Cap Designed for Decontamination of Multi-Dose Vials to Prevent Nosocomial Infections

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Abstract

Hospitals are spending an average of $36.5 billion annually due to nosocomial infections[1]. Nosocomial infections are illnesses patients acquire during their stay at the hospital. These infections can be spread through direct patient contact, improper hand washing, airborne vectors, and contaminated medical equipment. When following proper sterilization protocol, multi-dose vials demonstrated insignificant bioburden. If proper aseptic technique is compromised, multi-dose vials are susceptible to housing nosocomial infectious agents. Recently, multi-dose medication vials have shown to be sources of bacterial infection, with randomized testing showing that 4.2% of previously-used vials tested positive for bacteria[2]. While proper aseptic handling of these vials can successfully and adequately prevent the spread of infections, studies have shown that poor aseptic techniques are common causes of contamination[3, 4]. Furthermore, in one survey, 34% of anesthesiologists stated that they never or rarely disinfect the hub of these vials prior to use[5]. They are monetary and qualitatively costly because the patient’s health is now at risk, increasing their odds of death nearly 6-fold compared to a patient without a nosocomial infection[8]. Despite established protocols in the hospital, these methods can sometimes fail in practice during both routine injections and high-stress emergencies. These observations demonstrate the need for sterilization methods that are less prone to user error or negligence.

The goal of this project is to design a novel device to that curtails user error involving multi-dose vials and reduces the risk of nosocomial infections. The design encompasses an improved physical barrier that better prevents bacterial migration, and a built-in chemical barrier that would eliminate human error of standardized disinfecting protocols. The prototype has to be functional, sturdy, and efficient, as it will sometimes be used in emergency situations. The project utilizes a wide range of testing involving the evaluations of multi-dose vials and the prototype for the product. Isopropyl alcohol (IPA) evaporation tests were used to estimate the shelf life of the prototype. Dye ingress testing was conducted to analyze whether microorganisms could infiltrate the inside of the vial. The results of the dye ingress test showed there was no evidence of infiltration into the tested vials. A contamination and disinfection protocol was developed to prove that infection causing microorganisms are transferred from the vial hub to the sterile needle that is then being injected into the patient. The results of the disinfection testing confirmed this hypothesis, providing a further need for this cap design. Early prototype development provided promising results that showed disinfection of the vial hub after direct contamination. Utilizing the technology of 3D printing, the team hopes to produce a marketable disinfecting cap that can reduce human error during injections.
1. **Introduction**

Multi-dose vials are used in the hospital and outpatient settings to deliver drugs such as insulin, blood pressure medication, and immunosuppressants. The vial is considered “multi-use” because it can be penetrated with a sterile needle anywhere from 30-150 times for medication delivery. These multi-dose vials can be used for one or multiple patients. The medication in the vials contains a bacteriostatic preservative such as 0.25% phenol or 20% glycerin to reduce present bacteria [6]. According to the Centers for Disease Control and Prevention, the lifespan of the vial is about 28-30 days once the seal is removed [1]. The expiration date is established to prevent any bacterial growth that may infiltrate the vial or the ineffectiveness of the medication.

A vial is exposed to conditions that contain bacteria, fungi, and viruses throughout its lifespan. For example, an outbreak of streptococcal abscesses was reported after administration of diphtheria-tetanus toxoid-pertussis vaccines from contaminated multidose vials [6]. The vials are stored in varying temperatures which could also contribute to bacterial growth. Over the course of their use in hospitals, the vials are exposed to non-sterile environments: nurses often put the vial in their pocket, patient’s room, or at the nurses station for the sake of convenience. Susceptibility to these types of microorganisms can lead to nosocomial, or hospital-acquired, infections. The most common infections in a hospital are pneumonia, gastrointestinal illness, and urinary tract infections [2]. Infected patients typically show symptoms within 30-48 hours after exposure or shortly after they return home from the hospital. The infected patients find themselves back in the hospital for treatment and as a result, many hospitals face a lawsuit for malpractice.

The prevalence of infections that arise from hospitals is increasing, and as a result, insurance companies are giving hospitals less money to treat these returning patients. Hospital costs ranged anywhere from $900 for a urinary tract infection to upwards of $45,000 for bloodstream infections [4]. Insurance companies see patients being admitted again as a mistake on the hospital as these types of infections can be avoided if protocol is followed. For that reason, some insurances are not willing to cover the cost for the hospital to treat these patients.

Hospitals are now focusing efforts into proper sterilization of medical equipment to prevent patients from contracting nosocomial infections. Sources of infection have been sited from the environment, healthcare staff, and other infected patients [9]. Multi-dose vials present in a contaminated environment have been hypothesized to be a source of nosocomial infections. With the problem identified, a solution was engineered to maintain a sterile vial cap during routine handling and transport within a hospital in an effort stop the spread of infections from suspected multi-dose vials. The basics of the design involved creating a cap to be placed on the vial during storage and transportation. This cap will disinfect the rubber septum where the needle enters to draw medication, preventing any transfer of bacteria from the vial to the patient. With this type of decontamination method in place, the amount of nosocomial infections from injectables is intended to decrease.

2. **Methods and Materials**

**Design Requirements**

The design requirements for the cap include: ease of use, airtight environment under the cap, size versatility, and incorporation of a disinfectant. This cap has to be easy to use in both routine and emergency situations. Ease of use would promote a user friendly cap for patients who have to deliver medication at home. Additionally it would help eliminate human error. The airtight design requirement is to prevent the disinfectant from evaporating. Finally, the cap must have a disinfectant, isopropyl alcohol.

Vial Shield 2
(IPA). This is used to decontaminate the hub after the cap is removed for use. ASTM F1886/F1886M-16 was employed as the cap was designed to verify its functional and practical design.

Prototype Development

Developing the prototype of the cap required several iterations of the critical design process. Small tests were run at several steps to evaluate the performance of each specific aspect of the design. Testing the individual components of the design before testing the entire prototype ensured that each component would function as intended. It also allowed for design changes to be made easily and efficiently. Once all of the individual tests produced desirable results, the prototype was constructed and tested.

Construction of the prototype began with conceptualizing and finalizing the design components. SOLIDWORKS was then used to generate an initial 3D model of the design, shown in Figure 1.

![Figure 1: Initial 3D model of the cap design. Made in SOLIDWORKS](image)

This 3D model was then 3D printed using an Ultimaker2+ and silver acrylonitrile butadiene styrene polymer (ABS). This initial design was used to determine how the cap would actually fit on the vial as well as aid in further developing the design.

This design was the base for the following variations. For all the further designs, space was added into the height of the cap to allow room for the cotton pads that would hold the disinfection agent. The location and delivery of the isopropyl alcohol (IPA) was also reconsidered in further designs. An additional design incorporated ridges to better the hold on the vial and make it more secure. After further analysis, the pad design was rejected and replaced with an alcohol-soaked sponge, similar to on market IV line disinfectants such as the SwabCap®. This sponge design would theoretically be easier to use because it eliminates the need to dispose of a pad with each use. To protect the sponge and slow evaporation, a plastic film that breaks away when the cap is placed on the vial and then covers the sponge when the cap is off the vial would be incorporated. In continuation of the sponge prototype development, a 3D model was made with room for the sponge with three rings to snuggly fit onto the top of the vial. Figure 2 below illustrated this sponge incorporated prototype.
This 3D model of the prototype was printed using an Ultimaker 2+ with blue polylactide polymer (PLA) and white polycarbonate polymer (PC). Four prototypes were made and utilized in testing. Due to material constraints, the inner plastic film was forgone during the initial testing with the prototype. Additionally, cotton acted as the sponge to hold the isopropyl alcohol inside the prototype cap.

### Testing Methods

A multitude of testing trials were completed in order to achieve the design's intended performance. Alcohol evaporation evaluation was completed to obtain an estimate for the amount of IPA that could be used in the prototype. Dye ingress testing was conducted to study the effect of the multiple needle punctures on the vial rubber hub. Contamination and disinfection testing were completed to study the transfer of bacteria and the effectiveness of the prototype.

#### 2.3.1. IPA Evaporation

The isopropyl alcohol evaporation testing was conducted using cotton pads soaked with a measured amount of IPA as the temporary sponge design. Three scenarios were tested via weight analysis; a cap off of a vial exposed to the open air, a cap on a vial the entire duration of the test, and a cap exposed to the air and on the vial at two-minute intervals. The last scenario best represents the exposure that the cap will experience throughout its use. During this test, the dry weight of the cotton pads plus the prototype cap was collected. Following the addition of the IPA, the weights were recorded. The weight was then recorded as time elapsed since the IPA was added. The weight was used to determine the amount of IPA present at each time point to create an evaporation relation with time.

#### 2.3.2. Dye Ingress

Dye ingress testing is a standard industry test to evaluate the integrity of the rubber hub of the multidose vials. This test was run multiple times with various test vials and syringes. The dye ingress testing involved placing the used vials in a water bath with methylene blue dye. Methylene blue dye was chosen for its visual detection properties. A vacuum of -25 kPa was then pulled and held to create a pressure difference from the inside and outside of the vials. This was held for 30 minutes. The vacuum was then released and another 30 minutes passed before inspecting the vials. It was hypothesized that if the rubber hubs of the vials were compromised, when the vacuum was pulled air would leak out and then once the vacuum was released, the water with dye would infiltrate the vial. ASTM F3039-15 was utilized to confirm visual inspection regarding if the vials leak. Additionally, fluorometry was used to detect trace amount of dye in the vials for certain testing sets. Table 1 below outlines the various vial test sets and the collected results.
Table 1: Dye Ingress Testing and Results

<table>
<thead>
<tr>
<th>Vial Test Set</th>
<th>Preparations made to Vial</th>
<th>Results Collected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Used vials from hospital, Approx. 30 sticks with a 22G needle</td>
<td>None</td>
<td>Visually no dye detected</td>
</tr>
<tr>
<td>Used vials from hospital (same as above) w/ needle pin still inserted</td>
<td>Inserted pin into hub that was the same size as a 22G needle</td>
<td>Visually no dye detected</td>
</tr>
<tr>
<td>Used vials from hospital (same as above) w/ DI wash and needle pin still inserted</td>
<td>Washed out residual medicine and added 3ml of DI water to vial. Inserted pin into hub that was the same size as a 22G needle</td>
<td>Visually no dye detected. Fluorometry resulted in no dye detection</td>
</tr>
<tr>
<td>New vials w/ larger needle, 18G</td>
<td>Stick vials with 18G needle 1, 5, 10 times, fill with DI water</td>
<td>Visually no dye detected. Fluorometry resulted in no dye detection</td>
</tr>
</tbody>
</table>

2.3.3. Contamination and Disinfection Testing

The first step of the contamination and disinfection testing involved a “bulk contamination” which was the direct transmission of cultured Saccharomyces cerevisiae yeast colonies onto the hubs of sterile vials. The bulk contamination involved using previously grown yeast colonies of a selected concentration and directly contaminating sterile vials. Using Saccharomyces cerevisiae, a serial dilution was created and grown on WL Nutrient Agar Plates. The researchers chose the dilution that demonstrated high amounts of growth for the bulk contamination. A total of six Depyrogenated Sterile Empty Vials were used in this procedure, each with varying conditions to meet the experimental needs (Table 2). A sample of yeast was collected from the agar plate with a sterile swab; the vials were contaminated accordingly by swabbing each hub for three seconds to standardized the transfer of yeast. The contamination swab was discarded after each vial was contaminated.

Table 2: Six vials used in the experiment and their associated condition

<table>
<thead>
<tr>
<th>Vial</th>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (+)</td>
<td>Contaminated, no disinfection</td>
</tr>
<tr>
<td>Control (-)</td>
<td>Sterile</td>
</tr>
<tr>
<td>Vial 1</td>
<td>Contaminated, Nurses Protocol</td>
</tr>
<tr>
<td>Vial 2</td>
<td>Contaminated, Nurse’s Protocol</td>
</tr>
<tr>
<td>Vial 3</td>
<td>Contaminated, Prototype used for 5 minutes</td>
</tr>
<tr>
<td>Vial 4</td>
<td>Contaminated, Prototype used for 30 minutes</td>
</tr>
</tbody>
</table>

A multitude of disinfection techniques were used to ensure experimental validity. After contamination, the vials were tested according to the specified experimental conditions. The first two vials were disinfected using the nurse’s technique which consists of wiping an alcohol swab across the hub and the surrounding aluminum seal, allowing to dry for 30 seconds, and then penetrating the needle. The other two vials were used to test the prototype. One vial had the prototype on for 30 minutes (prototype 2) while the other vial had the prototype on for 5 minutes (prototype 1). The experimental variable of time was to determine the effectiveness of the prototype compared to other disinfecting caps such as the SwabCap®. According to in vitro studies, the SwabCap® was documented to cause bacterial cell death after 5 minutes of 70% IPA exposure[5]. All 4 vials were tested prior to disinfection to ensure they were
contaminated. This was done by swabbing the aluminum rim surrounding the hub. The swab was cut into a test tube with 1 mL of saline solution. The mixture was vortexed, and 100 μL of the mixture was plated on WL Nutrient Agar Plates and incubated at 37°C for 5 days. Following disinfection, the hubs were swabbed and plated, using the same technique that was previously described. The researchers utilized ASTM F2847-17 to assess the yeast growth on the vial septum and needle. This was done to determine if there were any remaining pathogens on the vials after disinfection from the nurse’s technique or the prototype.

3. Results

IPA Evaporation

The results of the IPA evaporation testing provided insight into the behavior of the alcohol in the cap. Initial evaporation testing using the first cap prototype is found in the appendices. The final cap prototype was used in additional evaporation testing to study the shelf life and performance of the cap. In this testing, three different parameters were used on the same cap design. Cap 1 was exposed to the open air, cap 2 was placed on top of a vial for the entire duration of the experiment, and cap 3 was placed on a vial and then removed and left open to the air and then placed back on the vial at 2 minute intervals.

![Figure 3: Results of IPA Evaporation with final cap prototype](image)

From the data collected, the amount of IPA was calculated based on the weight of the cap and the density of IPA. The amount of IPA over a sequence of time was fitted with a linear trendline. The slope of this linear trendline indicates how quickly the IPA evaporates from the cap. The constant in the equation represent the amount of IPA that was initially present. As suspected, the cap that was exposed to the open air, cap 1, has the highest evaporation rate of 0.000745 ml/min. Both parameters involving the cap being placed on a vial decreased the evaporation rate, meaning a longer shelf life.

Dye Ingress

The dye ingress testing was used to test the integrity of the rubber hubs on the vials. As shown previously in Table 1, several iterations of the dye ingress test were run with different vial set ups. Every vial used in testing was punctured with a 22 or 18 gauge needle at least 10 times to replicate use. The initial tests visually did not show any dye infiltration. The tests were repeated with the intent to collect samples from the vials before and after the test. These samples would be used in a fluorometer to detect any trace amount of dye. The results are shown below in Table 3. It was hypothesized that if the rubber hubs’
integrity was compromised by the needle, the absorbance detected would increase. This compromised integrity of the hub would indicate that there was a way for bacteria to infiltrate the vial.

**Table 3: Dye Ingress Fluorometer Results**

<table>
<thead>
<tr>
<th>Ingress Test</th>
<th>Absorbance (609nm)</th>
<th>Absorbance (668nm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before</td>
<td>After</td>
</tr>
<tr>
<td>No pin inserted</td>
<td>0.0406</td>
<td>0.0294</td>
</tr>
<tr>
<td>22G pin inserted during test</td>
<td>0.0352</td>
<td>0.0291</td>
</tr>
<tr>
<td>Punctured 1 time w/ 18G needle</td>
<td>0.0340</td>
<td>0.0258</td>
</tr>
<tr>
<td>Punctured 5 times w/ 18G needle</td>
<td>0.0389</td>
<td>0.0269</td>
</tr>
<tr>
<td>Punctured 10 times w/ 18G needle</td>
<td>0.0277</td>
<td>0.0341</td>
</tr>
</tbody>
</table>

As indicated by the above results, the absorbance did not consistently increase after the test. An increase in the absorbance would indicate the presence of the dye. Because the absorbance did not change, the alternative hypothesis could not be accepted. The change in absorbance could be accredited to the error in the fluorometer. Two different wavelengths were used to evaluate the absorbance to gather more data points. Both wavelengths indicated no increase in absorbance.

**Contamination and Disinfection Testing**

At the conclusion of the disinfection testing, results provided promising support for the need of this product. These initial results were obtained through visual observation. The researchers found that a sterile needle was contaminated after injection into the contaminated vial. Figure 4 below shows the agar plates of the contaminated hub, non-disinfected hub, and the sterile needle that became contaminated after puncturing the hub.
In addition to this result, the agar plates show that using the prototype effectively disinfected the contaminated vials. The current protocol used in hospitals also appeared to disinfect the contaminated vials. Figure 5 below shows the agar plates before disinfection of contaminated vials. Both the hub and the needles were sampled.
Figure 5: Agar plates of yeast growth. Left panel, results when using prototype. Right panel, results when using traditional protocol. Top plates are before disinfecting. Middle plates show hub after disinfecting. Bottom plates show needle after disinfecting the vial.

4. Discussion

After conducting the IPA evaporation test, dye ingress test, and the contamination and disinfection testing the researchers were able to gather supportive findings for the scope of their project. In the IPA evaporation testing it was found that the alcohol used in the disinfecting cap would not evaporate after one use. Based on simple calculations using the data obtained and shown in Figure 3, cap 1 would have run out of IPA after 15 and a half hours. Cap 2 would have run out of IPA after 11 days. And cap 3, would have run out of IPA after 28 and a half hours. Cap 2 would last much longer due to no exposure to air. The best representation for real would use is observed through cap 3. Based on the dimensions of the cap, the volume to hold the sponge and IPA is 1.56 ml. It was calculated with the data collected from cap 3 that with an initial amount 1.5 ml of IPA the cap would run out of IPA after 2 and a half days. This shelf life is an underestimate due to the fact that in potential use it is suspected that the cap will be on the vial for much longer stretches of times than exposed to open air. However, the cap will still be exposed to the open air at some points which is why the data from cap 3 was used to calculate this estimate.

Dye ingress testing further promoted the need for the prototype. The researcher’s hypothesis was rejected as all variations of the experiment indicated no leakage into the vial. By eliminating the possibility of bacteria infiltrating the vial, the researchers deducted that contamination can develop by the transfer of bacteria from a contaminated hub onto a sterile needle, or the human error of not performing thorough disinfection techniques. Disinfection techniques are well established in the healthcare setting, but the execution among employees is what leads to human error. Studies in the UK and USA confirm that nurses make errors when administering injections in 13-84% of all cases[7]. The prototype can further prevent human errors during injections, removing multi-dose vials as a source of nosocomial infections.

From the results collected, the most influential and promising were obtained from the contamination and disinfection study. As shown in figure 4, when a vial is not disinfected there is transfer of bacteria, in this
study yeast, from the top of the vial onto the needle that then penetrates the patient’s skin. Additionally, figure 5 indicates that the cap properly disinfects the vial just as the current nurse’s protocol does, and the cap removes human error. These results of the disinfection study validate the functionality of the prototype cap as well as confirm the need for the product.

5. Conclusion

This project effectively proves the need to disinfect multi uses vials before use. A contaminated hub will contaminate the needle. The needle will act as a transport for pathogens on the hub into the patient. The current practice is effective if performed correctly, or even, at all. Nurses are often faced with emergency situations, timely rounds, or simple forgetfulness; because of such, human error potentially plays a major role in nosocomial infections. Due to these circumstances, a contaminated hub is likely to remain contaminated; especially in settings such as a hospital where said demanding situations exist. In light of these potentials, the Vial Shield was engineered. With the Vial Shield, the hub is continuously disinfected so the event of a contaminated hub being used to treat a patient is null. Additionally, the Vial shield acts as a visual and tactile reminder. A vial with or without a Vial Shield is easily identifiable; therefore there is never a question as to whether a vial is disinfected or not.

The next steps for the development of the cap involve investigating a way to indicate when the cap is nearing the end of its shelf life. Research into the final materials for the cap production should be completed. Further testing with contamination to validate shelf life should also be completed.

6. Acknowledgements

The authors would like to acknowledge MedAssurance, LND Medical, and Rowan University, Department of Biomedical Engineering. Their continuous support and guidance is what made this project possible. ASTM standards would also be acknowledged for the desired testing that is planned. The first procedure that was performed is a dye ingress test which aimed at proving microorganisms can infiltrate the inside of the vial. ASTM F3039-15 was used to confirm the evaluations on the vials regarding if the vials leak. The second standard, F1886, aided in evaluating the prototype design. The prototype has to be functional, sturdy, and efficient as it will sometimes be used in emergency situations. The final protocol being performed in a sterility test. The goal of this test was prove that infection causing microorganisms are transferred from the vial hub to the needle that is then being injected into the patient. F2847-17 standard was used to quantify the sterility of the product and the vials during testing.

7. References


https://doi.org/10.1016/j.otohns.2008.05.013


http://dx.doi.org/10.1016/j.apjtb.2017.01.019
Appendix A. Previous prototype development images

Supplementary data and figures associated with this project can be accessed through the online version found at: create appendices into an online file and insert link here

Figure A1: Technical drawing and dimensions of prototype with reservoir. All dimensions are in centimeters. Visual picture of prototype with reservoir

Figure A2: Technical drawing and dimensions for the side reservoir design. All dimensions are in centimeters.
**Figure A3:** Technical drawing and dimensions for the inner screw and outer ridges design. All dimensions are in centimeters.

**Figure A4:** Technical drawing and dimensions for the spring loaded design. All dimensions are in centimeters.