO-Clean quickly and accurately assesses surface cleanliness, detecting protein residues by a color-changing reaction, with a faster and deeper purple color indicating higher contamination levels [32]. It provides results in 10 minutes. PRO-Clean produces four reagent colors, as illustrated in Figure 2.2: green (0), gray (1), light purple (2), and dark purple (3), with any color except green indicating a 'contaminated' surface. This color change must be observed visually.

Fig. 2.2.: The four potential color outcomes resulting from the protein test. Any color except green indicates contamination, image from [32].

3 Material validation

In the following chapter, the materials are validated for cleanability. In Section 3.1, the selected materials are discussed, Section 3.2 describes the methods used, and Section 3.3 presents the results. Section 3.4 provides the discussion, and Section 3.5 ends with a conclusion.

3.1 Materials

Due to the time and cost constraints of creating a mold, it is not feasible to create a PPSU injection-molded vela® at this stage [21]. Thus, this section explores alternative potential prototype materials. Vela® is a critical product; the official material must adhere to all the criteria of the complete decontamination cycle, as illustrated in Figure 2.1. However, in this research, the focus is on the cleaning of vela®. Therefore, different criteria apply to the material selection of the prototype than to the final material of vela®.

3.1.1 The final material of vela

PPSU is a commonly used thermoplastic in producing reusable medical devices, exhibiting excellent thermal and chemical resistance [35]. Hence, the material is expected to withstand aggressive reprocessing methods. Therefore, for now, PPSU was chosen as the final material of vela®. The PPSU will be injection molded. During injection molding, molten plastic is injected into a cold, empty cavity, called a mold, that has the desired shape of the product. The molten material solidifies, resulting in the product being ejected when the mold is opened. Injection molding is the main molding technique for thermoplastic polymers and is used to produce more than 30% of all plastic parts. It excels in high-volume production of complex plastic parts of various shapes and sizes [36].

3.1.2 The prototype material of vela

The production method was considered the primary constraint for the prototype's material. This method should allow for rapid production while permitting easy modifications if necessary, and it should be relatively low-cost. Rapid prototyping, also known as 3D printing, primarily focuses on quickly creating prototypes or foundational models, which are the basis for developing subsequent iterations and, ultimately, the final product [37]. Therefore, it is a highly suitable production method for the vela® prototype; however, there is a wide range of rapid prototyping techniques.

Two 3D printing methods were available during this project, fused deposition modeling (FDM) and stereolithography (SLA), both of which stand out as widely recognized and commonly utilized polymer-based 3D printing techniques [38]. The most well-known technique is FDM, which involves the controlled extrusion of material through a nozzle on a building plate, building layer by layer, and utilizes thermoplastic filaments [37]. FDM is a highly suitable production method for prototyping due to its cost-effectiveness, user-friendly operation, and the availability of a wide range of thermoplastic materials, making it an accessible and versatile option for quickly creating prototypes [39]. Then, SLA, a vat-based technique, solidifies a reservoir of resin layer by layer using a UV curing light and uses photopolymer resin. SLA could be interesting because it can print high-resolution parts and is known for its exceptional accuracy compared to other printers [38].

Subsequently, the material's criteria were examined to ensure it could be cleaned without getting damaged. Various criteria have been identified, considering the two different usage settings of vela®, namely the HIC and LMIC settings.

First, cleaning with water is a mandatory practice in every cleaning procedure. Thus, this necessitates the material be resistant to water flow [18].

Second, cleaning agents will be used during the cleaning process. Therefore, the following cleaning agents were considered:

- MediClean forte is often used in Dutch hospitals and, therefore, taken as a benchmark for the HIC setting. It is a soap with a pH range of 10.4-10.8 [40].
- Bleach (JIK) and soapy water are commonly used in LMICs to clean medical instruments; therefore, this is taken as a benchmark for the LMIC setting. Bleach water typically has a pH of approximately 9.5, while soapy water tends to have a pH of around 10.5 [41].

Hence, the material must be able to withstand both weak alkalis (pH 7-10) and strong alkalis (pH > 10) chemicals.

Third, the material should withstand high temperatures. In the HIC setting, during cleaning, temperatures up to 93 degrees Celsius are employed in the washer-disinfector, while in the LMIC setting, cold water is used [41].

Ultimately, these considerations have led to the following requirements as listed below:

1. The prototype material should be water-resistant.
2. The prototype material must be resistant to cleaning agents that contain weak alkalis (pH 7-10) and strong alkalis (pH > 10).
3. The prototype material should have a temperature resistance of at least 93 °C.

Considering the production method and these criteria, suitable materials were identified. Given that the printing was to be conducted at the 3mE faculty of TU Delft, the printers and materials provided by the 3mE workshop could be used. Consequently, the decision was made to opt for

FDM printing and to explore the materials accessible through their supply source, MakerPoint [42]. Additionally, an examination was carried out regarding the SLA printer and the available materials from their supply source, Formlabs [43]. An online investigation, along with the utilization of the materials database GRANTA EduPack, was undertaken to assess the suitability of materials [44]. Five materials are determined based on availability and prerequisite requirements, as Appendix B outlines.

These are the following materials with accompanying production methods:

- Material 1: acrylonitrile-butadiene-styrene (ABS) - FDM printer
- Material 2: co-polyester+ (CPE+) - FDM printer
- Material 3: polycarbonate (PC) - FDM printer
- Material 4: thermoplastic polyurethane 95A (TPU 95A) - FDM printer
- Material 5: tough 2000 resin (T2R) - SLA printer

3.2 Methods

The (prototype) materials of vela® are validated for cleanability. PPSU is validated as the final material for vela®, by means of an injection-molded PPSU object. Following this validation, other suitable prototype materials can be tested and compared to this PPSU object.

3.2.1 Preparation

To examine the effectiveness of cleaning PPSU, an existing injection-molded PPSU object was selected for this validation. A particular section of a water reservoir was cut out, measuring approximately 70 x 60 x 50 mm. This section exhibits intricate features that present challenging cleaning scenarios while maintaining symmetry. The symmetry is helpful for the *Clinical simulation tests*, as it allows for simultaneous testing of both ATP and protein tests on the left and right sides. Upon consultation with an expert on the CSSD of a Dutch hospital and literature, two specific areas were pinpointed as particularly challenging to clean. These areas were considered suitable for evaluating the cleanability of the material, as illustrated in Figure 3.1.

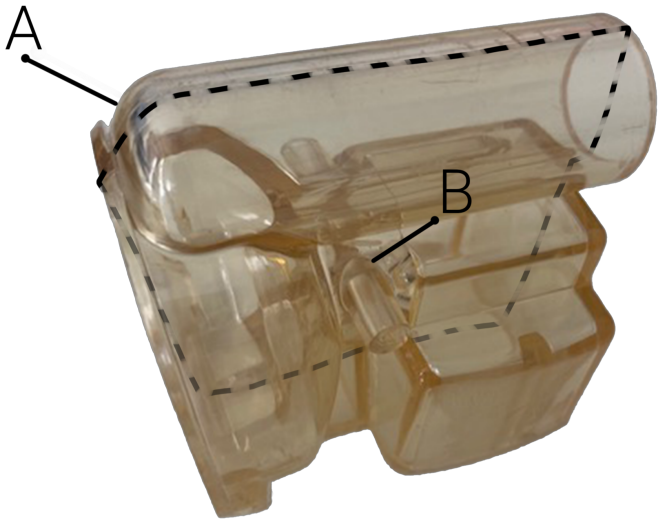


Fig. 3.1.: Oblique top view of PPSU test object with the test locations A and B indicated. A: The blind corner in the cylinder at the top. B: Around the round protrusion on the side. The dashed line on the test object represents the axis of symmetry, illustrating that testing can be done on both sides.

Afterward, this form was replicated using SolidWorks software to enable it to be 3D-printed in various materials, allowing for duplication. The SolidWorks model is depicted in Figure 3.2.

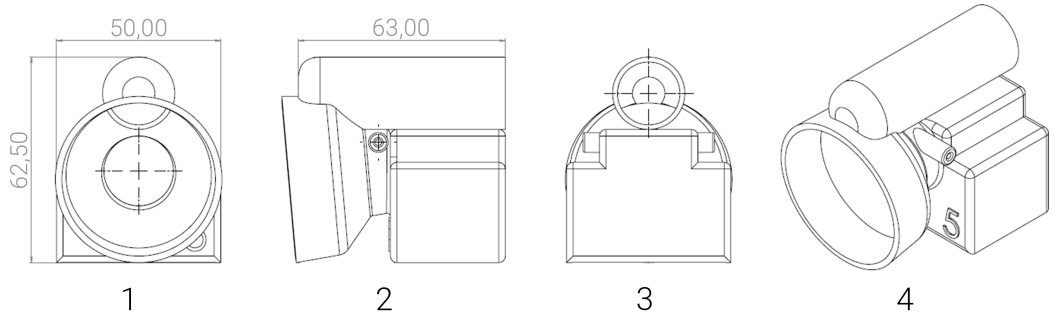


Fig. 3.2.: Different views of the test object in SolidWorks, including some dimensions (in mm) for reference. 1: Front view. 2: Side view. 3: Back view. 4: Oblique top view.

The SolidWorks model is subsequently 3D-printed using the five selected prototype materials. All the various prints were assigned distinct numbers (1 to 5) on the object to facilitate easy differentiation during testing, such as the '5' displayed on the model in Figure 3.2. In addition, all five prints were printed twice to ensure a spare print was always available during testing. The prints were post-processed by removing the support structures and smoothing the objects with sanding paper and a file. Figure 3.3 displays the six test objects, including the PPSU part, with the various materials indicated by the associated numbers.

Fig. 3.3.: Top view of the six test objects. 1: ABS. 2: CPE+. 3: PC. 4: TPU 95A. 5: T2R. 6: PPSU.

Two tests were conducted to perform this material validation. First, to validate the suitability of PPSU as a final material and to identify an appropriate prototype material that best represents PPSU (*Clinical simulation tests*). Second, in cases where multiple prototype materials appear suitable, a comprehensive analysis is conducted to evaluate the inherent distinctions within these materials (*Material analysis*).

The *Clinical simulation tests* aim to validate the suitability of PPSU for the final vela® device and, simultaneously, to identify a suitable material for the prototype that behaves similarly to the final vela® device in terms of cleanability. On paper, these five materials, ABS, CPE+, PC, TPU 95A, and T2R, appear suitable as they meet all the criteria outlined in Table B.1 and Table B.2 of Appendix B. However, in practice, it is imperative to empirically assess the materials' ability to withstand exposure to water, heat, the alkaline and acidic detergents employed in the washer-disinfector, and whether this affects their susceptibility to retaining dirt. Additionally, it is essential to evaluate the appropriateness of the 3D printed prototype, given that the layering technique of a 3D printed product may result in the formation of ridges and voids where dirt may accumulate. Finally, considering that plasticizers are frequently incorporated into materials in practice, which may impact the temperature resistance, it is necessary to determine whether they are compatible with this process [45].

When multiple materials appear suitable, gaining a deeper understanding of the material is imperative. For instance, the test objects are 3D-printed, and their surfaces may contain tiny pores, rendering them porous. The presence and extent of porosity can vary depending on the printing technique and the material used. If porosity is present, it can significantly influence cleanability [46]. Therefore, it is crucial to establish a method for distinguishing the material differences: the *Material analysis*.

3.2.2 Data collection

Clinical simulation tests
First, a pre-test was conducted involving placing all the test objects in the washer-disinfector to assess their resilience to the process. After that, the test objects were soiled with the Browne washer-disinfector test soil, subsequently cleaned, and validated for cleanliness using a ATP and protein tests. The tests were performed in the "dirty room" of the CSSD at the St. Antonius Hospital in Utrecht. The test objects were placed in the Ultrasonic machine (Nidsa) and the washer-disinfector (Belimed), following a predetermined test plan. This predetermined test plan can be found in Appendix C.

The data was collected using the two tests on the left and the right side of the test object. The ATP test was conducted by reading the results directly from the EnSure Touch ATP monitor and recording them. On the other hand, the protein test involved observing color changes, which were read and written down after a 10-minute interval. The data obtained from both tests were initially recorded manually on a pre-designed data sheet.

Material analysis
Suitable prototype materials were observed under a light microscope (Nikon Eclipse LV100 upright microscope with a digital sight DS-2MBWc camera). When the materials were examined under the microscope, the camera captured these images, which were subsequently analyzed.

Additionally, water absorption tests were conducted. The water absorption capacity is associated with the material's characteristics, particularly its porosity and the attributes of its pores. These tests are performed by first dehydrating the materials in a dehydrator (Concept) for one night. The materials were submerged in water for 30 minutes, extracted and dried, then weighed (wet material weight). After that, they were subjected to dehydration in the dehydrator for 120 minutes and then weighed again (dry material weight). The weighing scale was a digital pocket scale with a capacity of 100 grams and an accuracy of 0.01 grams. This process is repeated four times to quantify the amount of water retained by the materials, which, in turn, indicates the degree of surface porosity [47].

The water absorption capacity is defined as the ratio of the material weight in a hydrated and dehydrated state compared to the initial dry material weight for the water absorption tests.

It is categorized into mass water absorption W_{abs} and is calculated using the following formula:

$$W_{abs} = \left(\frac{m_1 - m_0}{m_0} \right) \times 100\% \quad [47]$$

W_{abs} : Mass water absorption (%)

m_0 : Initial dry material weight (g)

m_1 : Material weight after (de)hydration (g)

The initial dry material weight, m_0, was determined after the materials had been dehydrated in a dehydrator for one night. Then, after alternately measuring the wet and dry material weights, m_1, the W_{abs} was calculated.

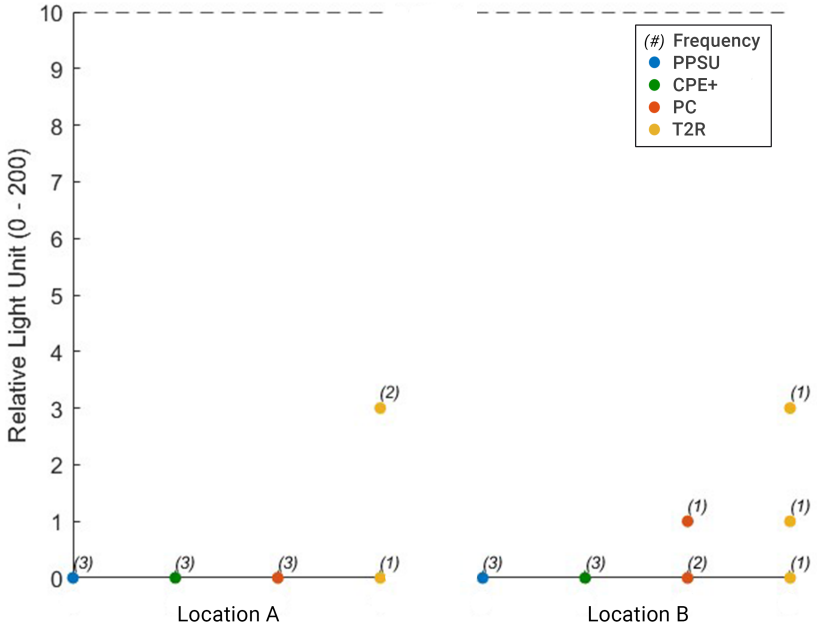
3.2.3 Data processing

For both the *Clinical simulation tests* and the *Material analysis*, the data was transferred to an Excel file for further analysis, and the final data analysis was performed and visualized using Matlab.

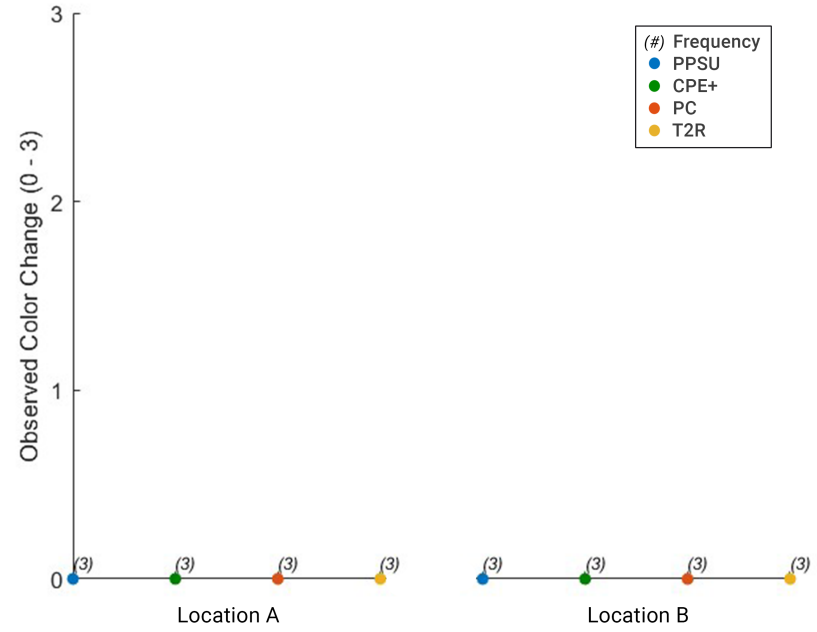
3.3 Results

Clinical simulation tests
The predetermined test plan was followed as described in Appendix C. In Appendix D, some photos of the study set-up are shown. After the pre-test, the test objects made from TPU 95A and ABS exhibited deformation, likely due to the addition of plasticizers. Consequently, these test objects were excluded from further analysis. The test objects of the following materials were further analyzed: PPSU, CPE+, PC, and T2R. These test objects underwent three cycles in the washer-disinfector and were subsequently tested.

As depicted in Figure 3.4, all the PPSU data points exhibit zero values for both location A (the blind corner) and location B (the round protrusion). Furthermore, the data points for all the other materials for the ATP tests also consistently remained below the predetermined threshold of 10 RLU, see Figure 3.4a. The same is true for the protein tests, where the data points for all the materials are 0; see Figure 3.4b. However, the test object made of CPE+ became brittle after undergoing multiple cycles in the washer-disinfector, as the test object developed cracks and started to crumble, see Figure D.1h in Appendix D.



(a) Scatter plot for the ATP test results. The Y-axis represents the degree of contamination in RLU, with a dotted line indicating the threshold value at 10 RLU.



(b) Scatter plot for the protein test results. The Y-axis represents the degree of contamination in observed color change on a scale of 0-3.

Fig. 3.4.: Test results for the material validation of the cleanability experiments. The Y-axis represents the degree of contamination. The X-axis displays each material and the associated contamination for Locations A (the blind corner) and B (the round protrusion). The frequency of occurrence is indicated in italics above each data point.

Material analysis

Figure 3.5 displays the PPSU, PC, and T2R materials observed under the microscope at 10 times and 20 times magnification.

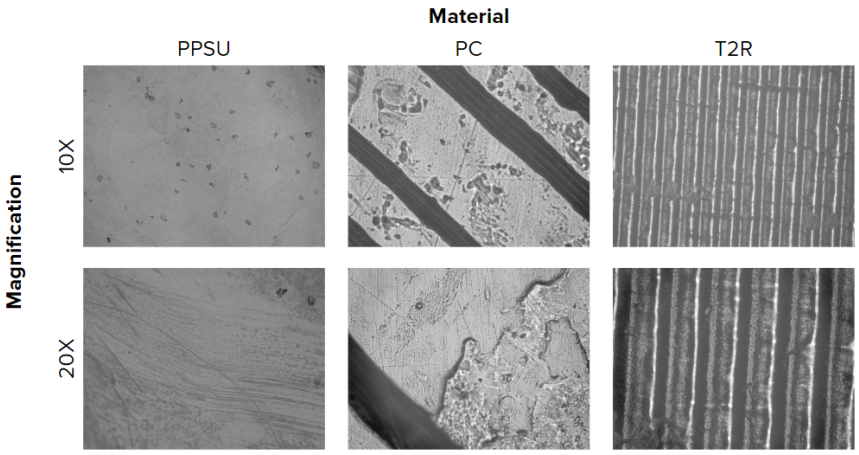


Fig. 3.5.: Microscopic image of PPSU, PC, and T2R at magnifications of 10x and 20x. Printing lines are visible in the materials PC and T2R. In all three materials, air bubbles are observable.

Visible 3D-print lines are apparent in the PC and T2R samples, and visible air bubbles are observed in all three objects. However, determining the depth is challenging.

Figure 3.6 presents a scatter plot depicting the percentage change of water absorption between the weight after absorption (wet material weight) and the weight after dehydration (dry material weight) compared to the initial dry material weight m_0 for PPSU, PC, and T2R. The m_0 of the PPSU test object was 68.84 grams. The m_0 of the PC test object was 30.79 grams. The m_0 of the T2R test object was 31.08 grams.

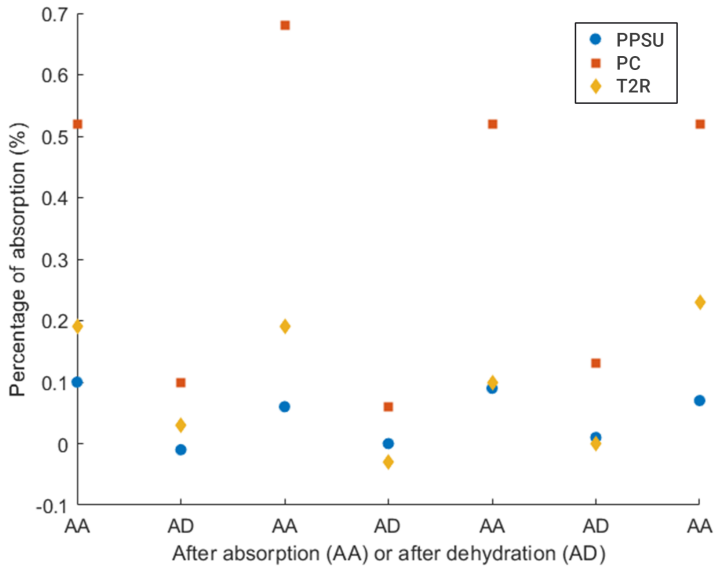


Fig. 3.6.: Scatter plot of the change in absorption percentage per material after absorption (AA) and dehydration (AD).

In general, PPSU exhibits the lowest water absorption rates (AA), followed by T2R, and PC exhibits the highest rates. This trend is also evident when considering the averages, as shown in Table 3.1.

Tab. 3.1.: Average water absorption per material after absorption and after dehydration.

	PPSU	**PC**	**T2R**
Mean after absorption (%)	0.08	0.56	0.18
Mean after dehydration (%)	0.00	0.10	0.00
Absolute weight change (g)	0.03	0.11	0.03

The Table also demonstrates that PC retains water after dehydration, unlike PPSU and T2R in this time frame of dehydration. Additionally, it is noteworthy that PC exhibits the highest average weight change among the materials studied.

3.4 Discussion

Two key conclusions can be drawn from the *Clinical simulation tests*. Firstly, PPSU proves to be a cleanable material and thus is suitable for vela® in terms of cleanibility. Secondly, both ABS and TPU 95A exhibited deformation after undergoing the washer-disinfector cycle, which is likely attributed to the presence of plasticizers [45]. While CPE+ initially withstood the testing, it eventually exhibited signs of brittleness, rendering it unsuitable as a prototype material. Consequently, the remaining suitable materials that share similarities with PPSU are PC and T2R. All these materials were confirmed as clean in the test, as shown in Figure 3.4.

Considering the *Material analysis*, the following conclusions can be drawn; firstly, on the microscopic images, as shown in Figure 3.5, it is visible that the print lines of the T2R print are smaller than those of the PC print, potentially contributing to a smoother surface texture. This observation aligns with the general understanding that SLA prints exhibit superior accuracy and surface finish compared to FDM prints [38]. Furthermore, the water absorption test was employed to provide a more robust validation of material absorption capacity and, by extension, porosity [47]. This test revealed distinctions among PPSU, PC, and T2R; notably, T2R exhibited characteristics most closely resembling those of PPSU, as illustrated in Figure 3.6. As a result, T2R emerged as the most suitable prototype material.

However, it is important to acknowledge the limitations of this study. The utilization of 3D printers at the TU Delft led to limitations in the range of available materials. Assessing various resins available at Formlabs led to selecting the most suitable one [43]. Similarly, at MakerPoint, an evaluation of materials compatible with an Ultimaker printer was conducted. The materials were chosen by considering online resources and utilizing the material information from the GRANTA EduPack software [42, 44]. As a result, potential suitable materials may have been overlooked. Furthermore, for the *Clinical simulation tests*, there are minor deviations in the outcomes observed for T2R in the ATP test; see Figure 3.4a. This could potentially be attributed

to the manual post-processing of the test objects. Lastly, for the *Material analysis*, the limited number of data points collected in the absorption test complicates executing a comprehensive statistical analysis.

The focus has been on 3D printing materials capable of withstanding multiple disinfection procedures in Dutch hospitals. In the future, it may be interesting to incorporate the entire reprocessing cycle into this process, including identifying 3D printing materials capable of withstanding elevated sterilization temperatures. Furthermore, the test objects were post-processed using sanding paper and a file. Alternative post-processing techniques could have resulted in an even smoother and less porous surface [48]; exploring these possibilities may be of interest to future research. Exploring an appropriate 3D printing material for the vela® prototype enhances the representativeness of test results, marking a positive step towards ensuring the reusability of vela®. Transitioning from single-use products to reusable medical equipment improves sustainability and accessibility [10, 12]. To facilitate this transition, it is essential to initially identify an appropriate 3D printing material for creating a prototype of the medical product and evaluating its cleanability.

3.5 Conclusion

This chapter aimed to validate the final material and identify an appropriate prototype material.

The first question validated the suitability of PPSU as the final material for vela®. PPSU was clean every time during the testing process; thus, it can be concluded that PPSU is indeed a suitable material choice for cleanability.

The second question identified a prototype material that most closely resembled the PPSU part in assessing cleanability. The results indicated that T2R print using an SLA printer showed the most remarkable similarity to the PPSU material. Thus, producing a prototype in T2R represents a straightforward and efficient approach for validation before its ultimate fabrication through injection molding in PPSU. Consequently, it is recommended that the use of T2R be considered in the following stages of the vela® tests.

4 Design validation

In the following chapter, the design of vela® is validated for cleanability. The design is validated in a HIC and a LMIC setting. In Section 4.1, materials and methods are discussed. Section 4.2 presents the results. Section 4.3 provides the discussion, and Section 4.4 ends with a conclusion.

4.1 Materials and methods

The first step involves preparing this design. After which, an analysis of the two test settings is conducted. Subsequently, data collection and processing are discussed.

4.1.1 Preparation

After the material validation is completed, vela® must be replicated as closely as possible to its final form. Ultimately, vela® will consist of five parts.

These are the following parts, as shown in Figure 4.1:

- Part 1: Tube & cup
- Part 2: Front handle
- Part 3: Silicone domes
- Part 4: Diaphragm with stem
- Part 5: Back handle

To validate the cleanability of vela®, creating a prototype resembling the final product is essential for testing its design. However, rapid prototyping techniques have limitations, resulting in imperfections that can lead to unintentional dirt collection [49]. Therefore, the five components must be smoothly constructed to ensure accurate test outcomes. Furthermore, some components have been externally sourced and consequently affixed to the parts using adhesive. This is the case with the connection between the front handle and the tube, which are a body and insert of a tube connector purchased at CPC. Since this is not how the final vela® will be produced, this component must be translated into a SolidWorks model to allow the parts to be printed as a unified part. Figure 4.2 shows a drawing of the connection consisting of three SolidWorks subparts. Subparts 1 and 2 represent body components and are one integral assembly due to the clamping system. They are not easy to separate without exerting force. Subpart 3 represents the insert. These subparts are assembled onto the associated vela® parts before printing to ensure

Fig. 4.1.: The five different parts of vela®. 1: Tube & cup. 2: Front handle. 3: Silicone domes. 4: Diaphragm with stem. 5: Back handle. Every part of vela® labeled with a number allows one to distinguish between the four prints. All parts of this vela® are labeled with the number '2'.

a smooth integration into the design. Appendix E provides a detailed breakdown of the three components for further clarification.

Additionally, the tube was molded in silicone, and silicone adhesive was used to ensure a secure attachment to the silicone tube. Furthermore, the silicone diaphragm is a component of Part 4; it is the only item purchased ready-made, see Figure 4.1.

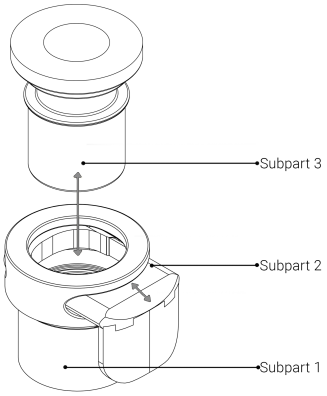


Fig. 4.2.: Assembly of the connection. Subparts 1 & 2 are the body; Subpart 3 is the insert. The arrows show movement to loosen and tighten the connection.

When the five SolidWorks parts of vela® were complete, it was printed several times in T2R. This decision stems from the requirement of conducting official validations with a minimum of three devices simultaneously tested, see Chapter 2.2. Four vela®'s were 3D printed to allow simultaneous testing in the HIC and LMIC settings. Furthermore, to ensure that the vela®'s can be easily distinguished during testing, each component will be labeled with numbers (1 to 4). This labeling will be applied to each part of the vela® that is printed in T2R, as illustrated in Figure 4.1. The prints were post-processed by removing the support structures and smoothing the objects with sanding paper.

Subsequently, it is crucial to identify the critical test locations on the device. Protuberances and cavities are recognized as the primary risk for dirt accumulation [17, 50, 51]. Thus, a selection of locations was made in consultation with an expert of the CSSD of a Dutch hospital and through consulting literature. Ultimately, six locations were chosen, as indicated in Figure 4.3.

Fig. 4.3.: Indication of the six different test locations. A: Inside the cup. B: Inside the tube. C: Connection from the handle to the tube. D: Above the head of the handle. E: Under the head of the handle. F: Between the stem and diaphragm. The back handle and the silicone domes are transparent, as no specific test locations have been chosen for these parts.

These locations were chosen due to their susceptibility to debris accumulation [17]. The inside of the tube, the upper part of the head of the handle, and the lower part of the head of the handle (Locations B, D, E) were selected due to the presence of cavities. The inside of the cup and the connection between the handle and the tube (Locations A and C) were chosen based on their intricate contours. The connection is particularly critical because it consists of two clamping

parts, as shown in Figure 4.2. Lastly, the location between the stem and diaphragm (Location F) was selected because the hard plastic stem and the silicone diaphragm clamp onto each other, potentially allowing for the accumulation of dirt in the space between them. Smooth surfaces do not pose a cleaning challenge [52]. Therefore, the back handle was not considered. Additionally, the silicone domes were intentionally excluded from consideration because the design of this component is still undergoing design iterations.

For the tests, first, the *Clinical simulation tests* were performed. Existing literature suggests that performing tests on the soiled device is a common control to distinguish differences before and after cleaning [53–57]. For the same reason, this study chose to add "dirty control tests" at the beginning of the tests. The design is validated in HIC and LMIC settings. For the "high-income procedure," the standard procedure of the CSSD at the St. Antonius Hospital in Utrecht can be followed [58]. The variation between the cycles is expected to be minimal for an automated process. Subsequently, these tests were also conducted in the LMIC setting, as vela® was initially designed to enhance the accessibility of medical equipment in LMICs. Therefore, these tests aim to determine if vela® can be effectively utilized in these nations, examining its sustainability and accessibility. To conduct targeted research, Kenya was chosen as the primary focus country for this setting. Since cleaning medical equipment is a manual process, having instructions for use (IFU) to ensure consistency in the cleaning procedure is crucial. Previous on-site research in Kenya was integrated into the cleaning and disinfecting setup, along with the IFUs used for similar settings [59]. Ultimately leading to the development of an IFU customized for vela®, which can be found in Appendix G. Since the cleaning process in the LMIC setting is manual, the vela®'s were cleaned individually.

Second, the *Layman's test* was conducted in the LMIC setting. Because the devices are manually cleaned in the LMIC setting, the research was influenced by the fact that the researcher knew the 6 test locations. Nevertheless, the *Clinical simulation tests* provide a good representation of the cleanability of these locations. However, it lacks a thorough understanding of the specific areas that may pose problems for those unfamiliar with the device. Hence, an experiment was designed in which vela®'s were soiled, and test subjects were tasked to clean it. After that, visual inspection determined whether the different locations were effectively cleaned. The test subjects of the *Layman's test* had to meet two conditions to create the most challenging and optimal testing scenario. These are the following:

- They should not be familiar with vela®.
- They should not have prior experience in cleaning medical equipment.

4.1.2 Scenarios for Clinical simulation tests

In the *Clinical simulation tests*, 75 tests were available for both the ATP and the protein tests, resulting in 150 tests in total. These tests must be distributed between the HIC and LMIC settings. After conducting the *Clinical simulation tests* for the material validation, it became evident that machine cleaning (HIC setting) was highly effective, resulting in many zero measurements.

Thus, scenarios were implemented in this test set-up to prevent depleting all tests to zero measurements. Testing commenced in the HIC setting, and after conducting tests on three vela®'s, an assessment was made, and one of the scenarios was chosen. Appendix H explains the four different scenarios. Scenario 4 is operated when all locations remain clean in the HIC setting; then, the remaining tests are allocated to the LMIC set-up. Scenarios 1 to 3 are operated if a certain number of locations are contaminated in the HIC setting. Depending on the number of contaminated locations, one of the scenarios and, thus, test distribution between the settings is chosen.

4.1.3 Data collection

During the *Clinical simulation tests*, the vela® devices were soiled with the Browne washer-disinfector test soil. Subsequently, the "dirty control tests" were conducted. Following this, the devices were cleaned according to the HIC or LMIC setting, after which the ATP and protein tests were performed. These tests were performed in the "dirty room" of the CSSD at the St. Antonius Hospital in Utrecht. Subsequently, testing begins in the HIC setting, while concurrent testing is also conducted in the LMIC setting. The complete pre-determined test plan can be found in Appendix F.

The data from these tests were collected using the ATP and protein tests. The ATP test was conducted by reading the results directly from the EnSure Touch ATP monitor and recording them. On the other hand, the protein test involved observing color changes, which were read and written down after a 10-minute interval.

4.1.3.1 Study set-up of the HIC setting

Clinical simulation tests
The vela® devices were placed simultaneously in the washer-disinfector (Belimed). After that, the tests were conducted. Given that this setting involves using machines, resulting in minimal chances of human error, these tests provide sufficient information about the design's cleanability in the HIC setting.

4.1.3.2 Study set-up of the LMIC setting

Clinical simulation tests
The required supplies, as outlined in the IFU, were obtained. JIK was replicated by simulating it with household bleach with a concentration of 4.5% and diluting it to 0.5% [22]. A photo of the final LMIC setting can be found in Figure I.1d of Appendix I. After that, the tests were conducted.

Layman's test

The vela®'s were soiled using the Browne washer-disinfector test soil, and test subjects (n=10) that fulfilled the required conditions were tasked to clean it. After performing the tests, data was observed and collected. This was done by visually inspecting each location and assigning a cleanliness score (0 = clean, 0.5 = slightly dirty, and 1 = dirty) to each location.

4.1.4 Data processing

Clinical simulation tests

The data obtained from both tests were initially recorded manually on a pre-designed data sheet. Subsequently, this data was transferred to an Excel file for further analysis, and the final data analysis was performed and visualized using Matlab. It is important to note that only descriptive statistics were used in the data analysis. However, inferential statistics were also considered, but due to the small sample size, no conclusive results could be drawn from them. More details about these statistics can be found in Appendix J.

Laymann's test

This data was entered directly into an Excel file for further analysis, and the final data analysis was performed and visualized using Matlab.

4.2 Results

For the *Clinical simulation tests*, the predetermined test plan was followed as described in Appendix F. In Appendix I, some photos of the study set-up are shown. By following the test plan and examining the scenarios, Scenario 3 was ultimately chosen for testing. Furthermore, the "dirty control tests" were performed as controls. In the ATP and protein tests, all the data points gathered in this control exceeded the predetermined threshold. Figure 4.4 illustrates how the tests were distributed among the different settings.

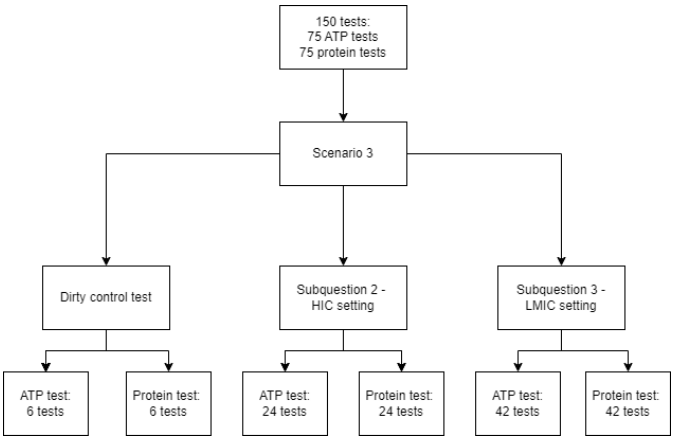


Fig. 4.4.: Flowchart for the test distribution for Scenario 3 of the Clinical simulation tests.

4.2.1 Validation of vela design in the HIC setting

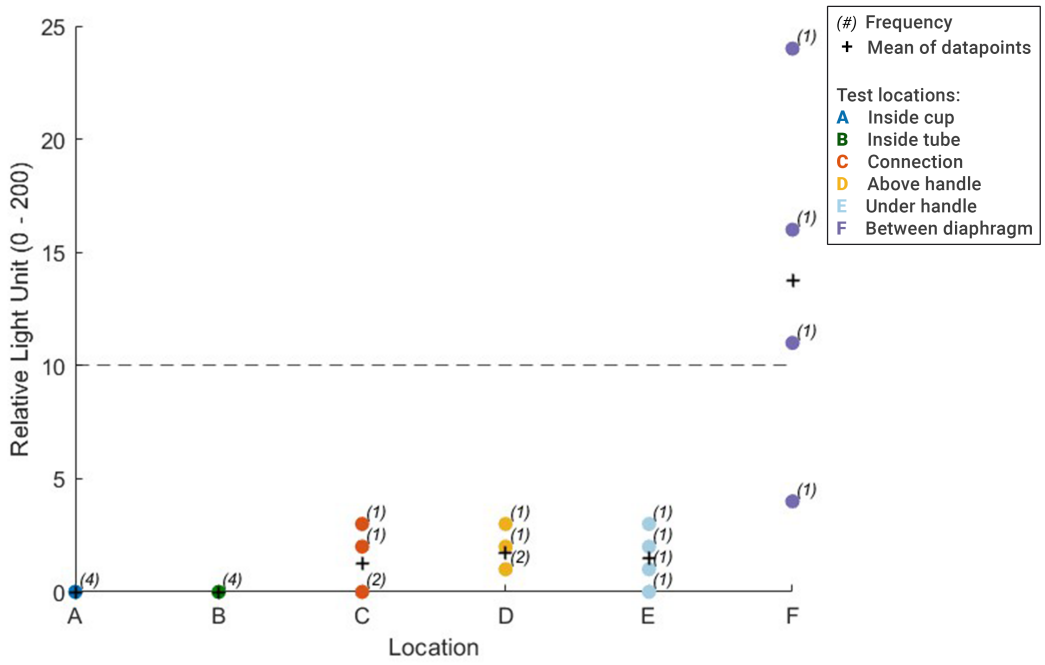
Clinical simulation tests in the HIC setting
Scenario 3 was chosen since, after conducting the initial three tests on vela®, it was observed that, except for one location, the results of the ATP test remained consistently below the predetermined threshold of 10 RLU. Similar observations were made in the protein tests, which further justified the selection of Scenario 3. Consequently, in the HIC setting, each location was tested four times with both tests. The results of these tests have been visualized in a scatterplot, as presented in Figure 4.5.

The outcomes of the tests exhibit little variation. In the ATP tests, data points exceeding the threshold are only observed at the location between the stem and diaphragm (Location F). Furthermore, the data points and the averages, marked with a "+", stayed below the threshold, as depicted in Figure 4.5a. In the protein tests, the data points exceed zero at the location between the stem and diaphragm (Location F). The other data points and their averages, marked with a "+", stayed below the threshold, except for one data point, on top of the head of the handle (Location D), as shown in Figure 4.5b.

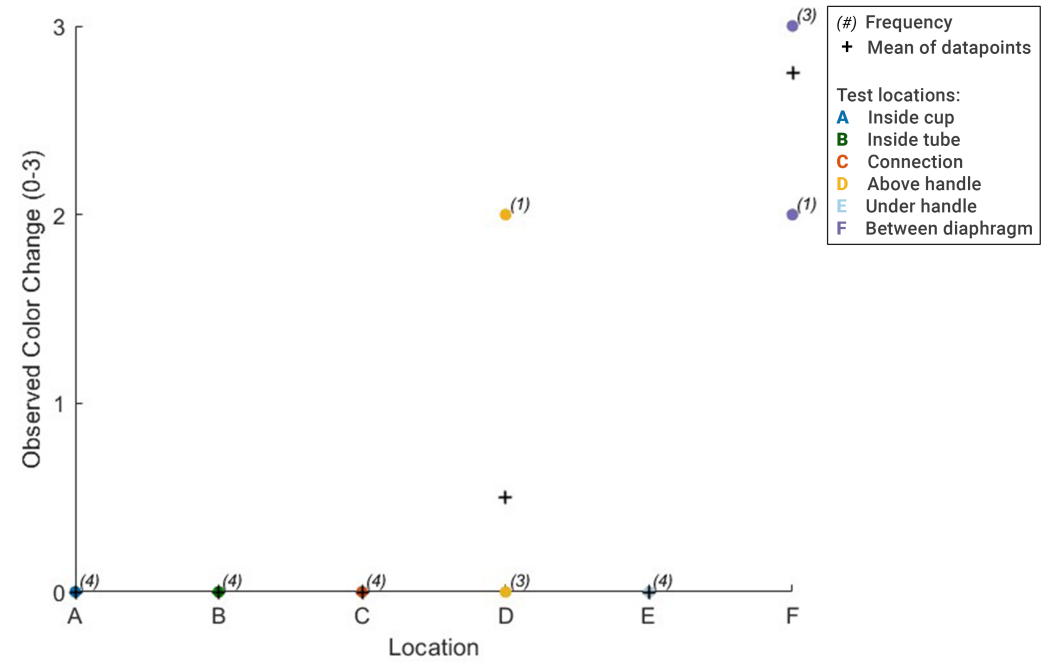
4.2.2 Validation of vela design in the LMIC setting

Clinical simulation tests in the LMIC setting
Scenario 3 entails that, in the LMIC setting, all the different locations are tested seven times with both tests. The outcomes of these experiments have been depicted in a scatterplot, as shown in Figure 4.6.

The results of these tests show considerable variation, even when comparing the location of the ATP test to the protein test. In the ATP test, data points above the predetermined threshold were observed at the connection, under the head of the handle, and between the stem and diaphragm (Locations C, E, and F). However, all the average scores, marked with a "+", remain below the predetermined threshold, as shown in Figure 4.6a. In the protein test, data points above zero were detected at the connection, above and under the head of the handle and between the stem and diaphragm (Location C, D, E, F). However, only the averages, marked with a "+", of the connection and on top of the head of the handle (Location C and D) exhibit a higher value, as depicted in Figure 4.6b. In both tests, the inside of the cup and the tube (Locations A and B) remained below the predetermined threshold.

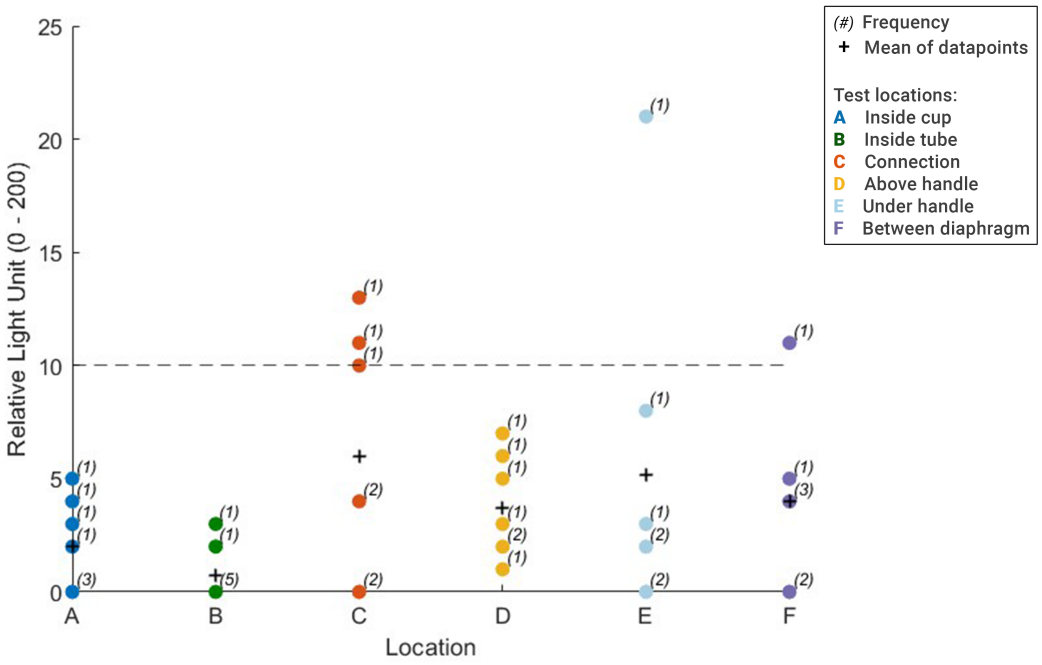


(a) Scatter plot for the ATP test results in the HIC setting. The Y-axis represents the degree of contamination in RLU, with a dotted line indicating the threshold value at 10 RLU.

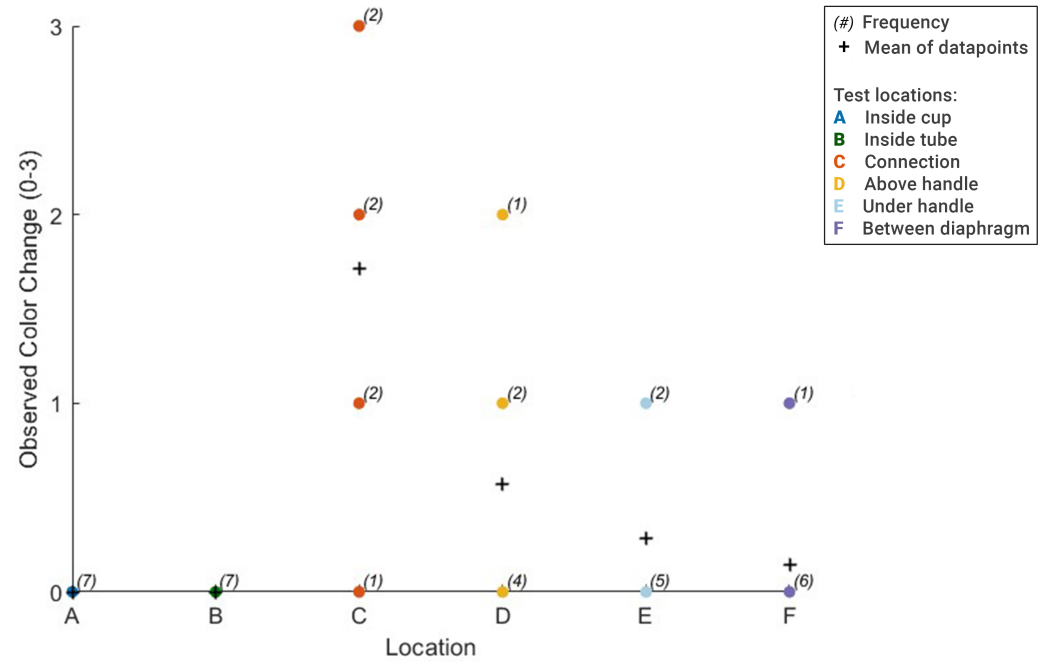


(b) Scatter plot for the protein test results in the HIC setting. The Y-axis represents the degree of contamination in observed color change on a scale of 0-3.

Fig. 4.5.: Test results for the design validation tested in the HIC setting. The Y-axis represents the degree of contamination. The X-axis displays the specific location. The frequency of occurrence is indicated in italics above each data point. The "+" symbol indicates the average score per location.



(a) Scatter plot for the ATP test results in the LMIC setting. The Y-axis represents the degree of contamination in RLU, with a dotted line indicating the threshold value at 10 RLU.



(b) Scatter plot for the protein test results in the LMIC setting. The Y-axis represents the degree of contamination in observed color change on a scale of 0-3.

Fig. 4.6.: Test results for the design validation tested in the LMIC setting. The Y-axis represents the degree of contamination. The X-axis displays the specific location. The frequency of occurrence is indicated in italics above each data point. The "+" symbol indicates the average score per location.

Layman's test

The results of Layman's test are presented in Figure 4.7. Ten test subjects participated in this test. For each location, the three categories add up to 100%.

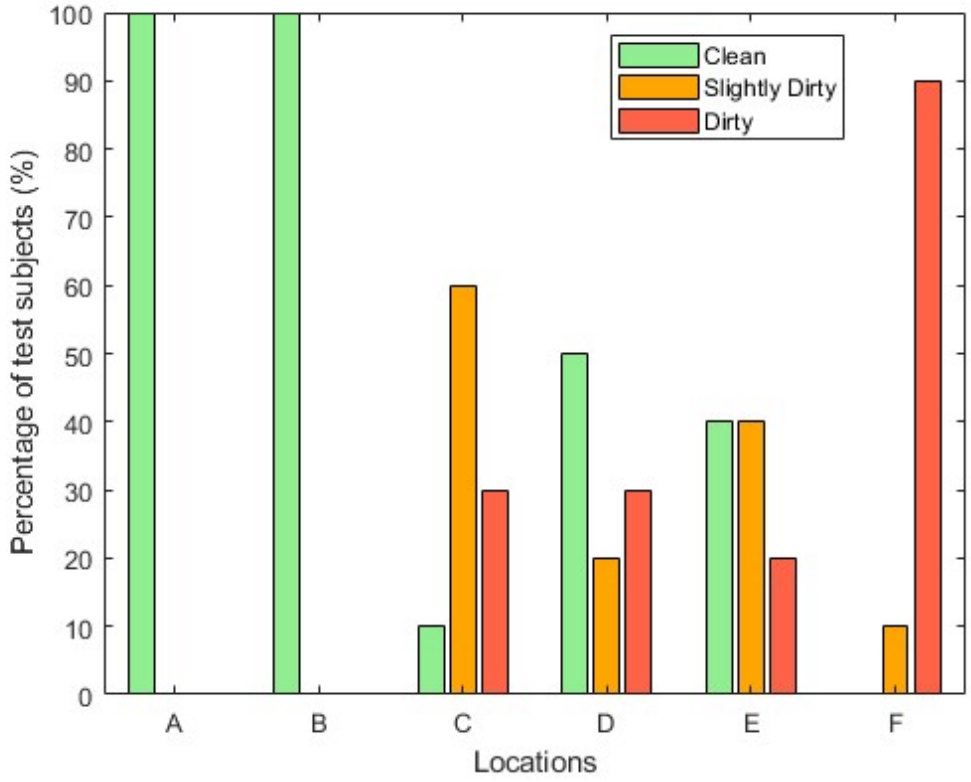


Fig. 4.7.: Bar chart displaying results of the manual cleaning by users unfamiliar with vela®. The Y-axis shows the number of test subjects per category in %. The three categories for each location add up to 100%. On the X-axis, the six locations are indicated (A: Inside the cup, B: Inside the tube, C: Connection for the handle to the tube, D: Above the head of the handle, E: Under the head of the handle, F: Between the diaphragm).

Table 4.1 presents the mean scores for all the locations to provide a more precise understanding of the outcome. The inside of the cup and tube (Location A and B) remain completely clean. Conversely, the location between the stem and diaphragm (Location F) appears dirty. However, the locations at the connection for the handle to the tube and above and under the head of the handle (Locations C, D, E) do not have uniform results. Table 4.1 shows the average scores, in which 0 = clean, 0.5 = slightly dirty, and 1 = dirty. It demonstrates that the connection (Location C) is the least cleaned, whereas above and under the head of the handle (Locations D and E) have a lower average.

Tab. 4.1.: Average cleanliness scores of the layman's test for the six locations.

	Loc. A	**Loc. B**	**Loc. C**	**Loc. D**	**Loc. E**	**Loc. F**
Mean score	0.0	0.0	0.6	0.4	0.4	1.0

4.3 Discussion

In this chapter, the findings of validating the design in the HIC and LMIC settings are discussed, ultimately converging into combined outcomes, as these findings must ultimately be synthesized in one design of vela®. Furthermore, limitations are addressed, and future recommendations are provided, including suggestions for design changes.

4.3.1 Findings

Below, the findings from both settings are discussed. Ultimately, these findings should be processed in one redesign.

4.3.1.1 Findings in the HIC setting

When examining the graphs in Figure 4.5 of the *Clinical simulation tests*, it appears that in the ATP test, only the location between the stem and diaphragm (Location F) was not sufficiently cleaned. These results are consistent with the findings of the protein tests. However, for the protein test, one of the data points from above the head of the handle (Location D) also indicates a lack of thorough cleanliness. Identifying the specific vela® in which these results were obtained reveals that this particular vela® exhibited a minor inaccuracy in its surface, which went unnoticed during post-processing. This inaccuracy in the surface could potentially account for the outlier observed. The fact that the space between the diaphragm does not get adequately cleaned can be explained by the tight fit between the silicone diaphragm and the hard plastic component in this area, as the diaphragm with stem (Part 4) shows in Figure 4.1. This location is challenging for a washer-disinfector to access and clean effectively. Therefore, it requires a redesign.

4.3.1.2 Findings in the LMIC setting

The *Clinical simulation tests* performed in the LMIC setting give less uniform results. In the ATP and protein tests, multiple data points exceed the threshold at the connection (Location C), implying that careful attention should be directed toward this location. On the other hand, the space between the diaphragm (Location F) has been cleaned more effectively; however, it should be noted that the individual conducting the tests was aware of which locations were being tested. Additionally, some data points and averages from above and under the head of the handle (Locations D and E) seem elevated, but most data remains within acceptable limits. Therefore, this may not pose a significant concern. In the protein test, only the data points gathered from the connection and above the head of the handle (Location C and D) indeed exhibit higher averages.

In the *Layman's tests*, the test subjects were unaware of the difficult-to-clean locations. Combined with the *Clinical simulation test* results, this provides valuable insights into which areas may

require redesign. Visual inspection shows that the inside of the cup and tube (Location A and B) consistently remain clean. The combination of the results from the *Clinical simulation test* and this test leads to the conclusion that these locations are cleanable. The space between the diaphragm (Location F) consistently appears dirty, indicating that a redesign may be necessary, as this location is challenging to clean for people unfamiliar with the device. The locations above and under the head of the handle (Locations D and E) present a borderline case, yielding varying results in the *Clinical simulation tests* and the *Layman's test*. One possible reason for this variability could be insufficient caution in cleaning due to a lack of attention or awareness regarding the presence of cavities. Nevertheless, with clear instructions in the IFU, these areas should no longer pose a problem [17]. The connection (Location C) presents challenges because the two subparts must be cleaned as one part, making it difficult to access between them. A redesign or clear instructions would likely be helpful in this case. In summary, the connection and the space between the diaphragm require a redesign.

4.3.1.3 Combined findings

Conducting these tests has revealed the specific locations of concern of vela® within each setting. Considering the results from both the tests conducted in the HIC and LMIC settings, it is advisable, in both cases, to consider a redesign that minimizes the space between the stem and diaphragm (Location F). Furthermore, when examining the LMIC tests, it is also recommended to consider a redesign for the connection (Location C). Inside the cup and the tube appear to pose no issues in both settings (Location A and B). As for the locations above and under the head of the handle (Location D and E), clear indications and cleaning instructions should be included in the IFU.

4.3.2 Limitations

Three main limitations of this project are discussed below.

Generalizing from a single country
In the study, the Netherlands was selected to represent the HIC setting, and Kenya was chosen as the representative of the LMIC setting. This generalization, however, may be considered somewhat oversimplified, as a single country may not comprehensively represent an entire group of countries. Nevertheless, this approach was adopted to enhance the specificity of the research, facilitating a more focused and practical examination.

LIMIC focus
Given that the primary focus of vela® is to enhance the availability of medical equipment in LMICs, it is a limitation that the product has not been tested directly in a natural LMIC environment. Despite best efforts to simulate these conditions, the results would have been more accurate if the testing had been conducted in a natural LMIC setting with the inclusion of local participants.

Sample size
Due to a combination of the current stage of the design of vela® and the associated costs associated with the tests, a decision was made regarding the number of tests purchased, resulting in a final generated dataset that is limited in size. Although descriptive statistics were used to draw conclusions, the data could not be further analyzed as none of the analyzed locations yielded statistical significance, as detailed in Appendix J.

4.3.3 Future research and recommendations

4.3.3.1 Design changes

For both the connection (Location C) and the space between the stem and diaphragm (Location F), it is beneficial to consider a redesign to facilitate the cleaning process. Below, a more in-depth examination of this recommendation is provided. Additionally, as suggested in a study by Branaghan et al. (2021) [17], it is advisable to make vela® transparent. This modification would improve the lumens' visibility, simplifying the manual cleaning process.

Redesign for the connection
In the case of the connection, the fact that the two subparts cannot be separated in combination with numerous protuberances and cavities results in potential oversights during manual cleaning. Therefore, it would be advantageous to reconfigure this section, allowing the subparts to be easily detachable during the cleaning process, as described in Figure 4.2. Additionally, a simplified design with fewer sharp angles should be considered. Figure 4.8 illustrates a concept for such a redesign, showing both the original design and the redesign and indicating the three main changes with colors.

In the redesign, the two subparts of the connection can easily slide in and out of each other due to the removal of the widening at the sides of Subpart 2, as shown in green in Figure 4.8. Because these parts can be easily detached during cleaning, facilitating a more visual inspection, thereby contributing to the ease of cleaning the corners [17]. In addition, this design change ensures that the tensile force applied to the tube during use is the same as before the redesign, ensuring the integrity of vela®'s operation.

Furthermore, since these subparts are disassembled for cleaning, Subpart 2 must be reassembled correctly after cleaning. First, the hole of Subpart 1 and the shape of Subpart 2 are engineered to ensure only one-way insertion, eliminating the need for orientation consideration, as shown in yellow in Figure 4.8. Second, Subpart 1 is designed symmetrically to allow Subpart 2 to be inserted from either side, as shown in blue in Figure 4.8. Last, both subparts have been simplified and rounded in design to reduce the likelihood of debris accumulation. These modifications are shown in Figure 4.8.

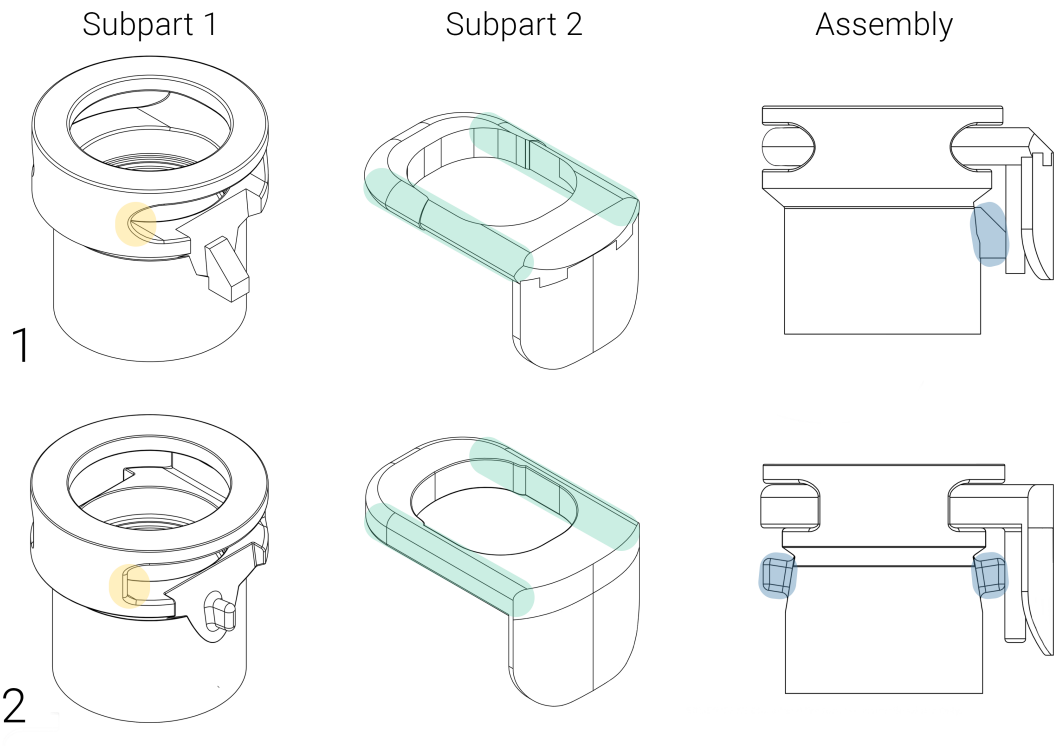


Fig. 4.8.: Redesign of the connection. 1: The old design of the connection. 2: The redesign of the connection. In both illustrations, the designs are shown separately and assembled. The green color indicates the change in widening; this has been removed in the redesign, making it easy to disassemble the subparts. The yellow part shows the change for reassembly; only one-way reassembly is possible in the redesign. The blue part makes subpart 1 symmetrical, and thus, the redesign cannot be inserted incorrectly.

Redesign for the space between the diaphragm

For the space between the stem and diaphragm, the challenge lies in accessing the space between the hard plastic component and the flexible silicone diaphragm. One potential solution for this issue is employing a two-component (2k) injection molding technique for this part. 2k injection molding is a technique that blends two distinct plastic materials within a single product [60]. This can be advantageous because the membrane and stem can be produced as one seamless part (see Part 4 in Figure 4.1). Which prevents the accumulation of dirt between the two materials, given that they are one unified part.

4.3.3.2 Method optimization

From both a sustainability and accessibility perspective, it appears more advantageous to transition from the prevalent single-use equipment to reusable devices [8, 10–14]. Reusable medical devices need to be designed with ease of cleaning in mind, an aspect often overlooked in discussions of reusability [17]. Consequently, exploring testing methodologies that focus on these considerations, as exemplified here, becomes particularly intriguing. This process, in turn, offers potential for optimization. Therefore, further refining this process is of interest, allowing manufacturers to conduct validation studies conveniently in the future.

4.4 Conclusion

This research aimed to investigate the potential of the design of vela® as a reusable vacuum extractor, focusing on validating the cleaning step. The material validation determined the choice of material for vela®, and in this chapter, the design of vela® was subjected to validation. This validation was conducted in a HIC and a LMIC setting. Conclusions were drawn by identifying the six most critical locations of the device and testing these locations. In the HIC setting, vela® demonstrated satisfactory cleanability at all locations, except for the space between the stem and diaphragm. In the LMIC setting, vela® exhibited good cleanability at all locations, except for the connection and the space between the diaphragm, with the condition that the cleaning procedure is clearly outlined in the IFU. As a result, a redesign was proposed for the connection, and the production method 2k injection molding was recommended for the diaphragm. With these modifications, it appears that vela® can be safely reprocessed in both the HIC and LMIC settings.

5 Overall conclusion

This research aims to answer the question: '*Can vela® function as a reusable vacuum extractor, focusing on its cleanability?*'.

In this phase, it is premature to manufacture a PPSU injection-molded vela® due to the associated time and costs of producing molds for the injection molding process. Therefore, the research is divided into a materials validation, focusing on test objects made of different materials, and a design validation, focusing on the design of vela®.

Clinical simulation tests are performed for both validations to understand the cleanability of the materials and the vela® design. Additional tests were included in both validations to answer the question as comprehensively as possible.

In the material validation, PPSU proves to be a suitable material for vela®, but at present, vela® lacks the resources, both in terms of cost and time, to undergo injection molding in PPSU. Consequently, to validate the reusability of vela®, it becomes imperative to identify a suitable 3D printing prototype material to assess its cleanability. Therefore, after analysis, T2R is considered suitable as a prototype material.

Furthermore, for the design validation, design-related improvements are needed. This emerged in the HIC and LMIC tested settings. However, these aspects will be collectively addressed, considering they must ultimately be synthesized in one design of vela®. By redesigning the connection of vela®, it can be easily disassembled for improved cleaning. By 2k injection molding the silicone diaphragm and hard plastic stem, there will be no room for contamination between the two materials. When incorporating these suggestions into the design, it can be concluded that a PPSU injection molded vela® can be safely cleaned and thus reused in both HICs and LMICs, contributing to the sustainability and accessibility of medical devices.

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Appendix

Literature review

A

This literature review has already been graded by the supervisors.

The following pages contain the literature review 'Exploring Validation Tests for Assessing the Cleanliness of Reprocessed Medical Devices'.

Exploring Validation Tests for Assessing the Cleanliness of Reprocessed Medical Devices

A Systematic Review

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July, 2023

Abstract

Introduction: The healthcare industry is shifting towards reusable medical devices to improve sustainability in general and provide accessibility in Low- and Middle-Income Countries. These devices must be reprocessed. Therefore, validation tests are necessary to ensure effective reprocessing. By strategically integrating these tests during the prototype phase, improvements in the final device design are achieved through the enhancement of cleanability. However, variations arise due to the utilisation of different production methods for prototypes (e.g. 3D printing) and final products (e.g. injection moulding), leading to differences in materials, surfaces, and porosities. The original objective focused on prototypes, but limited literature led this review to focus on reusable medical devices in general. This review aims to research which reprocessing tests are appropriate to validate the cleanliness of a reprocessed medical device.

Methods: Following the PRISMA guidelines, a systemic review was performed using Scopus and Medline databases. The articles were reviewed, and based on eligibility criteria, articles were included in the review.

Results: The systematic review examined a total of 455 articles, out of which 27 articles were included in the study, resulting in the analysis of fourteen different tests. Firstly, all the tests mentioned in the various articles were categorised based on their test type, instrument, instrument material, contaminant type, test moment in the reprocessing cycle, and the testing environment. Secondly, the tests were evaluated and compared using five key features: ease of use, precise localisation of the contamination site, specificity in identifying the type of contaminant, result reliability, and the time required to perform the test and obtain the results. After this comparison, the ATP, culture-based, fluorescence-based, and protein swab tests were identified as the most suitable options.

Conclusion: The tests mentioned above have certain limitations, but they are worth considering when evaluating cleanliness. Ultimately, these tests should be performed on a prototype, offering design insights before making the final medical device. In future studies, it is necessary to determine whether the results of a test performed on the prototype accurately reflect the results of the final product or whether there are differences between the two that must be addressed.

List of Abbreviations

ACC	Aerobic Colony Count
ATP	Adenosine Triphosphate
BCA	Bicinchoninic Acid
HAI	Healthcare-Associated Infection
LBT	Luminescent Bacteria Test
LMIC	Low- and Middle-Income Country
MRSA	Meticillin-Resistant Staphylococcus Aureus
OPA	Ortho-Phthalaldehyde
RUST	Rapid Use Scope Test
SUD	Single-Use Device
TOC	Total Organic Carbon

I. Introduction

A. The importance of reusable medical devices

In the past, most medical devices were (designed to be) reused multiple times. Due to concerns regarding safety, ease of use, and cleaning costs, the healthcare industry switched to utilising more and more single-use devices (SUDs). However, returning to reusable medical devices is relevant for sustainability and access to healthcare [1], [2]. Replacing SUDs with reusable medical devices will reduce environmental impact. According to a recent systemic review by Keil et al. (2023), this will positively affect 39 of the 40 measured aspects (e.g., acidification, global warming potential and ozone depletion); water use is the only aspect negatively impacted. Therefore, switching to reusable medical devices is worthwhile [3]. Secondly, reusable medical devices will provide better healthcare for Low- and Middle-Income Countries (LMICs) than SUDs. Due to economic constraints, it is unavoidable for LMICs to reuse SUDs, which imposes a risk of infection [2]. For this reason, medical devices with extended life cycles provide more efficient healthcare for people in LMICs [4].

B. The principle of reprocessing

The reuse of medical devices also implicates the need to "reprocess" the devices. According to the European Commission: "*'Reprocessing' refers to a process carried out on a used device in order to allow its safe reuse. It includes its cleaning, disinfection, sterilisation and related procedures, [...].*" [5]. During usage, a medical device becomes contaminated. Contamination refers to the presence of harmful, potentially infectious, or unwanted matter on inanimate objects or living material. When this device is reprocessed, it will be decontaminated [6]. The decontamination life cycle embodies the entire process of use to reprocessing and storage. This cycle is displayed in Figure 1.

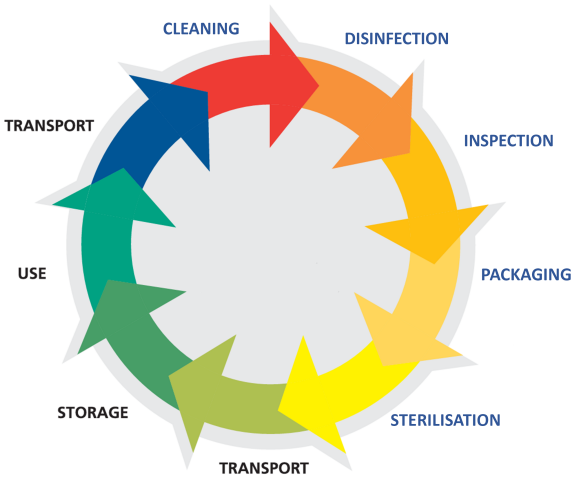

Fig. 1: The decontamination life cycle of reusable medical devices. In blue, the reprocessing steps within the cycle are indicated (adapted image [6]).

Reprocessing is divided into three consecutive steps: cleaning, disinfecting and sterilising. Cleaning is best described as a process of removing unwanted soil [7]. Disinfecting entails a process that eliminates many of all pathogenic microorganisms. Sterilising is a process that destroys all forms of microbial life [8]. The required reprocessing steps depend on the device: cleaning, cleaning & disinfecting or cleaning, disinfecting & sterilising. The higher the risk category, the more thorough the reprocessing process.

Over 50 years ago, in 1968, Dr. E. H. Spaulding developed a guiding classification system for the safe reprocessing of medical devices. This system, based on the risk category of the medical device, shows what steps of reprocessing the medical device needs [9]. Nowadays, this system is still in use. Medical devices are divided into three categories: non-critical use devices, semi-critical use devices and critical use devices. The applicable category determines what step(s) of reprocessing is/are needed [10]. Figure 2 shows the categories with accompanying steps of reprocessing and an example of a medical device.

Risk category	Steps of reprocessing	Examples of medical devices
Non-critical (Low) *Items in contact with intact skin*	Cleaning *(visibly clean)*	Blood pressure cuffs, stethoscopes
Semi-critical (Intermediate) *Items in contact with mucous membranes or body fluids*	Cleaning & Disinfection *(high level)*	Respiratory equipment, non-invasive flexible endoscopes, bedpans, urine bottles
Critical (High) *Items that are involved with a break in the skin or mucous membrane or entering a sterile body cavity*	Cleaning, Disinfection & Sterilisation	Surgical instruments, implants/prostheses, rigid endoscopes, syringes, needles

Fig. 2: Recommended steps of reprocessing according to Spaulding classification (adapted image [6]).

Cleaning is the first step in reprocessing medical devices and is essential across all three categories of reprocessing. Nevertheless, the importance of cleaning is often underestimated. However, it is crucial to recognise that the failure to perform this step correctly can lead to subsequent disinfection and sterilisation failures [10]–[15]. For example, if protein contamination is not removed from the instrument during cleaning, the protein contamination may adhere to the surface during subsequent disinfection and sterilisation instead of detaching [16].

C. Cleanability of medical device prototypes

Information on its cleanability must be gained during the development of a medical device. The FDA requires manufacturers of medical devices to validate cleaning instructions to demonstrate the successful cleanliness of a device [17], [18]. The manufacturers must demonstrate to users that the device is cleanable and document the suitable equipment for correctly reprocessing the device [19]. Performing the first cleaning tests on a prototype before finalisation offers advantages. It allows for more convenient design changes to enhance reprocessing compared to conducting tests on the final product, which requires full production. Prototyping typically uses 3D printing, an additive manufacturing technique [20], [21]. A study by Fleisher et al. (2020) demonstrated that using a 3D-printed medical device alters the product's mechanical properties due to the 3D printing process and the disinfection [22]. Hence, within this context, the prototype serves purely as an indication of the device's cleanability, emphasising its non-medical application. Beyond the difference in mechanical properties, there exist additional differences between a 3D-printed prototype and the final product [21]. The choice of production method is the primary factor distinguishing a prototype from a final medical device, often created through injection moulding. This results in notable differences between the two. Using a different production method leads to using different materials due to the need to process specific materials [20]. Furthermore, it leads to variations in the characteristics of the surface finish and differences in porosity. These factors may affect the cleanability of the prototype.

D. Different contaminants and tests

After using a device, contaminants are left behind on the device. What and how many contaminants are left behind depends on where in the body the device is used [23]. The medical device needs to be decontaminated and thus reprocessed. Insufficient reprocessing can result in adverse patient outcomes, including tissue irritation caused by residual reprocessing materials such as chemical disinfectants. Additionally, insufficient cleaning can lead to the accumulation of blood, tissue, and other biological debris. Such debris can enable the survival of microorganisms, potentially leading to Healthcare-Associated Infections (HAIs) [24].

Multiple tests and methods exist to determine whether reprocessing is executed correctly, each having pros and cons; the best practice within the industry has yet to be established [25]. Since the main focus is specifically on the cleaning step of reprocessing, the study entailed investigations into official cleaning validations [26], [27]. Furthermore, due to the high probability of encountering residual proteins on medical devices during usage, protein testing becomes noteworthy to incorporate into the research for a comprehensive assessment of cleanliness [28]. In addition, various tests for evaluating cleanliness post-cleaning were examined, including Adenosine Triphosphate (ATP) tests, microbiological culture tests, and chemical reagent tests such as protein, carbohydrate, and haemoglobin detection [13]. ATP testing also offers intriguing characteristics. The detection of ATP indirectly indicates organic matter and microbiological contamination. This method, successfully applied in the food industry for over three decades, is now finding relevance in the health industry [29]. This review explores various tests used to evaluate cleanliness in the context of medical device reprocessing.

E. Objective

Initially, the study aimed to review existing literature on conducting tests on prototypes to gain early-stage insights into both design and cleanability of the device. The mentioned prototype is not for medical use. However, due to the scarcity of literature on prototypes, the original objective was adjusted to focus on tests of medical devices in general. This study analyses and compares the tests, identifies limitations and literature gaps, and provides recommendations for future research.

In the end, this systematic review aims to answer the following research question: *What are the most appropriate tests to validate the cleanliness of a reprocessed medical device?*

II. Methods

This review was conducted following the guidelines written down by Page et al. (2021) concerning the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [30]. This section explains the methodology for the information collection, information selection, and data collection process.

A. Information sources

The articles used for this literature search were exported from the Scopus and Medline databases, which are bibliographic databases used for academic research. On April 19 2023, the final search run was performed.

B. Search strategy

A systematic and efficient search strategy was developed to conduct the search. An iterative process was followed in which the final search terms were defined utilising a framework provided by the TU Delft library [31]. Through this process, three concepts were defined. These concepts were: "cleaning", "tests", and "medical device".

Terms and synonyms were assigned to the different concepts. The search terms were fine-tuned by adding "AND", "OR", and proximity operators. During this iterative process, the terms were adjusted until the final search terms were determined. Table I shows the search terms per concept, including an explanation of the used operators.

For the concepts "cleaning" and "medical device", appropriate synonyms were added to the final search string. Subsequently, to narrow the search and enhance the review's focus, the concept of "tests" was concretised, allowing for a more targeted and precise examination of relevant tests specifically related to validating proper cleaning. In pursuit of this goal, the initial inspiration was drawn from official cleaning validations as a credible and reliable source of information for the selection of appropriate tests. In official tests for validating proper cleaning, the following five analytes are often taken as key starting points: Protein, Carbohydrate, Hemoglobin, ATP, and Total Organic Carbon (TOC) [26]. Therefore, these five terms were added to the search. To emphasise the importance of protein testing, two additional tests, namely "Bicinchoninic acid" and "Fluorescent," were included, as they specifically target protein detection [28]. Furthermore, microbial controls play a critical role in evaluating cleaning and disinfection procedures for medical devices. They help in detecting process failures and surface irregularities that can lead to microorganism persistence on reusable medical devices [32]. Thus, the broader term "microbial" was also added to encompass a wider range of articles related to microbiological aspects. Additionally, the search terms were expanded to include the "Aerobic Colony Count (ACC)" method, which is a relevant test for assessing microbial contamination levels on medical devices after cleaning [33]. Lastly, the search terms were expanded to include "Soil", considering the recommendation of cleaning experts who commonly employ soil testing in testing procedures.

Consequently, this resulted in a comprehensive compilation of tests. The final list of tests is described in the column "Tests" in Table I.

Furthermore, only articles from the year 2000 onwards were included. Appendix A displays the final search strings, including the used operators.

TABLE I
Different synonyms and terms for the three defined concepts

	Cleaning	Tests		Medical device	
Search terms	Cleaning	Adenosine triphosphate	Assay	Medical	Apparatus
	Washing	Aerobic colony count	Marker	Surgical	Device
		Bicinchoninic acid	Method		Instrument
		Carbohydrate	Test		Mechanism
		Fluorescent			Prototype
		Haemoglobin			Tool
		Microbial			
		Protein			
		Soil			
		Total organic carbon			

The different concepts are connected by the operator "AND".
The words within the concepts were combined with the operator "OR".
The words within the concepts before and after the dashed line were combined with the proximity operator.

C. Eligibility criteria

After obtaining the articles from Scopus and Medline, the duplicate articles were removed. Hereafter, all articles were thoroughly reviewed, taking into account the established inclusion and exclusion criteria.

Articles were included if the title and abstract:

- Described the cleaning of a medical device/healthcare product.
- Described one or multiple test(s) that validated the cleanliness of a medical device/healthcare product.
- Was performed after 2000.
- Is written in English.

Articles were excluded if the title and abstract described:

- The functioning of the cleaning equipment.
- The validation of a specific cleaning detergent.
- The effectiveness of changes in the reprocessing procedure or changes in the design of the medical device.

After reading the title and abstract of the articles, the full text of the articles was screened.

Articles were included based on the above inclusion criteria, and the full text had to describe a clearly documented and repeatable study.

Articles were excluded based on the above exclusion criteria and if there was no full text available.

The articles that remained after this selection were included in the analysis of this review.

D. Selection process

All articles were transferred to EndNote, in which the articles were analysed on different levels. Per level, a new library was created. In the first library, all the articles were collected. After that, the duplicates were removed. Then, using the inclusion and exclusion criteria, the articles were screened at two levels; title & abstract and full text. The final library contained all the articles used for this review. This library also included articles added via snowballing.

E. Data collection process

From the articles present in the final library, relevant information was extracted. This information was transferred from EndNote to a MS Excel spreadsheet. In addition, the validated tests were grouped, and relevant information per test was gathered and summarised in a MS Excel spreadsheet.

III. Results

This section gives a brief overview of the study selection, followed by an analysis of the results providing an overview of the different articles and an overview of the different tests.

A. Study selection

In this literature study, 531 scientific articles were extracted from the databases, of which 325 were extracted from Scopus, and 206 were extracted from Medline. First, the duplicates were removed (n=19), leaving 512 articles. Second, the titles and abstracts were reviewed. Through the eligibility criteria described in Section II-C, 441 articles were removed, leaving 71 articles. Third, the full text of the remaining articles was read. Using the eligibility criteria in Section II-C, 46 articles were removed, leaving 25 articles in total. An additional search was conducted by systematically reviewing the references of relevant articles, which yielded two additional articles. Therefore, a total of 27 articles were comprehensively reviewed. Figure 3 presents a flowchart of this process.

B. Analysis

This section presents the data collected from the articles through text and comparison tables. In the first part, Section III-B1, an overview of the tests was created using information

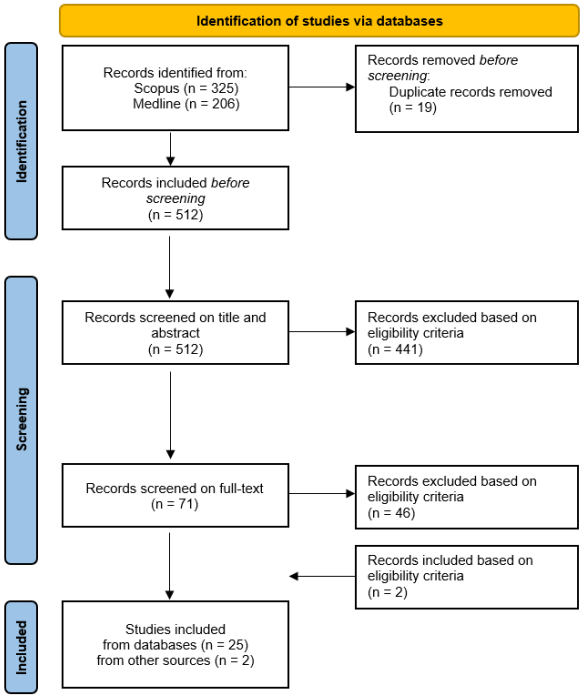

Fig. 3: PRISMA flowchart customised to this review [30].

gathered from the different articles, as presented in Table II. The second part, Section III-B2, focused on comparing the different tests, as illustrated in Table III.

1) Overview of the different tests: Table II provides a comprehensive overview of individual tests analysed in the articles. The categorisation of each test is based on its fundamental working principle, enabling the grouping of tests that share similar principles, such as the fluorescence-based technique. The table presents specific information from the respective articles. It displays:

- The test performed in the article, sometimes along with essential additional information.
- The instrument that is addressed in the article.
- The material of the instrument.
- The type of contaminant detected per used test, as stated in the article.
- The moment in the reprocessing cycle when the test is performed.
- The setting in which the test is conducted (simulated and/or clinical).
- The reference number of the respective articles.

Below, remarkable features of Table II are discussed.

Test - The mentioned tests are not specific to any particular brand; they represent different types of tests. However, it is important to note that the tests are described in greater detail in certain articles, while others provide more general descriptions. Additionally, a noteworthy observation is that many of the articles validate an ATP test.

Instrument - In many articles, the tests are performed on endoscopic instruments. Furthermore, none of the articles explicitly validates the cleanliness of medical device prototypes.

Material - A considerable number of articles did not provide specific information or lacked retrievable data regarding the instruments' material. Nevertheless, the materials mentioned in the articles predominantly consist of metals or include metals, among other materials.

Type of contaminant - The articles exhibit variations in terminology when describing the types of contaminants, even though they conduct the same test.

When tested in cycle - The tests were conducted at various stages of the reprocessing process, and there were distinctions between manual and automatic cleaning methods. Lichtenstein and Alfa (2019) display the different tests that can be performed in different reprocessing stages. The article highlights several cleaning monitoring tests employed to validate the cleanliness of gastrointestinal endoscopy equipment. It discusses rapid tests performed after cleaning, including those for monitoring organic residuals such as haemoglobin, carbohydrate, protein, and ATP residuals. However, when culture tests are performed to detect microbial contamination of flexible endoscopes, this should be performed after disinfection/sterilisation [18]. This suggests that not all tests can be conducted at the same stage of the reprocessing cycle.

Setting - The tests in the reviewed articles were conducted in diverse locations. In the clinical setting, the tests were performed in real-world hospital environments, while in the simulated setting, they were carried out in controlled laboratory conditions.

2) Comparison of the different tests: Table III compares all the tests discussed in the articles on five features.

The table lists the test type performed and the contaminant it detects, as stated in the articles. The tests are graded on the following five features:

- *Ease of use* - The easiness of performing and interpreting the results.
- *Locating* - The ability to determine the specific place on the medical device that is contaminated.
- *Precision* - The specificity of the test in detecting the type of contaminant.
- *Reliability* - The degree to which the result of the test is reliable.
- *Time* - The time required to test and obtain the results.

These five features are selected based on insights from various articles and input gathered from LAYCO:

- The first feature, ease of use, is supported by findings from various articles. It has been consistently emphasised that the practicality of a testing method is crucial [34]. For instance, it has been highlighted that employing a testing method that requires professionals and extensive equipment can be time-consuming, expensive, and potentially hazardous if not executed by qualified individuals [35].
- Then, locating emerged as a crucial feature based on LAYCO's input. Precisely identifying contamination lo-

cations in the tests conducted facilitated the easy detection of design bottlenecks, enabling necessary modifications to be implemented effectively. By targeting bottlenecks, specific locations can be identified and controlled [23], [25].

- Subsequently, precision emerged as another critical feature. It became evident that the level of precision varies among different tests, with some providing quantitative measurements and assessing the specificity of contaminants. In this context, innovative cleaning assessment tests that combine quantification and accuracy are considered essential [36], [37].
- Next up is reliability, a crucial aspect that surfaced during the research [33]. Ensuring reliable test results is essential, e.g., relying solely on human sensory perception may pose challenges in achieving this reliability [12]. Additionally, it is desirable to avoid the need for repeated test executions solely to establish reliable results [17].
- Finally, the time it takes to conduct the test and obtain the results is also of significant importance [33]. The research conducted by Alfa et al. (2012) specifically targeted reprocessing personnel and revealed that timely assessment is highly valued in environments where swift progress is necessary [15]. Furthermore, this timing indicates the potential speed at which the design can be adopted.

All the tests are rated on a grading scale per feature: "- -" = poor, "-" = fair, "+" = good, "+ +" = excellent, "x" is used when this feature is not specified in the articles and "xx" is used when articles are contradictory about this feature. Appendix B elaborates the reasoning behind the evaluation of the various tests in Table III.

Below, the various tests and their scores are discussed.

Aerobic colony count (ACC) method - The ACC method measures the actual bacterial load [33]. It quantitatively measures surface contamination by aerobic microorganisms and identifies surface contaminants that may not be immediately evident [38]. The ACC method involves taking a sample, typically by swabbing a specific location [33], [39]. Despite this exact localisation of the contamination site, it is time-consuming for frequent use and requires microbiology laboratory support [33], [38].

ATP test - This rapid indicator measures the amount of ATP using a swab. The device is swabbed on a specific spot, and the swab is mixed with a reagent that reacts with any ATP present, creating light. This light is measured using a luminometer. The more light produced, the more ATP and thus more organic material is present [37]. The ATP test has been subject to controversy. Different brands use different scales, making the measurement scale relative [40]. Some articles defined it as a not suited test for cleanliness control [13], [35], [41]–[43]. Given the varying perspectives on the test's reliability, Whiteley et al. (2022) found that incorporating a Cleaning Intervention Step, which involves adding a cleaning step, with the Simplified ATP test appears to offer a more reliable method [40]. Furthermore, the updated Association for the Advancement of Medical Instrumentation guideline for "flexible and semi-rigid endoscope processing in health care facilities" included ATP as one of the markers helpful in benchmarking the cleaning process [34].

Bicinchoninic acid (BCA) method - The BCA method is used to detect proteins [44]. In this method, the cleaned device is submerged in the BCA solution, and any proteins present will react with the solution, causing a noticeable colour change. The intensity of the resulting colour is measured using a spectrophotometer, which indicates the protein concentration [45]. While the BCA method is precise and capable of detecting all proteins, it does have a drawback: it requires a high-tech device to measure the colour change. This reliance on high-tech equipment makes the method less user-friendly [17].

Culture-based method - This test method relies on a broader approach. It involves cultivating microorganisms from the medical device on an agar plate or similar medium, allowing for the enumeration of microbial colonies. This method uses a pre-moistened polyester tip to swab a designated location on the device, facilitating accurate identification of the contamination site [35]. Nevertheless, cultures can be costly and require specific skills to be executed and interpreted accurately. They also rely on access to a microbiology laboratory and can take 1 to 2 days to obtain results [12], [25], [34], [35].

Fluorescence-based technique - The fluorescence-based technique relies on a common principle: using a reagent that binds to proteins, causing specific locations on the device to emit fluorescence when exposed to ultraviolet light. There are multiple approaches to achieve this; however, in this case, the focus is on the marker method [33], [38]. The test involves treating the cleaned device with the reagent and examining it under ultraviolet light, such as a portable black light. Any fluorescence observed is indicative of protein residues [46]. It is important to note that this method does not directly measure the cleanliness of surfaces. Instead, it visually confirms the physical removal of the applied substance by detecting residual fluorescence. Furthermore, this method does not provide data on the bioburden [33], [38]. For specific molecules, labelling of the molecules is required before they can be detected using this method [17]. Fluorescent marker systems offer several advantages, including simplicity, reliability, real-time assessment, and minimal equipment requirements [33], [38].

Haemoglobin assay - Haemoglobin assays detect the presence of blood residues on the device. This rapid and straightforward test utilises colourimetric blood test strips with nanogram sensitivity, which are read using a microplate reader. The procedure involves preparing microplates with modified blood test strips. The known device surface area is extracted using a specialised device and applied to the pad on the test strips. The measurement was conducted using a plate reader. Depending on the accuracy needed, multiple tests may be necessary [17].

Luminescent Bacteria Test (LBT) Method - The LBT method, also known as the Microtox test, is a rapid and sensitive bioassay used to assess a sample's toxicity or specific contaminants' presence. The LBT method can detect a wide

range of contaminants, but in this article, it is used to detect residual chemicals [47]. However, it is worth noting that information about the test's working principle is limited.

Meticillin-Resistant Staphylococcus Aureus (MRSA) detection - MRSA, a healthcare-associated pathogen, is a critical target for detection to reduce the risk of HAIs. The isolation of MRSA from the environment involves using saline-moistened cotton swabs. Following incubation and subculturing, colonies resembling MRSA are confirmed using standard microbiology methods, including coagulase testing and resistance confirmation [39]. The procedure is time-consuming and requires expertise; however, it effectively detects this specific type of contaminant.

Ortho-Phthalaldehyde (OPA) Method - The OPA method involves using OPA, a high-level disinfectant that creates a fluorescent substance by reacting with proteins. This fluorescence can be measured, with higher levels indicating more protein residue. The method is highly sensitive, but the high sensitivity of the OPA assay increases its susceptibility to accidental contamination, such as residual protein from the hands of those handling the test samples [48]. The OPA method provides a qualitative analysis, offering insights into identifying common contaminants that need removal [16]. In the modified OPA method, "modified" refers to specific alterations made to the standard OPA procedure [44].

Protein swab test - A protein swab test is a broad term used to describe a rapid indicator test. A swap is taken from the instrument on a specific location and tested for total protein presence [49]. The test results are indicated by a colour-changing solution [23]. The surface protein tests are easy to perform and have a 15-minute waiting time but have difficult comparisons with colour blocks [12]. The working principles of various protein swab tests can vary, but the overall testing procedure remains consistent across these tests.

Rapid bacteria test - The rapid bacteria test used in this study detects gram-negative bacteria. It provides quick results, and the test involves incubation and using a fluorometer to detect the presence of viable gram-negative bacteria. The minimum time to obtain a result is 12 hours. This study utilised the test for channel flush samples, but further research is necessary to validate its effectiveness and applicability [25].

Test strip system - The test strip system is a rapid indicator capable of detecting various types of contaminants. In the articles, these tests detect substances such as blood, protein, and carbohydrates [12], [15], [50]. The Rapid Use Scope Test (RUST) is a specific example of such a test strip [15]. For this test, sterile water is introduced into the lumen of the instrument and then collected in a sample cup [50]. A chemically treated strip is then immersed into this solution. The strip will change colour if the specific substance it tests for is present; this type of indication differs per test. The type of substance detected depends on the specific test used. Their simplicity, affordability and speed characterise this type of test [12], [15], [50]. Moreover, they do not leave any residue on the device. However, using fluid samples in these tests make it less specific for localising the contamination site. Additionally, the interpretation of colour changes poses a challenge because they are difficult to distinguish [12]. Furthermore, it exclusively identifies organic components and does not offer insights into the quantity of residual viable microorganisms [15].

TOC Method - The TOC method is a highly sensitive, non-specific analytical technique commonly used to detect carbon-containing compounds in environmental samples [36]. This method involves taking a swab from the device, which is then thoroughly mixed with a solution and subsequently examined. Since the TOC method is not based on living organisms, it tends to exhibit less variability in the results [47]. Additionally, TOC methods offer several advantages over conventional methods, including faster analysis, simplified procedures, and easier development of analytical methods [36].

Visual inspection - Visual inspection can be performed using a tool such as a borescope or magnifying glasses to examine the instrument's surface and detect visible contaminants [23], [43]. It is an easy and feasible method. Nonetheless, this method is limited to detecting contaminants greater than 50 micrograms on the instrument's surface or in superficial locations. Observing contaminants that are scattered, minor, or located within the lumen of the instrument poses challenges in this method [43], [51]. Furthermore, visual inspection is sometimes used as the sole means for evaluating the effectiveness of the cleaning process, which is shown to be ineffective [12], [43], [48].

The different tests encounter different contaminants; some are more specific than others, such as the OPA method, detecting proteins, compared to the TOC method, detecting organic carbon content. Others cover different types of contamination, such as the ACC method, detecting aerobic microorganisms, compared to MRSA detection, detecting MRSA bacteria.

Five of the fourteen tests in Table III directly detect protein. Protein is supposed to be a helpful marker [25]. There are very few exceptions in which a medical device will not encounter proteins; performing a test that detects proteins is valuable [28]. Nevertheless, studies have shown that cleaning validation studies should not solely focus on protein but attempt to test other contaminants as well [15].

TABLE II
Study characteristics of included studies*

Test	Instrument	Material	Type of contamination**	When tested in cycle**	Setting	Ref.
ACC method	High-touch surfaces	x	Aerobic microorganisms	Before and after cleaning	Clinical	[38]
	High-touch surfaces	x	Actual bacterial load	After terminal cleaning	Clinical	[33]
	Hospital surfaces	x	Bacteria	Before and after cleaning	Clinical	[39]
ATP test	Suction tip	Metal	Signature compound of all living cells	Before cleaning, after manual, and mechanical cleaning	Clinical	[50]
	High-touch surfaces	Metal	Microorganisms	Before and after cleaning	Clinical	[38]
	Flexible endoscope	x	Microbial/biological residue	At pre-cleaning, after manual cleaning, after disinfection and after storage	Clinical	[34]
	Surgical robotic instrument	x	ATP biological biofluorescence	After automatic ultrasonic cleaning and after automatic mechanical cleaning	Clinical	[43]
	Healthcare surfaces	Many (n=17), including metal	Contamination residual	After reprocessing	Simulated	[35]
	High-touch surfaces	x	Bacterial load and other residual bioburden	After terminal cleaning	Clinical	[33]
	Gastroscopes, Colonoscopes	x	ATP load	Before precleaning, after precleaning, and after manual cleaning	Clinical	[14]
	Endoscopes	x	ATP levels	After cleaning and after disinfecting	Clinical	[23]
	Duodenoscopes, Linear echoendoscopes	x	Residual organic material	After manual cleaning and after disinfecting	Clinical	[52]
	Duodenoscopes, Linear echoendoscopes	x	Gut flora	After manual cleaning	Clinical	[41]
	Gastroscopes	x	ATP levels	Before cleaning, after cleaning and after two times cleaning	Clinical	[13]
	Duodenoscopes	x	Bacteriologic/biologic residue	After precleaning, after manual cleaning and after disinfection	Clinical	[53]
	Hospital surfaces	x	ATP	Before and after cleaning	Clinical	[39]
	Duodenoscopes	x	High-concern microorganisms	Multiple moments	Simulated	[54]
	Duodenoscopes	x	Organic residue	After manual cleaning	Clinical	[42]
	Colonoscopes, Gastroscopes, Duodenoscopes	x	ATP residue	Before and after manual cleaning	Clinical	[12]
	Gastrointestinal endoscopes, Duodenoscopes	x	ATP	After cleaning, after disinfection and after storage	Clinical	[25]
	Hospital surface	x	ATP levels	After cleaning	Clinical	[37]
Simplified	Devices, surfaces, implements	x	ATP	After cleaning	Clinical	[40]

* "x" is used to represent a feature that is not specified
** verbatim as described in the article

TABLE II
(continued)

Test	Instrument	Material	Type of contamination**	When tested in cycle**	Setting	Ref.
BCA method	Soiled medical device materials	Silicon, Stainless steel, Teflon	Protein	After reprocessing	Simulated	[17]
	Gastroscopes	x	Protein	Before cleaning, after cleaning and after two times cleaning	Clinical	[13]
	Surgical robotic instrument	Metal	Residual protein soil	After three cycles of reprocessing	Simulated	[44]
Culture-based method	Flexible endoscope	x	Microbial/biological residue	After disinfection and after storage	Clinical	[34]
	Healthcare environment surfaces	Many (n=17), including metal	Microbial contamination	After reprocessing	Simulated	[35]
on Luria Bertani agar plates	Gastroscopes, Colonoscopes	x	Microbiological load	Before precleaning, after precleaning, and after manual cleaning	Clinical	[14]
	Endoscopes	x	Cultures	After cleaning and after disinfecting	Clinical	[23]
	Gastroscopes	x	Bioburden	Before cleaning, after cleaning and after two times cleaning	Clinical	[13]
on agar plate	Duodenoscopes	x	High-concern microorganisms	After storage	Simulated	[54]
	Duodenoscopes	x	Microbiological cultures	After disinfecting	Clinical	[42]
on agar plate	Gastrointestinal endoscopes, Duodenoscopes	x	Total bacteria	After cleaning, after disinfection and after storage	Clinical	[25]
Fluorescence-based technique	Soiled medical device materials	Silicon, Stainless steel, Teflon	Haemoglobin	After reprocessing	Simulated	[17]
Marker method	High-touch surfaces	x	Fluorescent marker	Before and after cleaning	Clinical	[38]
Marker method	High-touch surfaces	x	Residual fluorescent gel	After terminal cleaning	Clinical	[33]
	Surgical instruments	Metal	Prion proteins	After reprocessing	Simulated	[55]
Haemoglobin assay	Soiled medical device materials	Silicon, Stainless steel, Teflon	Haemoglobin	After reprocessing	Simulated	[17]
LBT Method	Medical device surface	Latex, PVC, Stainless steel	Chemical residue	After cleaning or disinfection	Simulated	[47]
MRSA detection	Hospital surfaces	x	MRSA	Before and after cleaning	Clinical	[39]

* "x" is used to represent a feature that is not specified
** verbatim as described in the article

TABLE II
(continued)

Test	Instrument	Material	Type of contamination**	When tested in cycle**	Setting	Ref.
OPA Method	Surgical instruments	Metal	Residual protein	After cleaning	Simulated	[48]
	Extraction forceps	Metal	Protein	After reprocessing	Combination clinical and simulated	[16]
Modified	Surgical robotic instrument	Metal	Residual protein soil	After three cycles of reprocessing	Simulated	[44]
Protein swab test	Surgical robotic instrument	x	Protein residue	After automatic ultrasonic cleaning and after automatic mechanical cleaning	Clinical	[43]
	Endoscopes	x	Protein residue	After cleaning and after disinfecting	Clinical	[23]
	Colonoscopes, Gastroscopes, Duodenoscopes	x	Protein residue	Before and after manual cleaning	Clinical	[12]
	Colonoscopes, Gastroscopes, Duodenoscopes	x	Protein	After cleaning, after disinfection and after storage	Clinical	[25]
Rapid bacteria test	Gastrointestinal endoscopes, Duodenoscopes	x	Gram-negative bacteria	After cleaning, after disinfection and after storage	Clinical	[25]
Test strip system	Suction tip	Metal	Blood, protein & carbohydrate	Before cleaning, after manual, and mechanical cleaning	Clinical	[50]
rapid use scope test strips (RUST)	Flexible endoscope	x	Protein, haemoglobin & carbohydrate	After manual cleaning	Clinical & simulated	[15]
	Colonoscopes, Gastroscopes, Duodenoscopes	x	Blood, protein residue	Before and after manual cleaning	Clinical	[12]
TOC Method	Medical device surface	Latex, PVC, Stainless steel	Chemical residue	After cleaning or disinfection	Simulated	[47]
	Pharmaceutical manufacturing equipment	Metal	Residual detergents	After cleaning	Simulated	[36]
Visual inspection	Surgical robotic instrument	x	Any visible blood and other stains	After automatic ultrasonic cleaning and after automatic mechanical cleaning	Clinical	[43]
	Endoscopes	x	Visible abnormalities	After reprocessing	Clinical	[23]
	Hospital surfaces	x	Visible soiling, moisture, staining, or poor surface condition	Before and after cleaning	Clinical	[39]
	Colonoscopes, Gastroscopes, Duodenoscopes	x	Visible apparent residue	Before and after manual cleaning	Clinical	[12]

* "x" is used to represent a feature that is not specified
** verbatim as described in the article

TABLE III
Comparison of the different tests*

Test	**Type of contaminant**	**Ease of use**	**Locating**	**Precision**	**Reliability**	**Time**
ACC method	Aerobic microorganism	- -	+ +	+	x	- -
ATP test	ATP	+ +	+ +	- -	xx	+ +
BCA method	Protein	- -	- -	+ +	+ +	x
Culture-based method	Microorganism	- -	+ +	+ +	+ +	- -
Fluorescence-based technique	Protein	+	+ +	- -	+	+
Haemoglobin assay	Haemoglobin (blood)	-	x	+ +	-	+
LBT Method	Chemicals	x	x	+	x	+
MRSA detection	MRSA bacteria	x	+ +	+ +	x	- -
OPA Method	Protein	x	x	+ +	-	x
Protein swab test	Protein	+ +	+ +	+	-	+ +
Rapid bacteria test	Gram-negative bacteria	x	- -	+ +	x	-
Test strip system	Protein, haemoglobin (and carbohydrates)	+ +	- -	+	-	+
TOC Method	Organic carbon content	x	x	- -	+ +	x
Visual inspection	Visible contamination	+ +	-	- -	- -	+ +

* "- -" = poor, "-" = fair, "+" = good, "++" = excellent, "x" = feature not specified, "xx" = contradictory findings

IV. Discussion

This systemic review gives an overview of different tests that validate the medical device's cleanliness during reprocessing, with the ultimate goal of translating these findings into tests for medical device prototypes in their early stages before medical use. Below, the findings of the articles and tests will be summarised, including the literature gap found, followed by the limitations.

A. Main findings and interpretation

This review aims to identify the most appropriate reprocessing tests for validating the cleanliness of a reusable medical device. With the resurgence of reusable medical devices in the healthcare industry, manufacturers are required to demonstrate successful device cleaning, emphasising the need for early implementation of these tests [1], [3], [17], [18]. This section focuses on the main findings of the tests from the articles and provides interpretations.

1) Comparison of the tests: Research has demonstrated that depending on where in the body the device is used, different types of contaminants will accumulate on the device [14], [23]. According to Chen et al. (2021), surgical instruments, mainly containing blood residue consisting of proteins, are better assessed for cleaning effects using the residual protein assay. Meanwhile, ATP tests are common for evaluating cleanliness in flexible endoscopy equipment [43]. Therefore, it is crucial to understand the associated type of contaminant when conducting tests on the device [56]. Thorough evaluation of medical devices entails testing for multiple contaminants and conducting tests across different areas of the device [12].

A comprehensive approach can involve a single test that detects multiple indicators. For instance, Alfa et al. (2012) conducted a validation study on the RUST test, selecting it as an appropriate method due to the prevalence of common contaminants such as proteins, carbohydrates, and haemoglobin on endoscopes [15]. Alternatively, multiple tests can be performed that indicate one contaminant. For example, Azizi et al. (2012) validated cleanliness using two different tests, namely the ATP test and a test strip system, as effective methods. Their study underscored the significance of employing both tests on a single instrument to achieve a comprehensive cleanliness assessment [50]. To ensure effective testing, it is essential to identify the specific types of contaminants that are likely to be present on the surface of a particular medical device. Based on this knowledge, one should select a test that can detect multiple contaminants or utilise multiple tests as needed. Moreover, to gain a comprehensive understanding of a device's cleanability, performing these test(s) at multiple locations on the device is necessary.

Comparing the different tests poses challenges due to the variations as observed in Table II. Nonetheless, a thorough comparison of the tests is conducted based on five different features, aiming to provide a comprehensive overview displayed in Table III and Appendix B.

Visual inspection alone has been demonstrated to be ineffective in reliably detecting contaminants [12], [43], [48]. Furthermore, while precision in detecting specific contaminants is essential, not all contaminants may be relevant for testing prototypes. Tests such as MRSA detection and ACC method may not be suitable for medical devices under development due to the specific nature of the contaminants they target. Location-specific testing plays a crucial role in identifying areas that require design adjustments. Therefore the BCA method, rapid bacteria test and the test strip system are unsuitable as they do not target specific areas of contamination. ATP tests, culture-based methods, fluorescence-based methods, and protein swab tests are viable options as they effectively indicate the specific contamination site. However, it is important to note that these tests also have limitations. For instance, although effective in identifying specific contaminants, culture-based methods entail longer testing times, result waiting periods, and expertise requirements [25], [34], [35], [42].

Another approach to assess a medical device's cleanliness is using artificial test soil. Although this type of testing was included in the search terms, as shown in Appendix A, no articles discussing this method were found. Some test soil methods utilise specific test soils combined with rapid indicators to identify the presence of those specific soils [11]. Additionally, there are coloured test soils that require visual inspection to determine the endpoint based on the residual colour [57]. This testing approach could be valuable for evaluating medical device prototypes as it visually highlights the precise areas of contamination accumulation. It is a quick and user-friendly test, although it does not provide specific information about the type of contamination. To ensure the device can be correctly cleaned, it is recommended to test this with two different types of tests [12]. It could be valuable to perform both a soil test in combination with a test with a specific indicator based on the type of contaminant it will encounter during use. Further research on this method would be worthwhile to explore its potential applications. For now, ATP tests, culture-based methods, fluorescence-based methods, and protein swab tests are promising options and worth considering when testing prototypes.

2) Comparison of the articles: Fourteen tests from a total of 27 articles were thoroughly reviewed, as shown in Table II. Remarkable results are discussed below:

- A literature gap was identified concerning the cleanliness assessment of medical device prototypes. None of the articles validated a medical device prototype, even though "prototypes" was explicitly mentioned in the search terms, as shown in Appendix A; hence, this objective was removed from the original scope. However, it remains the ultimate goal of the research. When conducting tests on a prototype, it becomes imperative to verify that the obtained results are accurately applicable and representative for the final medical device.
- Twelve of the 27 articles performed their test on an endoscopic instrument. Many HAI outbreaks have been

linked to contaminated endoscopes, more than with any other reusable device [18]. This risk of outbreaks could explain why there is much research on these devices. A result is that most tests have been tested on these devices and, therefore, have not been validated on other medical devices.

- Most of the instruments examined in the articles were predominantly made of metal. Considering that medical devices can be made of materials other than metal, such as plastic, it is desirable to ensure the applicability of these tests to non-metal devices as well.
- Comparing the validated tests used in the articles was challenging due to variations in their specificity. Some articles mentioned a specific type of test, such as the ACC method and the MRSA detection, while others used a broader term for the test, such as the culture-based method. This difference in specificity makes it challenging to compare the studies directly, as it is unclear from the articles which working mechanism these culture-based methods utilise. Moreover, articles used "tests", "methods", and "assays" interchangeably; this occasionally presented a challenge in ascertaining whether the articles were referring to identical test methodologies.
- Nineteen of the 27 articles included an ATP test as a primary method, sometimes along with other tests. However, the ATP test has been subject to varying opinions [13], [14], [34], [35], [40]–[43], [53]. This finding is intriguing, particularly when considering the relative frequency of usage of this specific test compared to other testing methods.
- The articles show variations in contaminant terminology despite performing the same test. This inconsistency is, for instance, revealed by a comparison between the ATP test conducted by Chan et al. [34] and the ATP test conducted by Chen et al. [43]. This variation can be attributed to multiple synonyms and differences in specificity among the articles. However, this diversity of terminology makes it challenging to compare the studies directly.
- Finally, the tests were conducted at various stages of the reprocessing cycle, and there were variations between manual and automatic equipment as well as differences in the testing environments.

3) Importance of early implementation of tests: Redesign of existing devices is crucial for reducing contamination risks, as design changes can significantly reduce transmission and potential risks of contamination [41]. The design of a medical device is recognised as a contributing factor to the persistence of contaminants on the device [14], [23]. This highlights the crucial importance of careful consideration during the design phase before medical implementation. Although the articles do not explicitly validate the cleanliness of medical device prototypes, they emphasise the need to include cleanliness testing in the medical device design process.

Early cleaning validation tests are particularly crucial in light of the resurgence of reusable medical devices in the healthcare industry. Conducting these tests during the design phase of medical device prototypes is essential for identifying potential problem areas and implementing effective measures to ensure device cleanliness and safety. This proactive approach allows for necessary design modifications that significantly enhance reprocessing procedures, improving the device's reprocessing capabilities early in development.

By conducting these tests at an early stage of development, simple design adjustments can be identified to effectively eliminate contaminants and prevent potential issues resulting from design oversights. Addressing contaminant accumulation in specific areas during the prototype stage contributes to the prevention of avoidable problems and enhances overall device performance. Such early validation tests play a vital role in optimizing the design before proceeding to test the final product, which requires full production.

When conducting tests on a prototype, it is crucial to ensure that the obtained results accurately reflect how they would apply to the final medical device. The prototyping of medical devices typically involves 3D printing, an additive manufacturing technique [20], [21]. While 3D printing can also be used for final production, its primary application currently revolves around prototyping [21]. A prototype created with 3D printing often differs from a final product produced with mass-production techniques in materials, surface finish, and porosity [20]. Ensuring that the distinctions observed in the prototype are accurately translated into the final medical device is essential. Otherwise, conducting tests solely on the prototype will not provide any tangible benefits to the manufacturer. It is, therefore, necessary to determine whether the results of a test performed on the prototype accurately reflect the results of the final product or whether there is a difference between the prototype and the final design that needs to be addressed.

B. Limitations

There are certain limitations to consider when reviewing the results of this systematic review. These limitations will be discussed below.

1) Limitations of the tests: Comparing the test described in the different articles proved to be complex due to several factors. These factors include limitations in instruments and materials, the lack of prototype testing, variations in test types, the presence of different contaminants, differing opinions about the tests and conducting the tests at different stages in the reprocessing cycle.

Furthermore, it is important to note that the interpretations and analysis of the data were solely conducted by the author of this review, introducing a potential bias that may have influenced the accuracy of the overall assessment. Moreover, including only 27 articles in this review could be considered a small number, which may impact the precision and reliability of the results and conclusions derived from the study.

2) Limitation of the comparison of the tests: The variation in the specificity of the tests further complicates the comparison among them. While some tests are explicitly mentioned, such as the ACC method and the MRSA detection, others may be broader categories that include various specific methods, such as the culture-based method. This difference in specificity adds complexity to the comparison process.

It is worth noting that the fourteen tests analysed and compared in this review do not encompass the entire spectrum of tests available to assess a medical device's cleanliness. The selection of these tests was based on the study's setup and search terms; therefore, other tests that could have been relevant may not have been included.

3) Prototype limitations: Some features were not taken into account when focusing on a prototype. These are discussed below:

- *Financial considerations* - The study did not factor in financial considerations when evaluating and rating the tests. Nonetheless, considering the economic aspect is crucial for cleaning procedures' smooth and efficient implementation. Manufacturers aim to prioritise cost-effective solutions that enable them to conduct multiple test iterations on the prototype while keeping expenses to a minimum.
- *Soil type* - In the prototype phase, the device undergoes cleaning after simulated use, and soil type selection becomes essential. The choice of soil affects the type of contaminants present on the device, which in turn influences the selection of appropriate tests. Thus, considering the soil type is an important feature to be taken into account.
- *Test settings* - The location and method of performing these tests raise some conflicting points. Differences in results may arise when testing for cleaning efficacy using a washing machine versus manual cleaning methods. Careful consideration should be given to the test setting and available cleaning methods in the final use setting to ensure accurate and relevant results, as it can significantly influence the outcome.

These limitations show a need to improve this translation from testing on a medical product to testing on a medical device prototype.

V. Conclusion

Both for the sustainability within the healthcare industry and for the accessibility of LMIC to the healthcare industry, it is necessary to make a switch from SUDs to reusable medical devices [1]–[3].

Redesign of current medical products is needed as they cannot be adequately cleaned [41]. This demonstrates the need to add more checks during the design of a medical device. This review aims to answer the question: *What are the most appropriate tests to validate the cleanliness of a reprocessed medical device?*

Different tests to validate the cleanliness of a medical device are compared on five different features. Some tests are more specific than others, and some tests test for other kinds of contaminants than others. This makes comparison of the tests harder. The most appropriate options are ATP tests, culture-based methods, fluorescence-based methods, and protein swab tests, as they can precisely identify the location of contamination. Although these tests have certain limitations, they are worth considering.

A comprehensive evaluation of medical devices involves testing for different types of contaminants and conducting tests across various areas of the device [12]. It is crucial to select tests that specifically target the contaminants expected to be present on the medical device. Additionally, combining these tests with coloured test soils could prove interesting. This test visually inspects the residual colour, providing clear indications of the areas where contaminants have accumulated [57].

In conclusion, no articles were found that specifically validated the cleanliness of prototypes before their medical use, which was the initial objective of this research. Prototype testing is useful in identifying potential design improvements and enhancements before the final medical device is produced and used. Therefore, it is strongly recommended to conduct further research in this area to fill the existing gap and address the cleanliness assessment of medical device prototypes before their eventual medical application. The production method is the primary distinction between a prototype and a final medical device, leading to material differences, surface finish variations, and porosity differences [20], [21]. To successfully transfer the results of testing on a prototype into the results of a final medical device, it is essential to determine whether the results of a test performed on the prototype accurately reflect the results of the final product or whether there is a difference between the prototype and the final product that needs to be addressed.

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APPENDIX

A. Final search terms on April 19, 2023

TABLE IV
Final Search Strings in Scopus and Web of Science

Database	**Search Strings***	**Results**
Scopus	(TITLE-ABS-KEY ((protein* OR polypeptide* OR haemoglobin* OR carbohydrate* OR microbial OR soil* OR fluorescent OR "Adenosine triphosphate" OR atp* OR "relative light unit*" OR "total organic carbon" OR toc OR "bicinchoninic acid" OR bca OR "aerobic colony count" OR acc) W/25 (test* OR assay* OR marker* OR method*)) AND TITLE-ABS-KEY (cleaning OR washing) AND TITLE-ABS-KEY ((medical OR surgical) W/25 (instrument* OR device* OR apparatus* OR tool* OR mechanism* OR prototyp*))) AND PUBYEAR $>$ 1999 AND PUBYEAR $<$ 2024	325 articles
Medline	((protein* [Title/Abstract] OR polypeptide* [Title/Abstract] OR haemoglobin* [Title/Abstract] OR carbohydrate* [Title/Abstract] OR microbial [Title/Abstract] OR soil* [Title/Abstract] OR fluorescent [Title/Abstract] OR "adenosine triphosphate*" [Title/Abstract] OR atp [Title/Abstract] OR rlu [Title/Abstract] OR "total organic carbon" [Title/Abstract] OR TOC [Title/Abstract] OR "aerobic colony count*" [Title/Abstract] OR ACC [Title/Abstract]) Near/25 test* [Title/Abstract] OR assay* [Title/Abstract] OR markers* [Title/Abstract]) AND cleaning* [Title/Abstract] OR washing* [Title/Abstract] AND (((medical* [Title/Abstract] OR surgical* [Title/Abstract]) Near/25 instrument* [Title/Abstract]) OR device* [Title/Abstract] OR apparatus* [Title/Abstract] OR tool* [Title/Abstract] OR mechanism* [Title/Abstract] OR prototyp* [Title/Abstract]) Filters: from 2000 - 2023	206 articles

* There is a small difference between the Scopus and Medline terms because of irrelevant search outcome

B. The evaluation of the various tests

TABLE V
Reasoning behind the evaluation of the various tests*

ACC method	
1. Ease of use	Microbiology laboratory support is needed to perform the test, which poses challenges in terms of usability and practicality [38].
2. Locating	To identify the location of contamination, a swab is utilised, providing a precise indication of the contaminated site.
3. Precision	This method directly measures the bacterial load, but limitations in precision [33].
4. Reliability	x
5. Time	Due to its time-consuming nature, this method is not suitable for frequent use [33], [38].
ATP test	
1. Ease of use	Easy to perform and requiring minimal training, enables results that are practical and easy to interpret [13], [14], [34].
2. Locating	To identify the location of contamination, a swab is utilised, providing a precise indication of the contaminated site.
3. Precision	Exhibit limitations in precision and may not provide a reliable indication of the level of contamination [35], [40].
4. Reliability	Opinions on this matter vary, with some articles regarding it as a reliable test while others have reservations.
5. Time	It requires minimal time to perform the test and obtain the results [12]–[14], [34], [35], [53].
BCA method	
1. Ease of use	Specialized equipment, such as photometers, is required for conducting measurements [44].
2. Locating	Fluid samples adds complexity to identifying the precise source of contamination [13].
3. Precision	Detects all proteins [17].
4. Reliability	Highly sensitive test for protein detection [13].
5. Time	x
Culture-based method	
1. Ease of use	The test is challenging to execute effectively and interpret accurately, as it necessitates access to a microbiology laboratory and trained staff and involves a labour-intensive process [25], [35], [42].
2. Locating	To identify the location of contamination, a swab can be utilised, providing a precise indication of the contaminated site.
3. Precision	This test has the capability to detect and identify (specific) bacteria.
4. Reliability	The results obtained are reliable due to the methods' specificity and the controlled laboratory conditions [42].
5. Time	Due to long incubation periods, the test inherently faces a 1- to 2-day delay for obtaining results, making them available only after a few days [25], [34], [35], [42].
Fluorescence-based technique	
1. Ease of use	Simple method that require minimal equipment, but surfaces of interest must be marked before terminal cleaning [33], [38].
2. Locating	The surfaces that fluoresce when exposed to the blacklight provide accurate indications of the location [38].
3. Precision	It does not provide quantitative data on bacterial contamination levels but indicates the presence of fluorescent markers and requires labelling of specific contamination [17], [38].
4. Reliability	It is reliable, but since the human eye is responsible for observing the fluorescence, it is prone to errors.
5. Time	Although preparation time is required for marking the surfaces, the method provides real-time indications [33], [38].
Haemoglobin assay	
1. Ease of use	Simple method, but requires the need and knowledge to handle a microplate reader [17].
2. Locating	x
3. Precision	High specific test.
4. Reliability	Device-based measurement enhances reliability, but variability over time and batches necessitates that each sample needs to be tested multiple times [17].
5. Time	Rapid assay, although the use of a device may slightly slow down the process.
LBT Method	
1. Ease of use	x
2. Locating	x
3. Precision	The method effectively detects residue presence at levels well below those known to cause mammalian cytotoxicity, with higher sensitivity for certain chemicals [47].
4. Reliability	x
5. Time	The method is described as rapid, but no further details are provided.

* "x" is used to represent a feature that is not specified

TABLE V
(continued)

MRSA detection	
1. Ease of use	x
2. Locating	To identify the location of contamination, a swab is utilised, providing a precise indication of the contaminated site.
3. Precision	This method detects a specific type of bacteria.
4. Reliability	x
5. Time	Time it takes to get the results is a least 48 hours [39].
OPA Method	
1. Ease of use	x
2. Locating	x
3. Precision	The method exhibits high sensitivity [48].
4. Reliability	The method is susceptible to accidental contamination, such as residual protein from the hands of individuals handling the test samples, making it less reliable [48].
5. Time	x
Protein swab test	
1. Ease of use	The tests are user-friendly, requiring minimal expertise and no external devices for operation [12].
2. Locating	To identify the location of contamination, a swab is utilised, providing a precise indication of the contaminated site.
3. Precision	It tests for a specific contaminant, but the results are displayed using colour changes instead of quantitative measurements.
4. Reliability	The results are manifested as colour changes, but discerning them accurately can be challenging, posing a risk of human error [12].
5. Time	The test can be conducted rapidly, with only 15 minutes for the results to be obtained [12].
Rapid bacteria test	
1. Ease of use	x
2. Locating	Sampling through flushing poses challenges in localising the specific site of contamination [25].
3. Precision	The test exhibited high sensitivity [25].
4. Reliability	x
5. Time	The minimum time required to obtain a result is 12 hours [25].
Test strip system	
1. Ease of use	This method serves as a simple and user-friendly audit tool [12], [15].
2. Locating	The requirement of fluid samples makes it more challenging to pinpoint the exact location of contamination [12].
3. Precision	It tests for a specific contaminant, but the results are displayed using colour changes instead of quantitative measurements.
4. Reliability	The results are manifested as colour changes, but discerning them accurately can be challenging, posing a risk of human error [12].
5. Time	This tool yields rapid results; however, obtaining the required fluid samples does involve a slightly longer time investment [15], [50].
TOC method	
1. Ease of use	x
2. Locating	x
3. Precision	It is a nonspecific technique that measures the total organic carbon content [36]
4. Reliability	Due to its non-reliance on living organisms, the method is less likely to introduce variability in results [36], [47].
5. Time	x
Visual inspection	
1. Ease of use	Very user-friendly and easy-to-use method [43].
2. Locating	Detecting significant contamination is relatively straightforward, but it is limited by factors such as user visual acuity, lighting conditions, and challenges in inspecting small internal passageways [48].
3. Precision	Not an accurate method [43].
4. Reliability	Relying solely on visual estimation is insufficient to detect the cleaning process's effectiveness adequately; the method is too subjective [39], [43].
5. Time	It is a very time-efficient method.

* "x" is used to represent a feature that is not specified

Material specification

B

Tab. B.1.: Material information from GRANTA EduPack [44].

Material	Durability - Water	Max. Service temperature	Durability - Weak alkalis	Durability - Strong alkalis
ABS	Excellent	62 - 77 °C *	Acceptable	Excellent
CPE	Excellent	100 - 110 °C	Acceptable	Limited use
PC	Excellent	101 - 116 °C *	Excellent	Excellent
TPU	Excellent	65 - 78 °C *	Acceptable	Limited use
Epoxy resin**	Excellent	130 - 150 °C *	Limited use	Excellent

* Estimations of GRANTA EduPack.
** Tough 2000 resin was not accessible within GRANTA EduPack; as a result, a material with similar characteristics was selected.

Tab. B.2.: Material information available online [42, 43, 61].

Material	Thermal resistance	Chemical resistance	Description
ABS	97 °C	Water, some acids and bases, alcohols	An easily printable material with limited warping, offering high impact resistance.
CPE+	100 °C	Alcohols (EtOH, IPA), water, acids and bases	Material is chemical resistant with high dimensional stability, with the added advantages of increased temperature resistance and higher impact strength compared to regular CPE.
PC	100 - 120 °C	Water and alcohols	Print parts that are tough, strong, and retain dimensional stability when subjected to high temperatures.
TPU (95A)	107 - 125 °C	Water (salts), glycol and fuels	A flexible material, making it ideal for applications that demand chemical resistance and the qualities of rubber and plastic.
Tough 2000 resin	Endured boiling water for an hour*	-**	The strongest and stiffest material in the Formlabs, it simulates both the feel and important mechanical properties of ABS plastic.

* Since there is little data, it was experimentally determined whether this material resisted boiling water for an hour
** Not determined or not available.

Test plan for the material validation

C

Specifications:

- St. Antonius Hospital Utrecht (Soestwetering 1, 3543 AZ Utrecht)
- Ultrasound: Nidsa brand
- Washer-disinfector: Belimed brand
- Test Soil: Washer-disinfector test soil, brand: Browne
- ATP Monitor: EnSure Touch ATP monitor
- ATP Swabs: Ultrasnap ATP swabs from Hygiena
- Protein Swabs: Pro-Clean residue test

Test objects:

- Material 1: ABS (Acrylonitrile Butadiene Styrene)
- Material 2: CPE+ (Copolyester+)
- Material 3: PC (Polycarbonate)
- Material 4: TPU 95A (Thermoplastic Polyurethane)
- Material 5: Tough 2000 resin

Tests:

- Test 1: Ultrasnap ATP swabs from Hygiena
- Test 2: Pro-Clean residue test

Test Locations:

- Location A: The blind corner in the cylinder at the top
- Location B: Around the round protrusion on the side

Procedure

Tests are scheduled to take place on the 6th of September, 2023. Safety glasses, gloves, a scrub cap, and protective clothing are worn during testing.

Pre-Test:

1. Run all test objects + PPSU (n=6) through the ultrasound once.
2. Run all test objects + PPSU (n=6) through the washer-disinfector once.
3. Determine which three out of the five materials will be tested along with the PPSU test object and which of the two duplicates will be chosen based on their reaction to the machines. If they all react well, refer to a predefined list.

4. Record in Excel which materials are Material 2, Material 3, and Material 4 and set aside the other objects.

Begin:

1. Record the time and identify which material corresponds to each test object in Excel.
2. Prepare the test soil:
    a) Add water to the top edge of the container.
    b) Shake it.
    c) Let it sit for 10 minutes.
3. Apply soil to PPSU and three test objects (n=4) and place them in a basket.
4. Following the Browne soil protocol, allow the soil to settle for 30 minutes.
5. Place the objects in the ultrasound machine.
6. Remove the objects from the ultrasound machine.
7. Place the objects in the washer-disinfector.
8. Remove the basket from the machine and place it on a table.
9. Remove the objects one by one from the basket.
10. Take a photo of the PPSU and start with the object's left side.
11. Swab Location A of PPSU, Test 2, following the instructions in the user manual.
12. Set a timer for 10 minutes, place it upright in a holder, and leave it on a printed sheet.
13. Wait and then read the result and record it in Excel.
14. Swab Location B of PPSU, Test 2, following the instructions in the user manual.
15. Set a timer for 10 minutes, place it upright in a holder, and leave it on a printed sheet.
16. Wait and then read the result and record it in Excel.
17. Take the right side of the PPSU object
18. Swab Location A of PPSU, Test 1.
19. Read the result and record it in Excel.
20. Swab Location B of PPSU, Test 1.
21. Read the result and record it in Excel.
22. Take a photo of Testobject 2 and start with the object's left side.
23. Swab Location A of Test object 2, Test 2, following the instructions in the user manual.
24. Set a timer for 10 minutes, place it upright in a holder, and leave it on a printed sheet.
25. Wait and then read the result and record it in Excel.
26. Swab Location B of Test object 2, Test 2, following the instructions in the user manual.
27. Set a timer for 10 minutes, place it upright in a holder, and leave it on a printed sheet.
28. Wait and then read the result and record it in Excel.
29. Take the right side of the test object
30. Swab Location A of Test object 2, Test 1.
31. Read the result and record it in Excel.
32. Swab Location B of Test object 2, Test 1.
33. Read the result and record it in Excel.

Repeat the above steps for Test objects 3 and 4 (order: Test object 1 (PPSU), Test object 2, Test object 3, Test object 4).

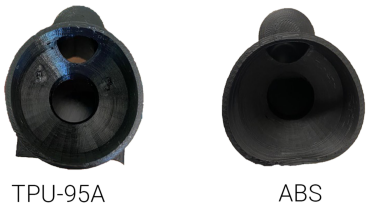
All data for Round 1 is now filled in Excel.

For round 2: Repeat all steps from 'Begin.' Test order: Test object 2, Test object 3, Test object 4, Test object 1. All data for Round 2 is now filled in Excel.

For round 3: Repeat all steps from 'Begin.' Object placement in machines according to the diagram. Test order: Test object 3, Test object 4, Test object 1, Test object 2. All data for Round 3 is now filled

D

Photo report of the material validation

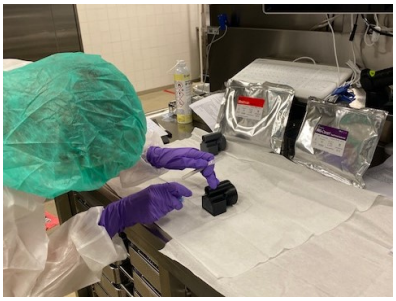


(a) After the pre-test, TPU-95A and ABS were deformed.

(b) The other four test subjects (PPSU, CPE+, PC, tough resin) soiled.

(c) The four test objects in the washer-desinfector

(d) The test location with the data entry sheet and the tests in the silver bags.



(e) Performing of the tests.

(f) Reading results from the ATP monitor.

(g) The protein test holder where protein tests were placed before the results could be read.

(h) The brittleness of CPE+ test objects after multiple cycles in the washer-disinfector.

Fig. D.1.: Eight photos that provide an insight into the testing process of the material validation.

E

Drawing of the SolidWorks parts of the connection

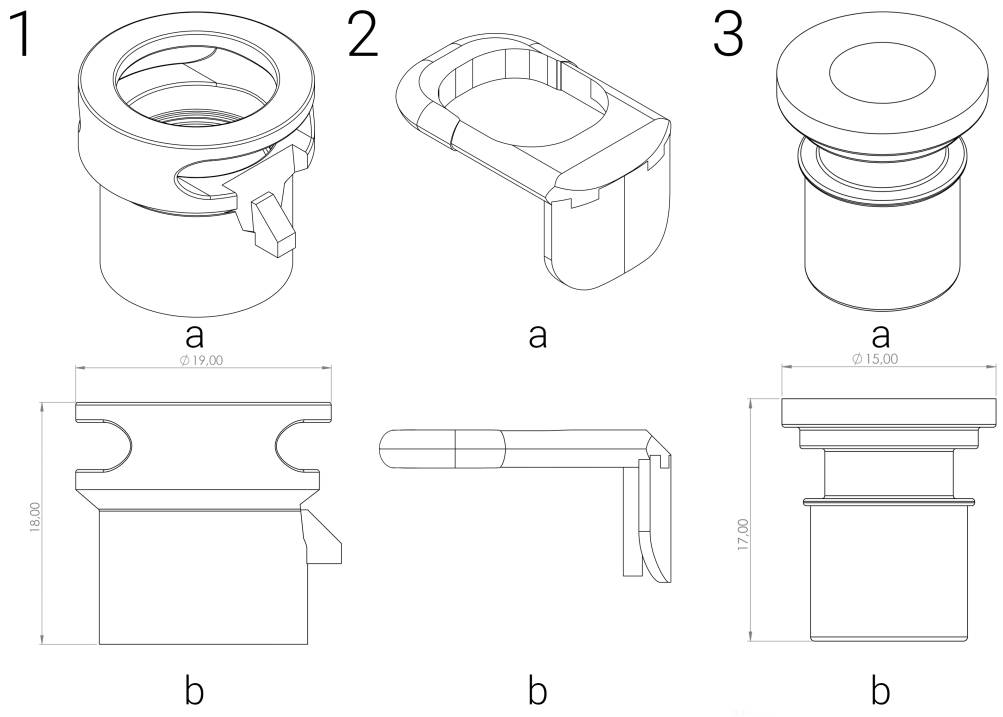


Fig. E.1.: SolidWorks drawing of the three subparts for the connection. Subparts 1 and 2 are interlocked and integrated into the design of the front handle. Subpart 3 is integrated into a small connector and glued to the tube with silicone adhesive. To lock the system, subpart 3 is pushed into subpart 1/2. To unlock the system, subpart 2 is pushed, which releases subpart 3. a: shows the oblique top view. b: shows the front view. Some dimensions are added (in mm) for reference.

F

Test plan for the design validation

Specifications:

- St. Antonius Hospital Utrecht (Soestwetering 1, 3543 AZ Utrecht)
- Ultrasound: Nidsa brand
- Washer-disinfector: Belimed brand
- Test Soil: Washer-disinfector test soil, brand: Browne
- ATP Monitor: EnSure Touch ATP monitor
- ATP Swabs: Ultrasnap ATP swabs from Hygiena
- Protein Swabs: Pro-Clean residue test

Test objects:

- Vela's (n=4), each made from tough 2000 resin and silicone, with each a unique identification number.
  Each Vela consists of 5 separate components. The numbers on the vela's serve solely for identifying the test sequence and do not indicate differences. They aid in tracing any anomalous results back to the specific Vela for further analysis.

Tests:

- Test 1: Ultrasnap ATP swabs from Hygiena
- Test 2: Pro-Clean residue test

Test Locations:

- Location A: Inside the cup
- Location B: Inside the tube
- Location C: Connection from the handle to the tube
- Location D: Above the head of the handle
- Location E: Under the head of the handle
- Location F: Between the stem and diaphragm

Procedure

Tests are scheduled to take place on the 5th of October, 2023. Safety glasses, gloves, a scrub cap, and protective clothing are worn during testing.

Pre-Test:

1. All vela's (n=4) are run once in the washer-disinfector.

Begin:

1. Record the date and time in Excel.
2. Prepare the test soil:
    a) Add water to the top edge of the container.
    b) Shake it.
    c) Let it sit for 10 minutes.
3. Apply soil to the vela's (n=4) and place them in a basket.
4. Following the Browne soil protocol, allow the soil to settle for 30 minutes.
   Testing the dirty vela's as a Reference Framework
5. Check vela 1; test all locations with ATP and record the results.
6. Check vela 2; test all locations with protein and record the results.
7. If necessary, reapply soil to vela 1 and 2.

Ensure that all the vela's are used approximately equally in the HIC and LMIC settings.

Design validation in HIC setting:

1. Place soiled velas (n=3) in the washer-disinfector.
2. Remove vela's from the washer-disinfector.
3. Record the number of the devices tested on the datasheet.
4. Take the first vela
5. Swab locations A to F of vela 1, Test 1.
6. Read the results and record them in Excel.
7. Take the second vela
8. Swab locations A to F of vela 2, Test 1.
9. Read the results and record them in Excel.
10. Take the third vela
11. Swab locations A to F of vela 3, Test 1.
12. Read the results and record them in Excel.
13. Apply soil to velas (n=3).
14. Allow the soil to soak for 30 minutes.
15. Place soiled velas (n=3) in the washer-disinfector.
16. Remove velas from the washer-disinfector.
17. Record the devices used on the datasheet.
18. Take the first vela
19. Swab locations A to F of vela 1, Test 2.
20. Record the time on a sheet, place it in a holder, and read it after 10 minutes. Record the results in Excel.
21. Take the second vela
22. Swab locations A to F of vela 2, Test 2.
23. Record the time on a sheet, place it in a holder, and read it after 10 minutes. Record the results in Excel.
24. Take the third vela

25. Swab locations A to F of vela 3, Test 2.
26. Record the time on a sheet, place it in a holder, and read it after 10 minutes. Record the results in Excel.

Based on the scenario, determine how often vela must go through the HIC setting.
(If so) Repeat from 'Design validation in HIC setting:'

Design validation in LMIC setting:

1. Set up the LMIC setting, see IFU LMIC vela.
2. Prepare soil:
    - Add water to the top edge of the container.
    - Shake it.
    - Let it sit for 10 minutes.
3. Apply soil to vela (n=1).
4. Allow the soil to soak for 30 minutes.
5. Follow the IFU LMIC vela procedure.
6. Record the number of the device tested on the datasheet.
7. Record the number of the device tested on the datasheet.
8. Swab locations A to F of the vela, Test 1.
9. Read the results and record them in Excel.
10. Apply soil to Vela (n=1).
11. Allow the soil to soak for 30 minutes.
12. Follow the IFU LMIC Vela procedure.
13. Record the number of the device tested on the datasheet.
14. Record the number of the device tested on the datasheet.
15. Swab locations A to F of the vela, Test 2.
16. Record the time on a sheet, place it in a holder, and read it after 10 minutes. Record the results in Excel.

Based on the scenario, determine how often vela must go through the LMIC setting.
(If so) Repeat from 'Design validation in LMIC setting:'

Instructions for Use

Tab. G.1.: Instructions for manual cleaning of vela®.

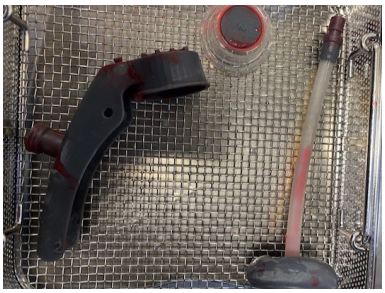
	Step	Instruction	Necessities
	(PRE-)CLEANING		
1.	Clean with water after use	Rinse vela thoroughly with clean water to remove any visible debris or contaminants.	
2.	Disassemble product	Separate the tube & cup, detach the back handle, remove the stem and diaphragm, and remove the silicone domes, leaving only the front handle. In total, there should be five individual parts. Place these parts in a designated container/place.	
3.	Clean with water and JIK	Prepare a cleaning solution by mixing water and JIK (0.5%) in a suitable container. Wipe and clean each part thoroughly using a clean piece of gauze soaked in the prepared cleaning solution. Discard the used gauze after cleaning. Place the cleaned parts into a designated container/place.	- JIK - Gauze
4.	Clean with soapy water	Wash and scrub all parts with mild soap and water in a separate container with brushes, ensuring that you flush water through the tube and use raggers to eliminate any visible contaminants.	- Mild soap - Brushes - Raggers
5.	Rinsing	Rinse vela thoroughly again with clean water to remove cleaning residues.	
6.	Drying	Dry all the cleaned parts with a clean gauze or cloth. After drying, place the parts in a designated container/place. Dispose of the used gauze or cloth properly.	-Gauze/cloth
	DISINFECTING/STERILIZING		
7.	Autoclave	Place the cleaned vela in an autoclave machine.	

Scenario's

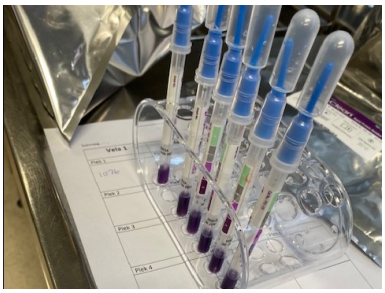
Tab. H.1.: Explanation of the four different scenarios.

Scenario	HIC/LMIC	Vela's per round	Number of rounds	Swaps at each location	Total tests conducted	Selection criteria after testing in HIC setting
1.	HIC	3	2	6	36	After testing 3 vela's, in 2/3 of the cases, $\geq$ 5 locations remain dirty
	LMIC	1	5	5	30	
2.	HIC	3	1 2/3	5	30	After testing 3 vela's, in 2/3 of the cases, $\geq$ 3 locations remain dirty
	LMIC	1	6	6	36	
3.	HIC	3	1 1/3	4	24	After testing 3 vela's, in 2/3 of the cases, $\geq$ 1 location(s) remain dirty
	LMIC	1	7	7	42	
4.	HIC	3	1	3	18	After testing 3 vela's, everything remains clean
	LMIC	1	8	8	48	

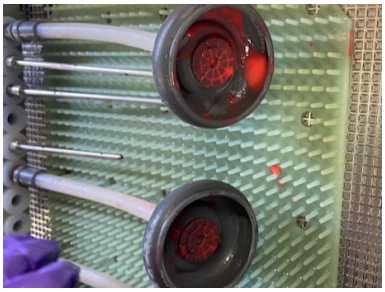
Photo report of the design validation



(a) The vela's are soiled after one cycle in the washer-disinfector.

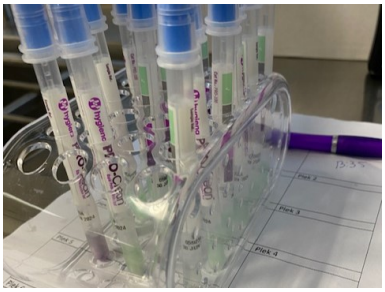


(b) A 'dirty test' is conducted; the protein tests are shown above.

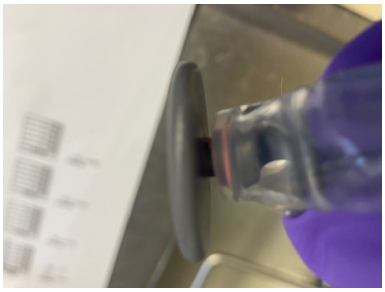


(c) In the HIC setting, the tube is clamped to facilitate a waterflow.

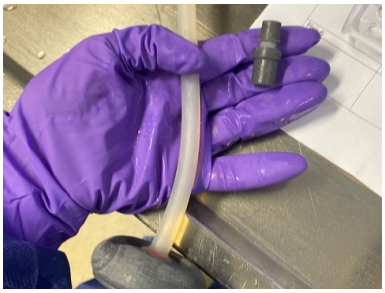
(d) Meanwhile the LMIC setting is prepared.



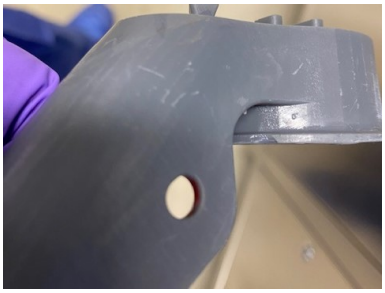
(e) Awaiting the protein test results of the three vela's tested in a HIC setting.



(f) In the HIC setting, only location 6 retained dirt.



(g) Detachment of the PPSU part after three runs in the washer-disinfector.



(h) Close-up of vela after cleaning in the LMIC setting.

Fig. I.1.: Eight photos that provide an insight into the testing process of the design validation. The tests are executed simultaneously for the HIC and LMIC settings.

J

Non-parametric statistics

This data analysis was performed in SPSS. Due to the limited sample size and the amount of baseline measurements that violate the assumption of normality, it was decided to use non-parametric tests for this data analysis. Two types of tests were used, and a threshold value was defined for each. In the ATP test, readings of 10 RLU or higher were categorized as dirty, while in the protein test, any reading above 0 was considered dirty. Therefore, all the data can be dichotomized, in which 1 is dirty, and 0 is clean. In this context, the decision was made to conduct binomial tests. The null hypothesis, H_0, states that the probability that a location is dirty equals the probability that a location is clean; therefore, the hypothesized proportion is set at 0.5. The alternative hypothesis, H_a, states that a location is dirty or clean, depending on the data. Figure J.1 shows the results for each location for the HIC setting (Figure J.1a) and the LMIC setting (Figure J.1b).

Hypothesis Test Summary

	Null Hypothesis	Test	Sig.[a,b]	Decision
1	The categories defined by ATP_LocationA = (dirty) and (clean) occur with probabilities ,500 and ,500.	One-Sample Binomial Test	,125[c]	Reject the null hypothesis.
2	The categories defined by ATP_LocationB = (dirty) and (clean) occur with probabilities ,500 and ,500.	One-Sample Binomial Test	,125[c]	Reject the null hypothesis.
3	The categories defined by ATP_LocationC = (dirty) and (clean) occur with probabilities ,500 and ,500.	One-Sample Binomial Test	,125[c]	Retain the null hypothesis.
4	The categories defined by ATP_LocationD = (dirty) and (clean) occur with probabilities ,500 and ,500.	One-Sample Binomial Test	,125[c]	Reject the null hypothesis.
5	The categories defined by ATP_LocationE = (dirty) and (clean) occur with probabilities ,500 and ,500.	One-Sample Binomial Test	,125[c]	Retain the null hypothesis.
6	The categories defined by ATP_LocationF = (dirty) and (clean) occur with probabilities ,500 and ,500.	One-Sample Binomial Test	,625[c]	Retain the null hypothesis.
7	The categories defined by Protein_LocationA = (dirty) and (clean) occur with probabilities ,500 and ,500.	One-Sample Binomial Test	,125[c]	Reject the null hypothesis.
8	The categories defined by Protein_LocationB = (dirty) and (clean) occur with probabilities ,500 and ,500.	One-Sample Binomial Test	,125[c]	Reject the null hypothesis.
9	The categories defined by Protein_LocationC = (dirty) and (clean) occur with probabilities ,500 and ,500.	One-Sample Binomial Test	,125[c]	Retain the null hypothesis.
10	The categories defined by Protein_LocationD = (dirty) and (clean) occur with probabilities ,500 and ,500.	One-Sample Binomial Test	,125[c]	Retain the null hypothesis.
11	The categories defined by Protein_LocationE = (dirty) and (clean) occur with probabilities ,500 and ,500.	One-Sample Binomial Test	,125[c]	Retain the null hypothesis.
12	The categories defined by Protein_LocationF = (dirty) and (clean) occur with probabilities ,500 and ,500.	One-Sample Binomial Test	,125[c]	Retain the null hypothesis.

a. The significance level is ,050.

b. Asymptotic significance is displayed.

c. Exact significance is displayed for this test.

(a) Statistic results of the HIC setting

Hypothesis Test Summary

	Null Hypothesis	Test	Sig.[a,b]	Decision
1	The categories defined by ATP_LocationA = (dirty) and (clean) occur with probabilities ,500 and ,500.	One-Sample Binomial Test	,016[c]	Reject the null hypothesis.
2	The categories defined by ATP_LocationB = (dirty) and (clean) occur with probabilities ,500 and ,500.	One-Sample Binomial Test	,016[c]	Reject the null hypothesis.
3	The categories defined by ATP_LocationC = (dirty) and (clean) occur with probabilities ,500 and ,500.	One-Sample Binomial Test	1,000[c]	Retain the null hypothesis.
4	The categories defined by ATP_LocationD = (dirty) and (clean) occur with probabilities ,500 and ,500.	One-Sample Binomial Test	,016[c]	Reject the null hypothesis.
5	The categories defined by ATP_LocationE = (dirty) and (clean) occur with probabilities ,500 and ,500.	One-Sample Binomial Test	,125[c]	Retain the null hypothesis.
6	The categories defined by ATP_LocationF = (dirty) and (clean) occur with probabilities ,500 and ,500.	One-Sample Binomial Test	,125[c]	Retain the null hypothesis.
7	The categories defined by Protein_LocationA = (dirty) and (clean) occur with probabilities ,500 and ,500.	One-Sample Binomial Test	,016[c]	Reject the null hypothesis.
8	The categories defined by Protein_LocationB = (dirty) and (clean) occur with probabilities ,500 and ,500.	One-Sample Binomial Test	,016[c]	Reject the null hypothesis.
9	The categories defined by Protein_LocationC = (dirty) and (clean) occur with probabilities ,500 and ,500.	One-Sample Binomial Test	,125[c]	Retain the null hypothesis.
10	The categories defined by Protein_LocationD = (dirty) and (clean) occur with probabilities ,500 and ,500.	One-Sample Binomial Test	1,000[c]	Retain the null hypothesis.
11	The categories defined by Protein_LocationE = (dirty) and (clean) occur with probabilities ,500 and ,500.	One-Sample Binomial Test	,453[c]	Retain the null hypothesis.
12	The categories defined by Protein_LocationF = (dirty) and (clean) occur with probabilities ,500 and ,500.	One-Sample Binomial Test	,125[c]	Retain the null hypothesis.

a. The significance level is ,050.

b. Asymptotic significance is displayed.

c. Exact significance is displayed for this test.

(b) Statistic results of the LMIC setting

Fig. J.1.: The statistical results of the binomial test, where 1 to 6 pertain to the ATP test and 7 to 12 to the protein test.

The assumed significance level is equal to or greater than 0.05. In that case, it becomes challenging to make definitive claims if a location is dirty or clean, making it difficult to draw meaningful conclusions from the data. Only within the LMIC setting is it possible to draw specific conclusions, as highlighted in Figure J.1b). It can be concluded that the cleanliness of locations A, B, and D (inside the cup, inside the tube, and on the head of the handle) of the ATP test and locations A and B (inside the cup and inside the tube) in the protein test as the H_0 is rejected. From the data, it can be observed that these locations are clean.