Reducing Patient Discomfort Through Self-Warming Skin Preparation Applicator

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Table of Contents

Authorship

Paper Section	Author	Editor
1 - Introduction	All	All
2.1 – Skin Preparation Procedure and Regulations	Ravneet Kaur, Alicia Costi	All
2.2 – Antiseptic Skin Preparation Products on the Market	Ravneet Kaur	All
2.3 – Prevalence of Medical Equipment Warming in Care Delivery	Ravneet Kaur	All
2.4 – Thermal Properties	Kalyn Ricciuti	All
2.5 – Importance of Patient Experience	Emily Kolaya	All
2.6 – Injection and Blow Molding of Disposable Medical Devices	Alicia Costi	All
2.7 – Prototyping Medical Devices	Ravneet Kaur	All
3.1 – Initial Client Statement	All	All
3.2 – Design Requirements – Technical	Kalyn Ricciuti	All
3.3 – Design Requirements – Standards	Alicia Costi	All
3.4 – Revised Client Statement	All	All
3.5 – Management Approach	Ravneet Kaur	All
4.1 – Needs Analysis	Alicia Costi	All
4.2 – Conceptual Design and Concept Map	Alicia Costi	All
4.3 – Alternative Designs	Ravneet Kaur, Emily Kolaya	All
4.4 – Final Design Selection	All	All
4.5 – Initial Testing	All	All
5.1 – Lithium Chloride and Water Testing	Alicia Costi	All
5.2 – Lithium Chloride, Water, and IPA Testing	Emily Kolaya	All
5.3 – Antimicrobial Testing	Alicia Costi	All
5.4 – Rapid Prototyping and 3D Prototype Evaluations	Ravneet Kaur	All
6.1 – Final Design Overview	Kalyn Ricciuti, Alicia Costi	All
6.2 – Applicable Engineering Standards	Alicia Costi	All
6.3 – Impact of Final Design	Alicia Costi, Emily Kolaya, Kalyn Ricciuti	All
7.1 – Final Design	Emily Kolaya	All
7.2 – Warming Results Achieved	Emily Kolaya	All
7.3 – Antimicrobial Properties Maintained	Ravneet Kaur	All
7.4 – Project Limitations	Kalyn Ricciuti	All
8.1 – Project Conclusions	Alicia Costi	All
8.2 – Future Recommendations	Alicia Costi	All

List of Tables

List of Figures

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1 Introduction

Surgeries and other invasive medical procedures are performed daily around the world. In the United States alone, an average of 48.3 million surgical and non-surgical procedures are performed every year. There is a broad range of procedures performed, such as those for the digestive system, musculoskeletal system, and nervous system (CDC, 2017). Prior to any procedure that is bound to breach the skin barrier, proper preparation of the surgical site is critical as the skin microbiome harbors a wide array of microorganisms. Though the majority of the microorganisms do not cause harm when on the skin, disruption of the skin barrier will allow the microorganisms to enter the body through the surgical site, or the incision. Consequently, antiseptic skin preparation applicators are routinely used to prepare the patient's skin because they aid in the elimination of bacteria that can cause surgical site infection (SSI). One of the most commonly utilized and trusted skin preparation products contains chlorhexidine gluconate in an alcohol-based solution, which has been shown to be effective against bacteria, viruses, and fungi (Skyes and Weese, 2014). Chlorhexidine gluconate (CHG) is a broad-spectrum biocide that disrupts the bacterial cellular membranes of both gram-negative and gram-positive bacteria. Additionally, CHG has broad activity against anaerobes, yeasts, and some lipid-enveloped viruses. Its fungal coverage, however, is reduced compared to other skin preparation solutions, such as iodophors and alcohols (Reichman & Greenberg, 2009). In an alcohol-based solution, specifically isopropyl alcohol, CHG remains active on the skin for up to 48 hours following the evaporation of the alcohol, which in turn improves its efficacy as an antiseptic.

While pre-surgical skin preparation is both important and a requirement, patients claim that the antiseptic solution is cold and uncomfortable when it comes in contact with their skin. The cause of this discomfort is the evaporative cooling properties of the isopropyl alcohol, which draws heat from the skin surface. This phenomenon is more commonly and comfortably experienced during perspiration. In an operating room, where ambient conditions are maintained at approximately 65 – 69 °F (18-20 °C) with a humidity of 70%, the body naturally responds through the vasoconstriction of blood vessels to maintain core body temperature of 97.7 - 99.5 °F (36.5-37.5°C) (Ballayante, 2009). When combined, the low ambient room temperature and the evaporative cooling on bare skin can be an unpleasant experience for the vulnerable patient. Furthermore, it is common to scrub the antiseptic solution in a layering method that requires

several applications to assure thorough surgical site preparation, which can easily amplify the extent of discomfort and poor experience for the patient.

In an effort to better understand the extent of the design need, the team created a survey (Appendix A) that clinical staff from the UMMS Interventional Radiology department would use to ask patients about their skin preparation experience. The team's goal was to receive quantitative and qualitative data that would validate the need for redesigning the current antiseptic applicator. After receiving IRB approval from WPI (Appendix B) and UMMS, the survey was given to Dr. Hussain and Dr. Ruppell, who then educated the staff on the context and manner in which the survey would be introduced to the patients. The team received 22 completed patient surveys from the UMMS staff and the results are provided in Appendix C. 91% of survey patients believed that a warm antiseptic solution would enhance their experience and 95% of patients found the antiseptic to be cold.

Although overall patient safety is always the top priority, it is important to prioritize efforts dedicated to enhancing patient experience as much as possible, especially during a vulnerable time such as surgery. Studies in various healthcare settings have shown that patient experience can affect recovery. Those who reported a poor experience and improper treatment during a medical visit were more likely to have a slower recovery and not follow post-treatment protocol (Chatterjee et. al, 2012). Unfortunately, such lack of adherence can lead to an increased healthcare cost burden as utilization of healthcare services will increase, which may result in greater patient dissatisfaction (Chatterjee et. al, 2012).

The overarching goal of this project is to reduce patient discomfort induced by the cold sensation felt after applying the antiseptic skin preparation solution during surgical preparation. Our project sponsor, Dr. Sarwat Hussain, and his team at University of Massachusetts Medical School (UMMS) perform a range of interventional radiology procedures that require the use of antiseptic skin preparation applicators as part of surgical preparation. A biomedical engineering design solution catered toward resolving some of the patient concerns can be integrated into the pre-surgical preparation phase of various procedures. Specifically, procedures that demand local or regional anesthesia, where the patient is still conscious or minimally sedated, could benefit from the design solution. Though the project's need is sourced from the staff's experience, the output of the research can benefit the large healthcare population due to the scope of surgical procedures worldwide.

2 Literature Review

This literature review provides an overview of pre-procedural and pre-surgical skin preparation. It highlights a variety of different topics, including: 1) skin preparation procedure and regulations, 2) preparation applicators currently on the market and their thermal properties, 3) the importance of patient experience. Patients have stated that skin preparation is an uncomfortable part of procedures and surgeries that negatively affects their overall patient experience. By researching the properties and mechanism of action of the current solutions, the reason for their dissatisfaction became clear. From this, the goal of this project is to lessen or eliminate the discomfort experienced by patients in the most effective manner possible.

2.1 Skin Preparation Procedures and Regulations

Every year, approximately 232.4 million major surgeries occur around the globe (Weiser, 2018). In the United States alone, over 48 million surgical and non-surgical procedures take place per year. In order to prevent a potentially life-threatening infection, the skin must first be properly prepared before a procedure. Post-procedural infections increase a patient's recovery time, decrease their overall experience, and can even be life-threatening. Due to the gravity of the potential consequences, special emphasis is placed on ensuring that skin preparation procedures follow certain regulations, such as those from the Association of Surgical Technologies (AST) and the U.S. Food and Drug Administration (FDA).

2.1.1 Skin Preparation Procedures

As previously stated, skin preparation is performed in order to prevent infection during any procedure or surgery that breaks the skin barrier. The skin microbiome is home to various types of microorganisms, such as *Staphylococcus epidermidis* and *Staphylococcus hominis* (World Health Organization, 2009). Although these microorganisms have no negative effect on the skin itself, the majority of surgical site infections occur when microbial flora enter the surgical wound. By properly preparing the skin, debris and microbes are removed, which prevents the growth of microbes during the procedure (AST Education and Professional Standards Committee, 2008). Thus, proper skin preparation is an integral part of any procedure that penetrates the skin barrier.

As to be discussed in section 2.2, there are multiple types of antiseptic skin preparation products currently on the market. Regardless of the product used, specific protocol is followed to

ensure that the patient's skin is properly prepared. Prior to performing skin preparation, the skin must first be cleansed of any soil, grease, blood, etc. with a fat solvent or degreaser (AST Education and Professional Standards Committee, 2008). Although this fat solvent or degreaser does not have to be aseptic, it must be non-irritating, non-flammable, and non-toxic. For the skin preparation itself, it is essential that sterile technique is utilized. Medical-grade gloves must be worn, and it must be ensured that they, along with the skin preparation applicator or sponge, do not come in contact with non-sterile items. There is currently not a standard skin preparation duration - it varies depending on the hospital and type of procedure being performed. However, enough preparation solution must be used, beginning at the incision site, to cover a circular four-inch radius (AST Education and Professional Standards Committee, 2008). Once a sufficient boundary of skin has been prepared, it is essential that the applicator or sponge does not again touch the clean areas. According to the AST, the most crucial aspect of skin preparation is that it progresses from a clean to dirty portion of the skin in order to prevent contamination (AST Education and Professional Standards Committee, 2008).

2.1.2 Skin Preparation Regulations

On account of the importance of skin preparation to the overall procedural or surgical experience, there are regulations in place from different organizations to ensure that protocol is followed. The first governing organization is the Association of Surgical Technologists - an organization of over 40,000 members that strives to ensure high quality patient care ("Association of Surgical Technologists", n.d.). The AST currently has ten standards of practice in place regarding various aspects of skin preparation of a surgical patient, however three are of particular interest and importance to this project. The organization recommends in Standard of Practice III that alcohol is not used alone as an antiseptic agent. Alcohol's antimicrobial action is the denaturing of proteins, with 60% to 95% alcohol being the most effective. It also possesses a broad spectrum of antimicrobial properties, such as the ability to destroy gram-positive and gram-negative bacteria and multidrug-resistant (MDR) pathogens like MRSA, VRE, Mycobacterium tuberculosis, and fungi (AST Education and Professional Standards Committee, 2008). However, it does not have a long-lasting, cumulative activity and therefore should not be the sole antimicrobial agent used for a procedure of long duration (AST Education and Professional Standards Committee, 2008). An additional AST Standard of Practice is Standard VIII, which

discusses manufacturer's instructions for warming antiseptic agents. This standard states that if a skin preparation solution is warmed, one must ensure that it is not so hot as to cause a burn on the patient's skin. Lastly, Standard of Practice II states that FDA-approved agents must be used that have immediate, cumulative, and persistent action (AST Education and Professional Standards Committee, 2008).

As mentioned by AST Standard II, FDA regulations must be followed in the design and usage of a skin preparation product. In the United States, antiseptic agents are currently regulated by the FDA's division of Over-the-Counter (OTC) Drug Products ("Safety and Effectiveness", 2017). The following standards should be accounted for, according to the FDA: 1) the ability to reduce transient microorganisms, 2) the possession of a broad range of antimicrobial properties, 3) fast-acting and long-lasting activity, and 4) avoiding irritation to the skin (AST Education and Professional Standards Committee, 2008). Additionally, the FDA stated in 2017 that as of December 20, 2018, chlorhexidine gluconate (CHG) and iodophors will not be Generally Recognized as Safe (GRAS) for use in a healthcare antiseptic. Due to this, any OTC antiseptic products containing these as active ingredients will need to be approved, prior to beginning a marketing campaign, under a New Drug Application (NDA) or Abbreviated New Drug Application (ANDA) ("Safety and Effectiveness", 2017). In the design of any new skin preparation solution, especially one that contains active ingredients not generally deemed safe, it is essential to take extra steps to gain FDA approval.

2.2 Antiseptic Skin Preparation Products on the Market

Depending on the medical procedure, there are various antiseptic skin preparation on the market for use. In 2013, the Association of Perioperative Registered Nurses (AORN), a leading advocate for "excellence in perioperative practice and healthcare", published the Perioperative Standards and Recommended Practices document (AORN, n.d.). Recommendation III in the document states that "the antiseptic agent should be selected based on the patient assessment", which includes assessing for allergies, sensitivities, contraindications, lesions and other tissue conditions (AORN, 2013). As published by the AORN, Table I and II below briefly summarize the activity and considerations for the most commonly used antiseptic solutions. More details regarding the common antiseptics are referenced in subsections below.

Table I. Activity and Considerations for Perioperative Skin Preparation Antisepsis

Antiseptic	Mechanism of Action	Gram-Positive Bacteria	Gram-Negative Bacteria	Viruses	Rapidity of Action	Persistent/ Residual Activity
Isopropyl Alcohol	Denaturation of proteins	Excellent	Excellent	Good	Excellent	None
Chlorhexidine Gluconate	Disruption of cell membrane	Excellent	Good	Good	Moderate	Excellent
Povidone-iodine (Betadine®□ Surgical Scrub)	Oxidation/ substitution with free iodine	Excellent	Good	Good	Moderate	Minimal
Chlorhexidine gluconate with alcohol (ChloraPrep™)	Disruption cell membrane and denaturation of proteins	Excellent	Excellent	Good	Excellent	Excellent
Iodine-based with Alcohol (DuraPrep™)	Oxidation/ substitution by free iodine and denaturation of proteins	Excellent	Excellent	Good	Excellent	Moderate

Note. Reprinted from *AORN: Perioperative Standards and Recommended Practices*, Retrieved from https://www.hqinstitute.org/sites/main/files/file-attachments/skin_antisepsis_0.pdf, 2013

Table II. Activity and Considerations for Perioperative Skin Preparation Antisepsis Contd.

Antiseptic	Use on Eyes and Ears	Use on Mucous Membranes	Contraindications	Cautions
Isopropyl Alcohol	Not allowed. Can cause corneal damage or nerve damage	Not allowed	N/A	Flammable. Does not penetrate organic material. Optimum concentration is 60% to 90%.
Chlorhexidine Gluconate	Not allowed. Can cause corneal damage and deafness if in contact with inner ear.	Not encouraged. Use with caution.	Known hypersensitivity to drug.	Prolonged skin contact may cause irritation in sensitive individuals.
Povidone-iodine (Betadine®□ Surgical Scrub)	Allowed. Moderate ocular irritant.	Allowed.	Known sensitivity (shellfish allergies are not a contraindication).	Prolonged skin contact may cause irritation. May cause iodism in susceptible individuals; avoid use in neonates. Inactivated by blood.
Chlorhexidine gluconate with alcohol (ChloraPrep™)	Not allowed. Can cause corneal damage and deafness if in contact with inner ear.	Not allowed.	Known hypersensitivity.	Flammable.
Iodine-based with Alcohol (DuraPrep™)	Not allowed. Can cause corneal damage or nerve damage.	Not allowed.	Sensitivity to povidone-iodine. (shellfish allergies are not a contraindication.)	Flammable.

Note. Reprinted from *AORN: Perioperative Standards and Recommended Practices*, Retrieved from https://www.hqinstitute.org/sites/main/files/file-attachments/skin_antisepsis_0.pdf, 2013

2.2.1 Alcohols

As reported by the Centers for Disease Control and Prevention (CDC) in 2008, the term "alcohol" in a hospital setting can refer to either ethyl alcohol or isopropyl alcohol, which are available as the OTC household rubbing alcohol (CDC, 2008).

Mechanism of Action

Alcohol penetrates the bacterial cell wall and denatures intracellular proteins by disrupting the side chain intramolecular hydrogen bonding (Elmhurst College, n.d.). Because protein function and activity are heavily dependent on protein structure, disruption of the tertiary structure (Figure I) of a protein will cease its activity.

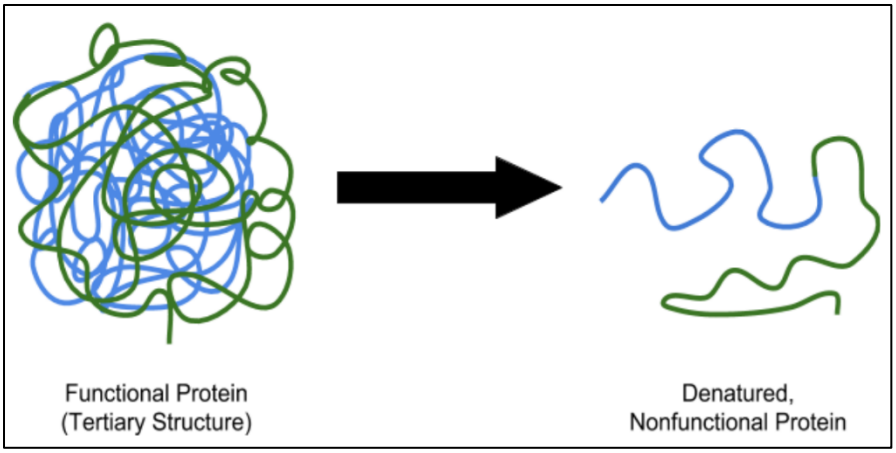


Figure I. Illustration of protein denaturation. Protein structure strongly dictates proper functionality. Therefore, if the tertiary structure is lost due to denaturation, protein will no longer perform its function. Alcohol-based antiseptics rely on the denaturation of protein as the primary mechanism of action to kill bacteria, viruses and fungi. Adapted from *Phys Org,* P. Rüegg, 2017, Retrieved from https://phys.org/news/2017-02-rare-proteins-collapse-earlier.html

Advantages

Alcohols, like ethyl alcohol and isopropyl alcohol, are widely accepted as they target broad-spectrum bacteria. Because alcohol molecules participate in two hydrogen bonds while water molecules participate in four, alcohols (180.7 °F) have a lower boiling point than water (212 °F) (UCSB ScienceLine, n.d.). A lower boiling point is advantageous because it allows alcohol-based antiseptic solutions to evaporate quicker than aqueous-based solutions. Ultimately, the reduced drying time on the skin makes alcohols a preferred base for preoperative skin antiseptic solutions.

Disadvantages

Although alcohol is recognized for its antimicrobial properties and is an accepted antiseptic agent, "it should not be used as the single agent but as part of the skin prep regimen" (AST Education and Professional Standards Committee, 2008). In simpler terms, alcohol is not a sufficient preoperative antiseptic solution when used alone. As previously mentioned, the AST states that although alcohol is suitable for skin preparation due to its rapid and antimicrobial activity, it alone does not have a persistent, cumulative activity. Persistent, cumulative activity is a desired and crucial property for antiseptics because it helps decrease rebound microbial growth after initial skin preparation.

2.2.2 Aqueous-Based and Alcohol-Based Chlorhexidine Gluconate

Chlorhexidine has been a trusted antimicrobial across various healthcare categories as it is incorporated in oral rinses, skin antiseptics, medical supplies and equipment, and antimicrobial dressings (Toomey, 2013). A stable salt form of free base chlorhexidine, chlorhexidine gluconate (CHG) is a widely used biguanide and biocidal agent in healthcare, mainly in dental hygiene and preoperative skin preparation (ChloraPrep™), because of its effectiveness against gram-positive bacteria, gram-negative bacteria, fungi, and viruses (McDonnell and Russell, 1999). Furthermore, CHG is a form of chlorhexidine salts that has the ability to dissolve in water and deliver the molecule in an effective way.

Mechanism of Action

Because CHG has a positive charge, it reacts with the negatively-charged microbial cell surface and absorbs into bacterial cells. CHG molecules disrupt the integrity of the cell wall and penetrate the cell well via passive diffusion, which subsequently damages the bacterial cytoplasm (McDonnell and Russell, 1999). Cell wall and cytoplasmic damage is then followed by the leakage of intracellular constituents and consequent cell death. CHG follows a similar mechanism of action against yeast. However, CHG's effectiveness against viruses is variable in that its activity is restricted to lipid-enveloped viruses, which suggests that CHG is not effective against nonenveloped viruses such as rotavirus, Hepatitis A virus, and poliovirus. Table III below summarizes the CHG's mechanism of action against various microorganisms.

Table III. Mechanisms of Antimicrobial Action of Chlorhexidine

Type of Microrganism	Action
Bacterial spores	Not sporicidal but prevents development of spores; inhibits spore outgrowth but not germination
Mycobacteria	Mycobacteristatic (mechanism unknown) but not mycobactericidal
Other non-sporulating bacteria	Membrane-active agent, causing protoplast and spheroplast lysis; high concentrations cause precipitation of proteins and nucleic acids
Yeasts	Membrane-active agent, causing protoplast lysis and intracellular leakage; high concentrations cause intracellular coagulation
Viruses	Low activity against many viruses; lipid-enveloped viruses more sensitive than non-enveloped viruses; effect possibly on viral envelope, perhaps the lipid moieties
Protozoa	Membrane activity (leakage) toward trophozoites, less toward cysts

Note. Reprinted from *Clinical Microbiology Review: Antiseptics and Disinfectants: Activity, Action, and Resistance*, Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC88911/, 1999

Advantages

Introduced in to the United States in the 1970s, CHG has been recognized as a gold-standard as there are several advantages of using it as an antimicrobial agent in skin preparation solutions. According to the World Health Organization, the antimicrobial activity of chlorhexidine is "not seriously affected by the presence of organic material, including blood" (2009). Furthermore, CHG is an even more effective antimicrobial agent when it is used in alcohol-based solutions, like 70% isopropyl alcohol. Attributed to its substantiativity, CHG can bind to proteins present on skin tissue and mucous membranes with limited systemic or bodily absorption. As a result, the protein-bound CHG adheres to the stratum corneum (uppermost top layer of skin) and provides an inhibitory effect on microbial growth by remaining on the skin after rinsing or drying. Nonetheless, alcohol-based CHG (ChloraPrep™) has a residual activity of up to 48 hours - about 8 times greater than that of aqueous-based CHG (World Health Organization, 2009).

Disadvantages

Because chlorhexidine is a cationic molecule, its activity can be reduced by natural soaps, various inorganic anions, non-ionic surfactants, and hand creams containing anionic emulsifying agents (World Health Organization, 2009). Although rare, prolonged contact can cause irritation and potentially dermatitis, making it less suitable for patients with sensitive skin. Specifically, chlorhexidine molecules can induce IgE-mediated anaphylaxis (Toomey, 2013). When individuals are exposed to a trigger antigen, like CHG, their immune system responds by activating production

IgE antibodies, which then attach to the surface membrane of mast cells and cause a "priming" effect (Toomey, 2013). Re-exposure or continued exposure to the antigen leads to rapid binding of antigen to the IgE antibodies of primed mast cells, which activates the mast cells that release allergenic mediators (histamine, cytokines, and leukotrienes) that account for the signs and symptoms of anaphylaxis.

2.2.3 Aqueous-Based and Alcohol-Based Iodine Solutions

In the early 1900s, iodine became recognized as an effective antimicrobial agent. However, following incidences of skin irritation and toxicity caused by iodine, povidone-iodine (PVP-I) was developed. PVP-I, or PI, is a stable chemical complex of polyvinylpyrrolidone (povidone/PVP) and elemental iodine (I) (Burks, 1998). PVP-I is safer than iodine alone as it has a lower concentration of free iodine at about 9-12%. Popular antiseptic skin preparation products that incorporate aqueous- based and alcohol-based iodine include Betadine® Surgical Scrub (PVP-I) and DuraPrep™ (iodine povacrylex in isopropyl alcohol), respectively.

Mechanism of Action

Apart from being effective against broad-spectrum bacteria, PVP-I can also kill viruses and fungi. PVP-I causes protein denaturation and precipitation of bacteria, which results in the death of the pathogenic microorganisms on the skin surface ("PubChem", n.d.). Specifically, iodine molecules "rapidly penetrate the cell wall of microorganisms" and "inactivate cells by forming complexes with amino acids and unsaturated fatty acids", which impairs protein synthesis and alters cell membranes (World Health Organization, 2009).

Advantages

One of the main advantages of aqueous-based PVP-I is that is can be used on the eye and ear unlike alcohols or CHG antiseptics. Apart from its versatility, PVP-I is effective against broad-spectrum bacteria, viruses, and fungi. In alcohol-based solutions, antimicrobial activity is improved, and the duration of persistent/residual activity increased from 2 hours (aqueous-based) to 48 hours (Hemani and Lepor, 2009).

Disadvantages

Despite its advantages, there are several disadvantages of PVP-I antiseptics. Unlike ChloraPrep™, Betadine®□ Surgical Scrub and DuraPrep™ are inactivated by presence blood and organic matter, which reduces the solution's antimicrobial properties (Hemani and Lepor, 2009). An in-vitro research study completed in the mid-1980s aims to explain this phenomenon as the team states that when iodine binds to organic substances like blood, pus, fat, and glove powder, there is decreased iodine availability to kill the bacteria present on the skin (Zamora et. al, 1985). Another study, which focused on comparing antiseptics to prevent catheter-related infections, suggested that povidone iodine is inactivated by protein-rich biomaterials, like blood, present on the skin (Goudet et. al, 2013). Additionally, prolonged skin contact can cause irritation and sensitivity.

2.3 Prevalence of Medical Equipment Warming in Care Delivery

In humans, normal core body temperature (normothermia) is 37°C (John et. al, 2014). When core body temperature drops below 36°C, a patient is considered to be hypothermic. Meanwhile, operating rooms are typically kept below 23°C. Although medical personnel wearing layers of clothing and personal protective equipment consider 23°C to be warm, patients that are undressed and simply covered by a surgical gown feel otherwise. Apart from a cold ambient room temperature, it has been shown that surgical patients lose 0.25°C of body temperature for every liter of intravenous (IV) fluid administered (Rose et. al, 2013). Although IV fluids are not administered for every procedure, a 0.25°C body temperature change is a significant temperature drop that should be considered.

Studies have shown that there is a relationship between hypothermia in surgical patients and their risk of surgical site infection. Clinically, hypothermia can induce perioperative wound infections by eliciting vasoconstriction and impaired immunity. Lack of tissue oxygen and collagen deposition, due to vasoconstriction, can then defer proper wound healing (Rose et. Al, 2013). Unfortunately, perioperative hypothermia has been shown to increase the length of hospital stays, cause cardiovascular stress, and decrease patient satisfaction (Rose et. al, 2013).

In an effort to mitigate the various causes of hypothermia, hospitals invest in warming equipment such as blanket and fluid warmers, which are discussed in more detail in section 4.3. Such equipment allows cotton blankets, intravenous fluid, and irrigation fluid to be kept at

temperatures above room temperature so that they can serve as a source of warmth to the patient when in use.

2.4 Thermal Properties

There are many thermal properties that contribute to the uncomfortable, cold sensation that patients experience when being prepared for a procedure or surgery. These properties and principles include evaporative cooling, as well as other physical and chemical properties of the ChloraPrep™ solution.

2.4.1 Evaporative Cooling

Evaporation is the process by which a liquid transforms to a gaseous state (Lohner, 2017). With a sufficient amount of energy any liquid can evaporate. The amount of energy needed for this phase change to occur is defined as the heat of vaporization. More specifically, the heat of vaporization is the amount of heat required to transform one gram of a liquid into a gas, without increasing the temperature of the liquid (Kirkham, 2014). It is important to note that the heat of vaporization is a latent heat. This means that the heat of vaporization is marked by a change in phase, not in temperature. The heat of vaporization varies depending on the liquid being observed as well as the surrounding temperature. For example, less energy is needed to vaporize liquid in warm temperatures than in cold temperatures (Lohner, 2017).

When a liquid changes to a gaseous state, hydrogen bonds must be broken. The more hydrogen bonds a molecule can form, the greater its heat of vaporization will be because more energy is required to break these bonds. Molecules with more hydrogen bonds will also have higher boiling points. Typically, liquids with lower boiling points will evaporate at a faster rate than liquids with higher boiling points (Lohner, 2017).

When gas flows over a liquid, it is called evaporative cooling (Bergman et al., 2011). Evaporation occurs when molecules at the surface of a liquid begin colliding with one another. For the process of evaporation to be sustained, internal energy must be provided from the liquid. This causes a reduction in temperature of the liquid, otherwise known as the cooling effect. However, to maintain steady-state conditions, the latent energy that the liquid loses needs to be restored through the transfer of energy to the liquid from its surroundings. This energy transfer can come from convection of energy from the gas or the addition of heat by other means.

An example of evaporative cooling that is present in daily life is the process of perspiration. Perspiration allows the human body to maintain homeostasis through the regulation of temperature. Typically, perspiration occurs due to an increase in environmental temperatures or the commencement of physical activity/exercise. The body is able to transform perspiration from its liquid form to a gaseous form. This process requires energy which is taken in the form of heat. The resulting heat transfer causes a cooling effect (Lohner, 2017).

2.4.2 Physical and Chemical Properties of ChloraPrep™ solution

As discussed in the previous section, there are certain properties of a liquid that will cause it to evaporate at a faster rate and have a greater heat of vaporization. As a baseline, water has a boiling temperature of 100℃ (212℉). Alcohol, on the other hand, has a boiling temperature of 82℃, which is significantly lower than that of water (Lohner, 2017). For this reason, alcohol will evaporate at a much faster rate than water. This means that the cooling effect of alcohol is greater.

Some other relevant properties of isopropyl alcohol and the ChloraPrep™ solution are compared in Tables IV and V below. Unfortunately, there are a lot of properties of the ChloraPrep™ solution that the manufacturer does not disclose. Because the solution contains isopropyl alcohol, those values will be utilized as estimates.

Table IV. Properties of Isopropyl Alcohol (Stockmen's Supply, 2018)

Property	Associated Value/Information
Color	Clear
pH	6-8
Melting Point	Not available
Freezing Point	-89.5℃
Boiling Point	190°F
Flash Point	77°F
Flammable Limits	2%-12%
Vapor Pressure	25 mm Hg at 66°F
Explosive Properties/Limits	Containers exposed to intense heat should be cooled with water to prevent vapor pressure build-up, which could result in container rupture.

Table V. Properties of ChloraPrep™ Solution (Medline, 2017)

Property	Associated Value/Information
Color	Clear, orange, or teal
pH	7 - 7.5
Melting Point	Not available
Freezing Point	Not available
Boiling Point	Not available
Flash Point	67°F
Flammable Limits	2%-12%
Vapor Pressure	Not available
Explosive Properties/Limits	Not available

2.5 Importance of Patient Experience

Patient experience is a subjective factor in every hospital that should not be overlooked. It reflects the healthcare system and therefore should optimally serve society by satisfying its customers (Jackson, 2001). One way of quantifying this service is given by The Centers for Medicare and Medicaid Services who has a Value-Based Purchasing Program that includes Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS) scores. The HCAHPS scores measures the patient's' impression of care during their stay at a hospital or healthcare facility and is mandatory for hospitals to receive any payments from Medicare. Those facilities that do not meet a defined performance standard are penalized through reductions in Medicare payments (Ehwerhemuepha, 2018). Hospitals enrolled in Medicare care plans have better performance in dealing with customer service and obtaining information on health plans in the US (Jha, 2008).

The HCAHPS survey asks 27 questions about the patients' experience in the hospital and demographics. A few questions relate to communications with physicians, nurses, about medication, quality of nursing services, planning for discharge, pain management, room

cleanliness and quietness. The survey also asks a global rating of the hospital on a 0 to 10 scale and whether the patient would recommend the hospital to family and friends, Hospitals with a high level of patient satisfaction such as those in the top quartile of HCAHPS ratings are of better quality than those in the bottom quartile (Jha, 2008).

One study examined the effects of three variables on patient experience. These three variables pertaining to the nurse staffing included staffing levels, skill mix, and staffing flexibility. They found that staffing flexibility has the most positive impact on patient experience. Many nurses work part-time because their job can be stressful with increased understaffing and irritable patients. Part-time employment can reduce burnout for employees of this profession and improve performance. A less taxing working environment can elicit better patient care compared to full-time nurses (Oppel, 2018). Although nurses do not prepare the skin, this provides useful insight into what factors affect patient experience. A friendly staff member who mentions that a cold sensation will be felt gains the patients trust. A patient who trusts their caregivers will feel more comfortable and satisfied with their experience. Warm sensations can elicit feelings of comfort that a cold sensation cannot. A warm antiseptic solution could make a small impact on the patients' experience before a procedure. Nurse staffing could help with this type of impact on patient experience based on how they are trained to treat the patient.

Patients of all ages must be considered. In pediatrics, a study analyzed clinical variables and psychosocial factors as well as the child HCAHPS survey responses (Ehwerhemuepha, 2018). A few of the clinical variables mentioned were length of stay, pain intensity scores, number of chronic conditions, number of hospitalizations, and inpatient surgeries. Some psychosocial variables included were legal custody issues, domestic concerns, alternate medical care and request for spiritual care. They found that parents who are dealing with custody issues, have a male child, or have a child with a chronic medical condition are less likely to recommend the hospital. This may relate to the stress of going through custody battles and familial hardships. If the parents feel like the caregiver did not explain what to look for after they were discharged or that the doctor did not listen to them or ask questions that a family member would know best about the child, they are less likely to recommend the hospital and perceive that the nurses did were not respectful and courteous. Meanwhile parents of low socioeconomic status and those with children who do not have chronic medical conditions are more likely to recommend the hospital. This may relate to different expectations of care and the need for more complex care. Although the child HCAHPS

scores give a general indicator of the importance of hospital to patient communication, the responses are from the children's parents, not the patient themselves.

The adult HCAHPS scores are taken from the adult patients themselves. About 2429 scores had low scores in pain control and discharge instructions. Patient experience can vary across regions and reflects the difference in quality management and organizational leadership (Jha, 2008). Unmeasured variables such as cultural differences and expectations of care at for-profit and not-for-profit hospitals may have an impact in experience as well. While people who are older are more likely to give positive recommendations compared to younger people as reported by a study on the predictors of patient satisfaction, this only accounts for a small percentage of the total effect on satisfaction after adjustments are made according to their satisfaction models (Jackson, 2001). Communication barriers such as unfriendly doctors, lack of empathy and enthusiasm, failure to consider patient's concerns, lack of explanation about the patient's condition, and excessive use of medical jargon are also only a small portion of the significant factors. Poor mental and physical health may influence satisfaction, but not as much as the health outcomes of the visit. While this study only used how patients would in theory judge satisfaction, 80% said that the health outcome was the most important variable along with unmet expectations, of which hospital staff are not aware. The team hopes to alleviate one source of unease for the patient in an attempt to increase satisfaction.

2.6 Injection and Blow Molding of Disposable Medical Devices

In the manufacturing of medical devices with plastic components, there are two types of molding processes that are regularly used – injection molding and blow molding. Both manufacturing processes have their benefits, however, choosing one is typically based on the type of product being produced.

While utilized to produce medical devices, injection molding is also used to manufacture common, everyday items – from small plastic parts, to chairs, to automobile parts. Injection molding has become of interest to the team as the manufacturing method of a redesigned skin preparation applicator due to its economic viability and the volume of product it can quickly produce. Additionally, injection molding allows for complex parts to be produced in a single rapid and automatic operation, unlike other manufacturing processes (Ebnesajjad, 2015). It is this single

operation that allows injection molding to be economically feasible, despite the high cost of molding press machines and molds due to the high pressures they are required to withstand.

Conventional injection molding is a simple, understandable principle. Simply put, during injection molding, a melted polymer is injected into a mold where it can cool and mold to the shape of the desired product (Seow and Lam, 1997). To go into more detail, the chosen plastic resin, a thermoplastic polymer, is heated until it converts from a solid polymer to a molten fluid with low viscosity. The melted resin is then injected into a closed mold of the chosen product shape within the molding press. The low viscosity of the molten resin allows for the mold to fill completely. High injection pressures are needed due to the viscosity of the melts, so a large amount of force is needed to hold the mold closed while it is filling. The material is then cooled until it solidifies, and then the mold is open, and the finished part is removed (Ebnesajjad, 2015). Although the principle is simple to understand, the practice of injection molding can be complex due to the complexity of some plastic melts and the design of molds needed to produce a product.

While conventional molding is useful for solid parts, it does not allow for the manufacturing of hollow or thin-walled products. Gas-assist injection molding was created in order to overcome this shortcoming. The process to produce a gas-assist injection process differs from the conventional process: first, pressurized nitrogen gas is injected into the melt and permeates the part (Hansen, 2005). Next, compressed nitrogen gas is injected. During the injection of this gas through the plastic's core, a portion of the molten plastic is displaced. Following the gassing phase, pressure is released by gas recycling or by releasing the gas back into the atmosphere. Once ambient pressure is obtained, the final part is then ejected from the mold (Hansen, 2005). Gas-assist can be used for simple hollow, tube-shaped parts and thin-walled parts, and is more versatile than conventional injection molding.

In addition to injection molding, blow molding is also a manufacturing method being considered by the team. Blow molding is typically used to manufacture high volume, one-piece hollow products. Products that are typically blow molded are items such as water or soda bottles, shampoo bottles, or any other hollow plastic product. Like injection molding, the shape of the end product is determined by the mold details (Lee, 2000).

The blow-molding process utilizes a parison, or pre-form, that is a plastic resin hot tube (Lee, 2000). This pre-form is placed within a split mold that has a hollow cavity. The sides of the mold are then clamped shut together, which seals the pre-form. Air is blown into the tube, expanding

the wall of the melted resin into the desired shape of the cavity. Following this, the mold is cooled with water. This solidifies the resin into the shape of the part so that it can be ejected from the mold. Once the part is ejected, it typically requires trimming of excess product and finishing (Lee, 2000). The blow molds used have a number of parts, but most commonly consist of two halves. These halves, when closed, form a cavity that enclose the pre-form, mentioned above, for blowing. These mold haves contain built-in channels for the cooling water used to solidify the molded product (Lee, 2000).

Unlike injection molding, blow molding does not require high clamping or blow pressures (Lee, 2000). Therefore, the blowing mold does not need to be made with a high tensile strength material. However, a high tensile strength material is typically recommended for molds with a long production run – these molds are usually made of steel. Typically, though, blow molds are machined from aluminum billet, cast aluminum alloys, zinc alloys, or bronze (Lee, 2000).

Both injection and blow-molding are practical manufacturing options for the redesigned skin preparation applicator. The selection of a final manufacturing method will be based on the final product design, and the volume of sticks to be produced.

2.7 Prototyping of Medical Devices

While a medical device design is still being finalized, it is essential to create prototypes. These prototypes allow the design team to create improved iterations of the device, by putting each prototype through a set of different tests. Once the final prototype is perfected, the design can then go on to be mass manufactured. If the final design includes plastic components, the manufacturing process often includes injection or blow molding, as discussed in section 2.6.

The MQP team will begin by creating prototypes of their final chosen design. When prototyping, typically designers have the option to 3D print components. For this project the team will send a SolidWorks model to a rapid prototyping lab in order to 3D print the stick component of our skin preparation stick. However, the team also must purchase additional materials such as sponges and rubber and self-assemble them with the 3D printed stick. This step is necessary in order to fully test our prototype and identify any changes that need to be made.

Prototyping often does not stop at just one prototype. Time depending, the team expects to have three different iterations of their design by the end of this project. Each design will include

minor changes and any improvements we deem necessary during testing. It is not until the final prototype functions optimally that the design is able to be manufactured.

3 Project Strategy

A project strategy has been established in order to ensure that the project has a positive final outcome. This section of the report outlines ideas about the solution to the team's design, and what the team intends to do in the project. It first begins with the initial client statement. Then, technical design requirements are discussed along with design requirements based on standards. A revised client statement is discussed. Lastly, a management approach of the project is explained.

3.1 Initial Client Statement

As presented by the team's advisor, Professor Jeannine M. Coburn, PhD and sponsor, Dr. Sarwat Hussain, MD, the initial client statement is:

> *"Develop a method to integrate warming into skin preparation applicators for interventional or surgical applications."*

This statement is sourced from Dr. Hussain's personal experiences when attending patients in the Interventional Radiology department at UMass Medical School. As previously mentioned, Dr. Hussain states that the alcohol-based antiseptic solution causes discomfort in patients in the form of a chilling sensation upon application.

Throughout the course of the team's initial literature review, along with discussions with both Professor Coburn and Dr. Hussain, a revised client statement has been developed in Chapter 3.4.

3.2 Design Requirements – Technical

This section discusses the various design requirements of the project. First, the project objectives will be identified. Then, the different constraints will be outlined. Lastly, design functions and specifications will be presented.

3.2.1 Objectives

Based on the initial client statement, the team gathered more information through meetings with their advisor as well as through research. Using this information, the team was able to develop

several objectives, which are listed below. These objectives are ranked based on importance in a pairwise comparison chart.

1. **Design or develop a device or method for pre-warming the skin preparation applicator:** The problem that Dr. Hussain has observed with the current process of skin preparation is the shocking cold sensation experienced during skin preparation. The low boiling point of isopropyl alcohol causes it to evaporate at a faster rate than water. This property combined with the ambient temperature in the operating/procedure room (which is below typical room temperature) causes an extremely cold sensation when the antiseptic is applied.
2. **Improve overall patient experience:** Surgical and other medical procedures put patients in an already vulnerable and anxious position. Any discomfort that can be avoided/eliminated during a surgery or procedure should be taken into consideration. Increased patient comfort and satisfaction has been shown to improve the healing process.
3. **Create a universal design that could be applied to comparable skin preparation applicators on the market:** For the purposes of research and design, the team is focusing on the ChloraPrep™ skin preparation applicator. Despite this, it is the team's goal to develop a device or method that could be easily adapted to any other skin preparation applicators on the market. This would allow the team's device to be accessible to a wider patient population.
4. **Ensure safety of the patient and medical staff:** The antiseptic solution used in the skin preparation applicators can be flammable or even explosive when heated past certain temperatures. The team must ensure that the applicator is warmed to a temperature that will not put the patient or medical team in danger.
5. **Create a cost-effective device that is not a significant cost increase from the current devices on the market:** While patient experience is important, it may not be prioritized over cost if the new device is significantly more expensive than current devices. For this reason, the added cost must be worth the added value. **The team will add current product cost from a reliable source. We plan to ask Dr. Hussain how much UMMS pays*

for the product in bulk and how the insurance company reimburses the hospital. Once this information is obtained, this objective will be clarified and expanded on. *

6. **The device should maintain its original functionality:** Skin preparation applicators are ultimately used to eliminate bacteria and other contaminants from the surgical site. The new design must maintain the antimicrobial properties of the current devices on the market.

3.2.2 Constraints

Something necessary to consider in the design requirements of the project are different constraints. The constraints that were identified must be considered to define the limitations of the project, along with its success. The identified constraints and their definitions can be seen in the Table VI below.

Table VI. Applicable Project Constraints

Constraint	Definition
Budget	A total budget of $1000
Time	Project must be completed by April 19, 2019
Sterility	Device must be contained in a sterile package
User Friendly	Should not require additional training to medical personnel
Inexpensive Fabrication	Cost increase should be less than 25% (subject to change)
FDA & AST Regulations	Must satisfy current regulations regarding proper surgical preparation procedures

The project team must work within these limitations to successfully complete the project. The first constraint identified is the budget. The team has an overall budget of $1000, or $250 per team member, for testing, prototyping, and purchasing materials. The second constraint is time. The project must be completed by project presentation day, which falls on April 19, 2019. School breaks (e.g. WPI vacation days, national holidays) must also be accounted for within this constraint. The third constraint is sterility. Currently, skin preparation applicators are contained in a sterilized package and any modification made must not interfere with the device's ability to be contained in a sterile package. Additionally, modifications to the device designed must also be sterilized. Regarding device handling and use, the device must remain user-friendly and require no additional training to medical personnel. It should also be inexpensive to fabricate, and not require a price increase of more than 25%. Lastly, the device should continue to satisfy FDA and AST standards for surgical preparation procedures.

3.2.3 Functions

The team identified the key functions for the redesigned skin preparation applicator, which are explained in Table VII. The primary function of this project includes reducing the amount of patient discomfort by warming the antiseptic solution by approximately 10°C. Through various heat loss calculations performed, it was determined that raising the temperature by 10°C should essentially eliminate the initial chilling sensation when the antiseptic fluid is applied on the patient's skin. Ideally, the temperature of the antiseptic be about that of skin. However, to prevent skin irritation or burns, the temperature of the antiseptic should not be increased to a value beyond body temperature. Possible means of achieving the function of warming the antiseptic solution include dry heat, hot water bath, or heat of mixing reaction. Dry heat such as steam or hot glass beads could warm the solution and sterilize at the same time, however this requires additional machinery which is expensive and takes up space. A hot water bath will not maintain sterility if the device is opened outside of its original packaging. If the device is still in the original sterile packaging, the whole package would have to be submerged into the bath. This would include the paper materials and safety sheet along with the device which is not ideal because the goal is to warm the antiseptic solution, not the whole device including material and safety sheet. The last means of achieving the function is the heat of mixing reactions. This mean was chosen because the reaction can take place directly outside of the antiseptic solution holding tube. The materials are inexpensive, accessible, and do not require additional machinery since they can be used inside of the device.

The second design function is a method of releasing the antiseptic solution from its container. At first a shaking mechanism could be used in order to break a membrane that separated the solution from outside of the device. This was ruled out because depending on how sensitive or fragile the membrane was, it could be easily broken or fractured during transport thereby starting the reaction prematurely. Another means was to squeeze the inner tube to break and release the solution. This is how the solution is administered in the current applicator stick, but this method does not include a warming function. Squeezing to fracture was ruled out because there exists the possibility of the antiseptic solution mixing with the heat of mixing reaction. If mixing occurs, the solution may lose antiseptic properties and the reaction products could end up being administered onto the patient's skin. The last mean was the use of pull tabs. Separate chambers each holding either the antiseptic solution or the heat of mixing products would be sealed using rubber pieces

cut to fit the opening of the chambers. When these rubber tabs are pulled, the contents of that chamber will be allowed to flow to the destination.

Table VII. Design Functions

Design Function	Means of Achieving Function		
Warming antiseptic solution	Dry heat	Hot water bath	Heat of mixing reaction
Release of antiseptic from inner tube	Shaking device	Squeezing inner tube to fracture	Pull tabs

3.2.4 Specifications

The design must fall under specifications determined by the team. These specifications include warming the antiseptic solution to 40°C that will reduce patient discomfort. Additionally, the device must hold no less than 10.5 mL of antiseptic solution because this is the smallest amount of fluid one applicator can hold. The device must also maintain its original antiseptic properties in order to reduce the risk of infection. This is quantified by a 4-log It is essential that the warmed antiseptic solution kill just as much bacteria as the currently used model. The device must also be able to undergo a sterilization process before use. Since skin preparation sticks are often used in surgical suites, they must be contained in sterile packaging in order to avoid bring contaminated items into the suite. Finally, the team determined that the new device should not have a significantly higher price than those currently on the market. The team's prototype cost $57 to produce, however this was 3d printed as a single device. When manufactured on a large scale, this price should decrease significantly. For the most patients to benefit from the warming skin preparation applicator, insurance companies must be willing to cover the cost of the new device.

3.3 Design Requirements – Standards

This section discusses different industry, engineering, and regulatory standards. Topics such as sterility and the warming of antiseptic agents will be discussed. Additionally, the team will also cover other standards such as those from the Association of Surgical Technologists (AST), US Food and Drug Administration (FDA), and the International Organization for Standardization (ISO).

3.3.1 Association of Surgical Technologists (AST)

The first set of standards that the team will adhere to are the ones set in place by the Association of Surgical Technologists (AST). The AST has ten standards of practice for skin preparation on a surgical patient. The ChloraPrep^{TM} applicator that is currently used, along with the team's future modifications, are expected to follow these standards. Although skin preparation applicators fall within the overarching category of skin preparation, three AST standards are directly relevant to them: Standard of Practice II, Standard of Practice III, and Standard of Practice VIII. It is critical that the team's final design satisfy these AST standards in order to ensure a safe device that is able to benefit patients during their pre-procedural skin preparation.

Standard of Practice II specifies that for pre-procedural skin preparation, healthcare facilities should use FDA-approved agents that possess immediate and persistent antimicrobial properties (AST Education and Professional Standard Committee, 2008). FDA standards will be discussed in section 3.3.2. Standard of Practice III states that alcohol should not be used as a single agent for pre-procedural antiseptic purposes. For the team's design to be considered effective by the AST, alcohol may be used, but an additional, longer-lasting antiseptic agent must be included (AST Education and Professional Standards Committee, 2008). Standard of Practice VIII states that if a skin preparation solution is flammable, it must not be warmed, per manufacturer's instructions. This standard is of particular interest and concern to the team, as warming skin preparation solution is one of the goals of the project.

3.3.2 U.S. Food and Drug Administration (FDA)

The project team also must abide by current FDA regulations. Antiseptic agents, such as those within a skin preparation applicator, are regulated under the FDA's Over-the-Counter Drug Products division ("Safety and Effectiveness", 2017). It is stated that when antiseptic agents are being chosen, the following factors must be considered:

1. The ability to reduce transient microorganisms
2. The possession of a broad range of antimicrobial properties
3. Fast-acting and long-lasting activity
4. Potential irritation to the skin

Additionally, the team's final design would require additional FDA approval. As of December 20, 2018, chlorhexidine-gluconate and iodophors will not be generally recognized by the FDA as safe

for use in antiseptics (“Safety and Effectiveness”, 2018). The team’s current plan is to modify a pre-existing skin preparation applicator that contains chlorhexidine-gluconate. This means that in order for modification and updated product to be FDA approved, a New Drug Application will need to be submitted.

3.3.3 International Organization of Standardization (ISO)

The final set of standards to be considered by the team are ISO standards. The first ISO standard of importance to this project is ISO 11737-2:2009 – Sterilization of Medical Devices. This standard “specifies the general criteria for tests of sterility on medical devices that have been exposed to a treatment with the sterilizing agent reduced relative to that anticipated to be used in routine sterilization processing” (“ISO”, 2015). The standard states that the tests should be done while defining, validating, or maintaining a sterilization process. Additionally, ISO 13485:2016 must be considered. This standard sets requirements for the quality management systems within the medical device industry (“ISO”, 2016). Furthermore, ISO 15378:2017 is an application standard regarding the packaging materials used for medical devices. If the team decides to alter the ChloraPrep™ packing material, or applicator material itself, then this standard must be considered ("ISO”, 2017). Additionally, with any modifications of materials comes further material testing. ISO 10933-1:2018 is a standard that applies to any medical devices that indirect or direct contact with the patient’s body during intended use (“ISO”, 2018). This document specifies how to assess the biological safety of a medical device through appropriate methods and tests. This standard will be adhered to by the team in order to ensure proper testing is performed regarding the safety of our device.

3.3.4 European Standards and Criteria

To confirm that the redesign of the device does not jeopardize the effectiveness of the antiseptic solution, the team considered the European standards and criteria that the ChloraPrep™ antiseptic solution is currently compliant with. European (EN) standards are voluntary standards ratified by one of three European Standards Organizations ("What is a European Standard”, 2019). According to the ChloraPrep™ Summary of Product Characteristics document, because it a product used worldwide, the antiseptic solution meets the following criteria from chemical disinfectants and antiseptic products established by European Standards: EN 1040, EN 1275, EN

13727, and EN 13624 (ChloraPrep™, 2016). Although the team's new product was designed in the United States, in order to effectively market it it in the future, all current standards should be upheld. The following text explains each standard the performance criteria to meet the standard, and the general protocol each standard follows (Accuratus Lab Services, n.d.).

- EN 1040: Basic Bactericidal Activity of Chemical Disinfectants
    - EN 1040 is designed to evaluate the basic bactericidal activity of chemical disinfectants and antiseptics.
    - For an antiseptic agent to meet the criteria of EN 1040, there must be at least a 5-log reduction in test organism viability after exposure to the antiseptic for a maximum of 5 minutes.

- EN 1275: Basic Fungicidal or Basic Yeasticidal Activity of Chemical Disinfectants
    - EN 1275 is designed to evaluate the basic fungicidal or yeasticidal activity of chemical disinfectants and antiseptics.
    - For an antiseptic agent to meet the criteria of EN 1275, there must be at least a 4-log reduction in test organism viability after exposure to the antiseptic for a maximum of 15 minutes.

- EN 13727: Bactericidal Activity in the Medical Area
    - EN 13727 is designed to evaluate the bactericidal activity of products (i.e. handwashes and disinfectants) that are used in the medical area.
    - For an antiseptic agent to meet the criteria of EN 13727, there must be a 3- to 5-log reduction in test organism viability after exposure to the antiseptic for 1 to 5 minutes, based on the specific protocol or claim.

- EN 13624: Fungicidal or Yeasticidal Activity in the Medical Area
    - EN 13624 is designed to evaluate the fungicidal or yeasticidal activity of products that are used in the medical area.
    - For an antiseptic agent to meet the criteria of EN 136274, there must be a 4-log reduction in test organism viability after exposure to the antiseptic for a maximum of 60 minutes.

The European Standards mentioned above all call for of a suspension-based study to be completed, in which the test organism (i.e. microbial/bacterial agent) is exposed to a test sample (i.e. chlorhexidine gluconate in isopropyl alcohol). After reaching the target exposure time, the test suspension solution in neutralized to halt further antimicrobial activity of the antiseptic solution. To test for test organism survival, samples from the suspension solution are plated and incubated. After incubation, a reduction in viability is determined by comparing the plated sample to the initial bacterial count and the bacterial count on the control plate.

3.4 Revised Client Statement

Following further discussion of the project requirements, the revised client statement for the project is:

> *"Develop a device improvement or a skin preparation method that can reduce patient discomfort during antiseptic application."*

The team revised the client statement in an effort to broaden the scope of project design. Rather than limiting the scope to adding an element in the current device design that will warm the patient's skin, the team understands that root source of the project need is the patient discomfort. Any design that will reduce discomfort with improve patient experience.

3.5 Management Approach

In an effort to address the constraint of time, the team is following a Gantt chart (Figure II) that was created to display key hard and soft deadlines and project phases.

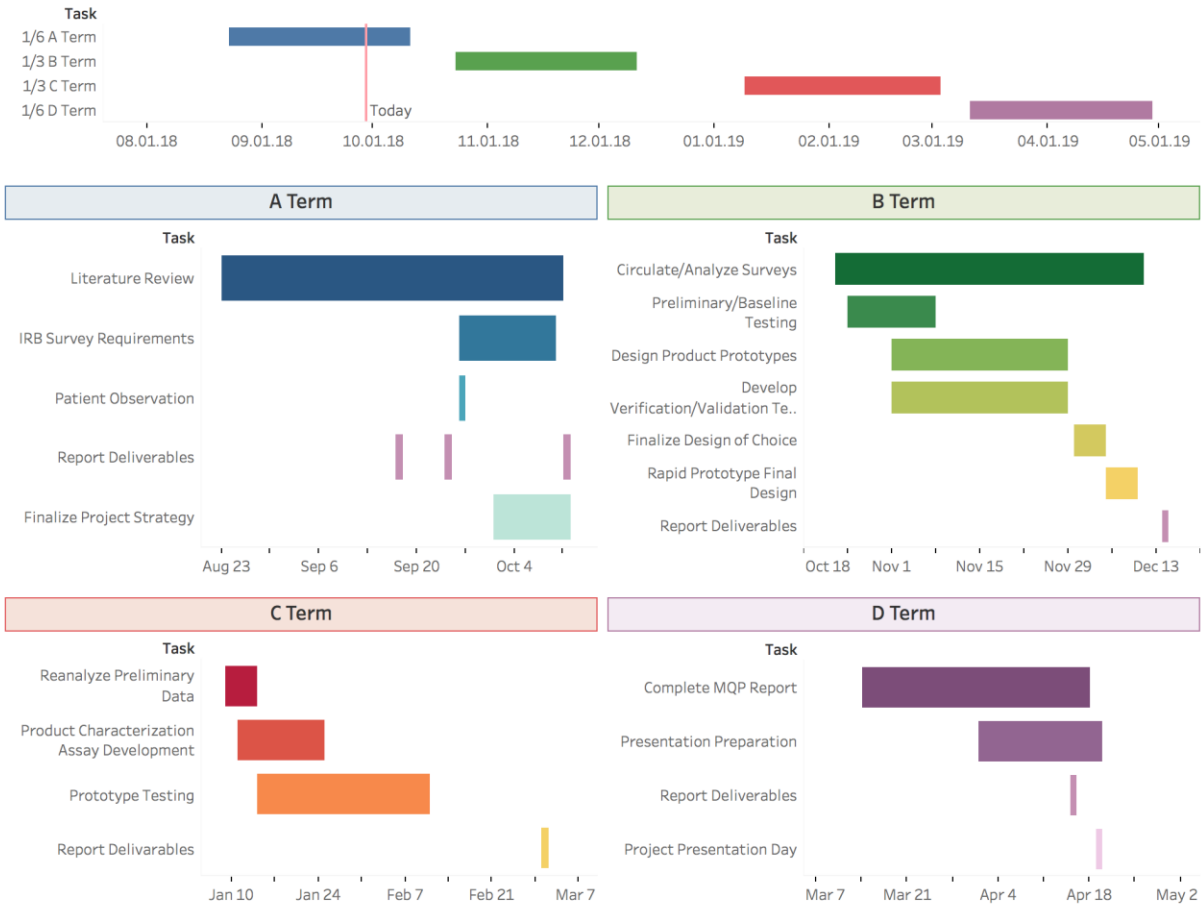


Figure II. Gantt Chart

4 Design Process

Following the development of a project strategy, the design process begins. The project strategy is how the team created a plan for the successful completion of this project. Within the project strategy, the design requirements for the project were stated and ranked based on importance. This chapter will begin with a need analysis, which will rank objectives by weight. It then moves into a discussion regarding conceptual design. The different means by which the project objectives could be accomplished are then identified and discussed. Finally, all alternative designs are evaluated in order to choose the most feasible and effective final design.

4.1 Needs Analysis

The project objectives were ranked by importance by the project team. Table VIII below lists the project objectives in order of importance.

Table VIII. Pairwise Comparison of Project Objectives

	Patient Experience	Universal	Safe	Cost-Effective	Functional
Patient Experience	-	0.5	1	0.5	1
Universal	1	-	1	1	1
Safe	0.5	0.5	-	0.5	0.5
Cost-Effective	1	0.5	1	-	1
Functional	0.5	0.5	1	0.5	-
Total	**3**	**2**	**4**	**2.5**	**3**.5

In Table VIII above, the - symbol represents a null value and is used when comparing two identical needs. A score of 0.5 is given when the need in the column is deemed less important than the need it is being compared to in the row. Finally, a score of 1 means that the need in the row was identified as less important than the need in the column.

Following the prioritization of the project objectives, the team identified the wants and needs. In this case, a need is something that is essential for the project to be successful. Based on the ranked objectives seen in Table 2, the needs for this project were identified to be: safety, functionality, and improved patient experience.

For this project, a "want" is something that, while it may beneficial to have, is not critical. Although the identified "wants" could improve the outcome of the project, they are not necessary in order to complete the project successfully. Based on the ranked objectives from the table above, the wants were identified to be cost effectiveness and a warming method.

4.1.1 Objective Definitions

Following the ranking of the project objectives, it is important to understand what is meant by each of them. The first objective considered was patient experience. When designing a new skin preparation applicator, one of the team's goals is to enhance the overall patient experience. The team hopes that this can be achieved by providing them with an improved preparation process for their procedures. The next objective was universality. Although the team is primarily designing a skin preparation application that contains Chlorhexidine Gluconate, the team hopes to create a universal design that can also be used for other skin preparation solutions. Next is safety. It is imperative that the skin preparation procedure remains safe for both the patient and medical personnel, with no risk of injury. Another objective is for the device to be cost-effective. For the team's new design to have the largest impact on patient experience, it is critical that the design is covered by insurance companies. To ensure this, the price of the new device should not increase substantially. Finally, the team considered functionality. While our goal is to enhance the patient experience, it remains vitally important that the applicator performs its original function – to reduce the presence of bacteria on the skin before a procedure.

4.2 Conceptual Design and Concept Map

In order to produce a preliminary conceptual design for a skin preparation applicator with warmed solution, it is easiest to divide the design into smaller sections. The first part to consider is the type of antiseptic being used in the updated skin preparation applicator. Dr. Hussain, the team's sponsor, would like to continue using ChloraPrep^{TM} applicators as skin preparation agents. Thus, this is the primary target for the design team. However, alternative antiseptic solutions, such as those that contain povidone iodine, should be considered to determine which can be heated most efficiently while retaining their antiseptic properties. Next, the general warming method must be selected. The sponsor's preference is to warm the antiseptic solution by way of a modification to the physical skin preparation applicator. The team will also consider other options, such as

externally warming the applicator or a method of pre-treating the patient's applicator, to ensure that an applicator modification is the best choice. The specific warming mechanism will then be chosen by the team. For example, if the team decides on designing a modification to the applicator, the specific warming method then needs to be determined. The team will consider different options, such as various exothermic reactions. Finally, any new device designs or modifications needed to house the warming method will be created. These steps to creating a final conceptual design can be seen in Figure III below.

Figure III. Concept map for the warming of a skin preparation applicators

4.3 Alternative Designs

Based on the team's initial research, it was clear that there were three general methods that could be executed to fulfill the needs of the client: external warming, internal warming, and desensitization of the skin. These methods have been analyzed in depth in the following sections. Ultimately, one method will be selected as the final design solution.

4.3.1 External Warming Methods

Warming the skin preparation applicator using an external method would involve increasing the temperature of the antiseptic solution via a heating source that is not integrated with the existing device. In other words, an external heating method would not require any changes be made to the existing device. Instead, an external device would be designed/utilized as a source of heat for the skin preparation applicators. The following are potential solutions utilizing an external method of warming.

4.3.1.1 *Dry Heating Unit*

The team could design a device, much like an incubator, that utilizes a form of dry heat (such as steam or hot glass beads) to keep the antiseptic solution in the device warm. This device would be installed permanently in procedure rooms and/or operating rooms and the skin

preparation applicators would be stored inside until use. Currently, healthcare settings, including UMMS, rely on warming cabinets that warm medical blankets to comfort patients and increase a patient's body temperature. Pedigo, a medical equipment company, manufactures warming cabinets that warm cotton blankets. Additionally, Pedigo manufactures fluid warming cabinets that are designed to warm medical irrigation and intravenous fluids. Warming fluids above room temperature can reduce the severity and potentially lower the incidence of perioperative hypothermia (Singh et. al, 2014). In addition to blanket and fluid warming cabinets, healthcare settings also utilize warmers, like the THERMASONIC® Gel Warmer, to warm ultrasound gels to body temperature prior to use. Although these solutions exist and are used in industry, a barrier or disadvantage of such equipment is the cost. Table IX below provides the manufacturer's suggested retail price (MSRP) of the equipment mentioned above (Universal Medical Inc., 2019). The retail cost of the equipment appears to be the main drawback. For example, if a hospital were to supply every unit that uses irrigation or intravenous fluid with a fluid warming cabinet like the Pedigo Solution Warming Cabinet, the total cost would easily reach hundreds of thousands of dollars.

Table IX. Cost of External Medical Product Warming Equipment (Universal Medical Inc., 2019)

Blanket Warmer	Fluid Warmer	Ultrasound Gel Warmer
Pedigo Blanket Warming Cabinet Compartment Size: 2.3 cubic feet MSRP: $4,438.70	**Pedigo ivNow Fluid Warming Pod** Compartment Size: 3 fluid bags MSRP: $3,846.00	**THERMASONIC® Gel Warmer** Compartment Size: 3 gel bottles MSRP: $223.00
Pedigo Blanket Warmer with Dual Glass Compartment Size: 20.6 cubic feet MSRP: $13,991.40	**Pedigo Solution Warming Cabinet** Compartment Size: 7.7 cubic feet MSRP: $15,394.90	

4.3.1.2 *Hot Water Bath*

The team could design a hot water bath with temperature controls to warm the skin preparation applicators prior to use. This hot water bath would ideally by stored in the procedure/operating room and the skin preparation applicators could be retrieved as needed before the procedure. The biggest challenge with this design idea is the ability to maintain the sterility of the skin preparation applicator. Skin preparation applicators are contained within sterilized packaging. Placing the packaged skin preparation applicator in a hot water bath would jeopardize

the sterility of the skin preparation applicator (as the water would likely soak through the packaging, which is partially composed of paper).

4.3.2 Internal Warming Methods

Warming the skin preparation applicators using an internal warming method would involve integrating a heating component directly into the design of the skin preparation applicator. This would require a redesign of the existing device to incorporate a heating element. The following are some potential solutions that utilize an internal method of warming.

4.3.2.1 *Exothermic Reactions*

By definition, exothermic reactions are chemical reactions that release energy in the form of heat into the surrounding as a product of the reaction (Bergman et. al, 2011). The following equation represents this phenomenon:

$$A + B \rightarrow C$$

The team researched three exothermic reactions that could potentially warm the antiseptic solution stored inside the glass ampoule of the ChloraPrep™ applicator. The three exothermic reactions are as follows:

<u>Sodium Acetate Crystallization</u>

$$CH_3COO^- (aq) + H_2O (l) \rightarrow CH_3OOH (aq) + OH^- (aq)$$

With a heat of fusion ranging from 264–289 kJ/kg, the crystallization of sodium acetate from a supersaturate solution is a phenomenon that is used in conventional hand warmers. A solution of concentrated aqueous salts is sealed in a flexible container with a metallic activator strip usually made of stainless steel. The metal strip is bent, and crystals begin to precipitate. When the first crystal forms, the whole pack fills with solid crystalline needles of sodium acetate. This crystal formation releases heat and the temperature rises to 130 °F for approximately 30 minutes (Supersaturated solution, 2013). In small quantities with controlled heat production, this reaction could be beneficial towards our objective of internally warming the antiseptic solution.

Quicklime and Water

$$CaO\ (s) + H_2O\ (l) \rightarrow Ca(OH)_2\ (aq)$$

Quicklime (calcium oxide) and water are known to produce an exothermic reaction (United States Patent, 1985). It is used as a device for heating food in a sealed container such as a tin, can or carton without the use of external heat. The benefits of this approach are that it does not generate hydrogen gas as a byproduct as other common exothermic reaction do such as magnesium and water (Researchers Submit Patent Application, 2013). The quicklime is separated from the water by a watertight seal or membrane that is easily broken using mechanical means. Water and quicklime produce heat, which is transferred by conduction to the food in the container. Some drawbacks of this method are the amount of water needed to produce this reaction, more than three-parts water by weight to one-part by weight of quicklime. This could pose a problem to the team's design because the preparation applicator must be comfortable to hold. A large amount of water in the device would increase the size. Also, the presence of humidity of the air can damage the quicklime and reduce the heating capacity. The energy of the system is low, approximately 1.2 kJ/g of calcium oxide (Researchers Submit Patent Application, 2013). The mixture is not homogeneous, so uneven heating may occur. Strong heating causes the production of water vapor which increases the pressure inside the vessel and can cause explosions.

Porous Oxygen Activated Heater

$$Mg\ (s) + 2H_2O\ (l) \rightarrow Mg(OH)_2\ (s) + H_2\ (g)$$

While current flameless heaters use water to produce heat, water can be a hassle to carry in the device and the hydrogen gas byproducts create safety, storage, and disposal concerns. Oxygen-based heaters do not require water to generate heat. They only generate heat in the presence of oxygen which allows the reaction to be stopped and started by preventing or allowing oxygen access. Since oxygen is abundant in the atmosphere, this reaction does not require additional components in order to be initiated, only oxygen from the atmosphere. The porosity of the composite is what determines the efficiency of the heater. Since the Rechargeable Battery

Corporation sought a patent for porous oxygen activated heaters, more information needs to be researched. An example of this can be seen in Flameless Ration Heater (FRH). An improved flameless ration heater is used in US Army Meals Ready to Eat (MRE) which does not require water to heat the meals. This lowers the cost, weight and transportation burden of the other heating method. There is no hydrogen gas produced and the air activated heater can heat the meal 100 degrees Fahrenheit in less than 10 minutes (No water needed in new Army MRE heaters, 2015).

The team will use this research regarding existing exothermic reactions to redesign the ChloraPrep™ applicators to incorporate an internal warming method.

4.3.3 Desensitization of Patient Skin

Desensitization of the patient's skin is a method that does not involve changing the skin preparation applicators in any way. Instead, the patient's skin would be treated to reduce sensation in the area that required preparation. Desensitization techniques to decrease nerve pain include a program where the patient can either put the wounded area in baths with contrasting temperatures. This eventually trains the skin to feel cooler in the cold bath and warmer in the warm bath. Another technique is touch stimulation. Starting with a cotton ball, the painful area is stroked in one direction followed by a soft fabric such as silk, then a rougher fabric such as a towel. Eventually pain tolerance is increased with the stimulations in the wounded area (Back in Motion Physical Therapy, 2018).

4.3.4 Pre-warming of Patient Skin

Pre-warming the patient's skin could reduce the shockingly cold sensation felt during the application of the antiseptic solution. One way in which this pre-warming can be achieved is through capsaicin. Capsaicin is "a selective activator of the chemo- and heat-sensitive transient receptor potential (TRP) V1 cation channel", that also gives chili peppers their intense heat (Janos, 2015). In humans it has been found that at a concentration of 2×10^{-7} g/ml, capsaicin causes a warm sensation. In animal experiments, capsaicin has also shown to cause sensory desensitization (Janos, 2015). If applied to the patient's skin before the antiseptic solution, capsaicin can potentially reduce the sensation of the evaporative cooling from the ChloraPrep™.

Additionally, prior to the application of the antiseptic solution, the skin could be warmed using a forced-air blanket. Forced-air blankets are commonly used to warm a patient's skin surface

prior to the induction of anesthesia, in order to avoid hypothermia during surgery (Shin, 2015). One study showed that these blankets can increase core body temperature before surgery by as much as 0.5°C. Although patients' body temperatures still decreased throughout the procedure, by starting with a higher core temperature, they only dropped to 36°C as opposed to 35°C (Shin, 2015). Pre-warming the patient's skin with forced-air blankets could increase their starting skin temperature, and potentially decrease the cold sensation of ChloraPrep™.

4.4 Final Design Selection

At this stage in the completion of the project, the team has finalized their design. In order to come to reach this final design, the team conducted literature review and calculations to determine an effective chemical reaction to cause heating. Additionally, the team designed multiple physical applicator prototypes, constrained by the current size of the ChloraPrep™ stick and the preferences of our sponsor. Additionally, antimicrobial testing was completed in order to ensure the effectiveness of the ChloraPrep™ solution as a disinfectant after being warmed.

4.4.1 Heat Loss Background Information

Energy can take three main forms: kinetic energy, potential energy, and internal energy. Kinetic energy, E_k, is the energy possessed by a moving system due to its velocity. Potential energy, E_p, is a result of the position of a system in a gravitational or electromagnetic field or do to the conformation of the system relative to equilibrium. Internal energy, U, is the energy transferred as a result of any driving force, excluding a difference in temperature.

Energy can be transferred as heat or work. Heat energy is a type of energy that causes flow across system boundaries due to a temperature difference between the system and its surroundings. Work is energy transferred as a result of any driving force, excluding a difference in temperature.

Enthalpy, H, is the combination of two energy terms. It can be described by the following equation:

$$H = U + pV$$

The variables are defined as follows:

$U = internal\ energy$

$p = pressure$

$V = volume$

Specific enthalpy, h, is calculated using a similar, but slightly different equation:

$$h = u + pv$$

The variables are defined as follows:

$u = specific\ internal\ energy$

$p = pressure$

$v = volume$

Enthalpy, H, is an extensive value meaning that it is dependent on the size of the system. Specific enthalpy, h, on the other hand, is a specific quantity.

To understand the mechanism of heat transfer, it is crucial to understand the general principles of energy balances. In an energy balance, energy can be neither created nor destroyed. Instead, energy is transferred from one form to another. This can be expressed as a simple mathematical idea by saying the energy that leaves the system can be subtracted from the energy that enters the system to determine the amount of energy that has accumulate in the system. This idea can be expressed in the following variable form:

$$M_i(u + e_k + e_p + pv)_i - M_o(u + e_k + e_p + pv)_o - Q + W_s = \Delta E$$

The variables are defined as follows:

$M_i = mass\ in$

$M_o = mass\ out$

$u = specific\ internal\ energy$

$e_k = kinetic\ energy$

$e_p = potential\ energy$

$pv = work$

$Q = energy\ leaving\ the\ system\ as\ heat$

$W_s = shaft\ work\ performed\ on\ the\ system\ by\ the\ surroundings$

$\Delta E = total\ change\ in\ energy$

This equation can be simplified if kinetic and potential energy are negligible. The following is the simplified form of the equation:

$$\sum_{input} Mh - \sum_{output} Mh - Q + W_s = \Delta E$$

The variables are defined as follows:

$M = mass$

$h = specific\ internal\ energy$

$Q = heat\ energy$

$W_s = shaft\ work$

$\Delta E = change\ in\ energy$

Using this equation, it is possible to predict how much heat must be removed from or added to a system to achieve optimal conditions.

Enthalpy can occur as a result of a temperature change, phase change, mixing, or reaction. For the purposes of this study, enthalpy as a result of a temperature change will be the focus. Sensible heat is defined as the energy transfer required to increase or decrease the temperature. This can be determined using the heat capacity at constant air pressure, c_p. Specific heat capacity (or just specific heat) is a term used to describe c_p on a per-unit-mass basis. Change in enthalpy cannot be determined without the specific heat capacity. The following equation can be used to determine change in enthalpy, ΔH:

$$\Delta H = Mc_p\Delta T = Mc_p(T_2 - T_1)$$

Heat of reaction, ΔH_{rxn}, is the energy released or absorbed during a reaction.

$$\Delta H_{rxn} = \sum_{products} Mh - \sum_{reactants} Mh$$

$$\Delta H_{rxn} = \sum_{products} nh - \sum_{reactants} nh$$

M or n involves the actual mass or moles involved in the reaction.

An exothermic reaction occurs when the energy required to hold the atoms of the product together is less than the energy required to hold the reactants together. This results in the release of surplus energy, causing a negative value for ΔH_{rxn}.

Specific heat of reaction, Δh_{rxn}, depends on the reactants and products as well as the temperature and pressure. For this reason, it is not possible to calculate all possible values for Δh_{rxn}. Instead, Δh_{rxn} can be calculated using the heats of combustion, Δh_c. Δh_c is the heat that evolves during a reaction of a substance with oxygen to yield oxidative products such as gaseous carbon dioxide, gaseous nitrogen, and liquid water.

4.4.2 Heat Loss Calculations

The information in the previous section was used to determine the cooling of the skin / actual change in temperate of the skin during standard application of the Chlorhexidine skin preparation stick.

The following assumptions can be made:

1. Steady state system
2. $\Delta E = 0$

The following equation is used to perform the calculations:

$$m_1 \Delta h_v = m_2 c_p \Delta T$$

The variables are defined as followed:

$m_1 = mass\ evaporated\ of\ IPA$

$\Delta h_v = latent\ heat\ of\ IPA$

$m_2 = mass\ of\ skin$

$c_p = specific\ heat\ capacity\ of\ skin$

$\Delta T = T_1 - T_2\ = change\ in\ temperature\ (before\ and\ after\ the\ application\ of\ IPA)$

Some preliminary calculations were necessary to determine the values of the variables listed above. These calculations are shown below:

$m_1 = \rho_1 v_1$

$\rho_1 = density\ of\ IPA = 786 \frac{kg}{m^3}$ (PubChem, 2019)

$v_1 = volume\ of\ antiseptic = 1\ mL * \frac{10^{-6} m^3}{1\ mL} = \ 1 \times 10^{-6}\ m^3$

Above, the team assumed that a 1ml volume sufficiently covered a 4 cm radius of application site.

$m_1 = \ 7.86 \times 10^{-4} kg = 0.786\ g$

$\Delta h_v = 44.8 \frac{kJ}{mol} \times \frac{1}{Molecular\ Weight\ of\ IPA} = 44.8 \frac{kJ}{mol} \times \frac{1}{60.0950 \frac{g}{mol}} = 0.745 \frac{kJ}{g}$

$\Delta h_v = \ 745 \frac{J}{g}$ (NIST, 2018)

$m_2 = \rho_2\ A_2$

Typically, at the University of Massachusetts Medical School, the antiseptic is applied in an outward circular motion to create a radius of about 4 cm. Thus, this is the value that the team used to calculate the area of the skin below:

$\rho_2 = skin\ mass\ density = 1.02 \frac{g}{cm^3}$ $(Liang, 2010)$

$A_2 = \ area\ of\ skin = \pi(radius\ of\ skin\ \ being\ prepped)^2 = \pi(4cm)^2 = 50.265\ cm^2$

$$m_2 = \left(1.02 \frac{g}{cm^2}\right)(50.265\ cm^2) = 51.27\ g$$

$c_p = 4.186 \frac{J}{g℃}$ $(Bergman, 2011)$

$T_1 = 35.02℃$ $(Bierman, 1936)$

$T_2 = ?$

The following calculation was performed to determine the change in temperature:

$$m_1 \Delta h_v = m_2 c_p \Delta T$$

$$(0.786\ g)\left(745 \frac{J}{g}\right) = (51.27\ g)(4.186 \frac{J}{g℃})(35.02℃ - T_2)$$

$$T_2 = 32.29℃ \therefore \Delta T = 2.73℃$$

4.4.3 Heat of Mixing Calculations

Once the team calculated the heat loss on the skin caused by the application of the Chlorhexidine and Isopropyl alcohol solution, exothermic reactions were then further considered. The team calculated the necessary amounts of water and solvent for three different reactions to raise the temperature of the antiseptic solution to 40°C. After further discussion, the team decided to consider three reactions of salt in water, rather than those mentioned in section 4.3.2.1. The three salt and water reactions considered were lithium bromide and water, copper chloride and water, and lithium chloride and water. The following assumptions were made:

1. There is 100% efficiency of heat transfer between water, 70% isopropyl alcohol, and the given salt.
2. Chlorhexidine's effects are negligible.

The first equation used for this calculation is:

$$Q_{H_2O} = Q_{\text{IPA}}\ , where\ Q = energy = mc_p \Delta T$$

Since the applicator contains 70% isopropyl alcohol, Q_{IPA} was calculated assuming the solution to be 30% water and 70% isopropyl alcohol:

$$Q_{\text{IPA}} = 0.3\left(mc_p \Delta T\right)_{H_2O} + 0.7\left(mc_p \Delta T\right)_{\text{IPA}}$$

The values used for this calculation are shown in Table X below.

Table X. Properties of Water and Isopropyl Alcohol

	Water	Isopropyl Alcohol (IPA)
Density (g/mL)	1	0.785
Volume (mL)	10.5	10.5
Specific Heat (J/molK)	75.34	161.2
Change in Temp. (K)	2.73	2.73

The calculation is performed below:

$$Q_{IPA} = \left[(0.3)\left(\frac{1g}{mL}\right)(10.5\,mL)\left(\frac{1mol}{18.02\,g}\right)\left(75.34\frac{J}{mol*K}\right)(18°C)\right]$$
$$+\left[(0.7)\left(0.755\frac{g}{mL}\right)(10.5\,mL)\left(\frac{1mol}{18.02\,g}\right)\left(161.2\frac{J}{mol*K}\right)(18°C)\right]$$

$$Q_{IPA} = 237.1\,J + 893.5\,J = 1130.6\,J$$

Because energy is neither created nor destroyed, Q_{IPA} can be set equal to Q of the water needed for the exothermic reaction to take place:

$$m_{H_2O} * C_{p_{H_2O}} * \Delta T = 1130.6\,J \therefore m_{H_2O} * 75.34\frac{J}{mol*K} * 18K - 1130.6\,J$$

In the equation above, delta T of 18 K is the difference in temperature regarding the temperature of Chlorhexidine we are attempting to achieve. The team determined that the target temperature of the solution is 40°C, which would be an 18°C increase from where it currently sits at room temperature, 22 C. All temperatures were then converted to Kelvin for the calculations. Solving for the moles of H_2O, and multiplying by water's molar weight of 18.02 g/mol, the required amount of water for an exothermic reaction is:

$$m_{H_2O} = 0.834\ mol * 18.02 \frac{g}{mol} = 15g\ of\ H_2O$$

From here, each of the three chosen reactions were analyzed individually in order to determine the quantity of salt required.

Lithium Bromide

The first reaction considered was lithium bromide in water. To determine how much lithium bromide is necessary to heat the applicator solution, the heat of mixing was first determined to be:

$$\Delta H_{LiBr} = -8127 \frac{J}{mol}\ (Apelblat, 1986)$$

The number of moles of LiBr needed were then calculated using the following equation:

$$m_{LiBr} = \frac{Q}{\Delta HLiBr} = \frac{1130.6\ J}{8127\ \frac{J}{mol}} = 0.139\ mol\ LiBr$$

Multiplying this value by the molar mass of LiBr, the mass of LiBr was determined:

$$86.85\ \frac{g}{mol} * 0.139\ mol = 12\ g\ LiBr$$

Copper Chloride

The second reaction considered was copper chloride in water. To determine how much copper chloride is necessary to heat the applicator solution, the same procedure was followed as for lithium bromide above.

$$\Delta H_{CuCl_2} = -51.78 \frac{kJ}{mol}\ (Vandyshev, 2003)$$

The number of moles of $CuCl_2$ needed were then calculated using the following equation:

$$m_{CuCl2} = \frac{Q}{\Delta HLiBr} = \frac{1130.6\,J}{51780\,\frac{J}{mol}} = 0.0218\,mol\,CuCl2$$

Multiplying this value by the molar mass of $CuCl_2$, the mass of $CuCl_2$ was determined:

$$134.5\,\frac{g}{mol} * 0.0218\,mol = 2.93g\,CuCl2$$

Lithium Chloride

The final reaction considered was lithium chloride (LiCl) in water. To determine how much LiCl is necessary to heat the applicator solution, the same procedure was followed as for lithium bromide and copper chloride above.

$$\Delta H_{LiCl} = -37.1\,\frac{kJ}{mol}\ (Apelblat, 1984)$$

The number of moles of LiCl needed were then calculated using the following equation:

$$m_{LiCl} = \frac{Q}{\Delta HLiBr} = \frac{1130.6\,J}{37100\,\frac{J}{mol}} = 0.03047\,mol\,LiCl$$

Multiplying this value by the molar mass of LiCl, the mass of LiCl was determined:

$$42.39\,\frac{g}{mol} * 0.03047\,mol = 1.29\,g\,LiCl$$

4.4.4 Proposed Designs

The following sections will discuss the first few design iterations that the team created. These were preliminary designs, which were eventually ruled out.

4.4.4.1 *Dual Chamber*

A dual chamber design would allow for a water-activated exothermic reaction to occur. The antiseptic application would be comprised of two chambers that are separated by a C-slide plastic cover slip that resembles a C-slide plastic webcam cover that is used to protect webcam privacy (Figure IV). The first chamber (toward the end of the applicator) would contain the exothermic salt that is separated from the antiseptic solution by a thin impermeable membrane and the glass ampoule containing the antiseptic solution. The bottom of the applicator would resemble a PTFE/silicone vial septum that can be punctured by a needle to introduce water to the salt chamber. Upon activation of the exothermic reaction, adequate heat transfer would occur through the impermeable membrane and glass ampoule to warm the antiseptic solution. Once warm (determined by an indicator). The C-slide cover slip can be opened to allow the warmed antiseptic solution to transfer into the second chamber. In the second chamber, the two plastic wings on the side of the applicator would be squeezed to break the glass and expel the warm antiseptic solution through the cotton pledget containing orange dye and then the foam sponge.

Some of the advantages of this design is that the exothermic reaction will not be in direct contact with the antiseptic solution as there are two protective barriers separation the two. The two chambers allow for the exothermic reaction to warm the antiseptic solutions without interfering with the breaking of the glass ampoule. However, the disadvantages include the following:

- There are additional resources (i.e. sterile water, sterile syringe, and sterile needle) that required to activate the exothermic reaction. This is an entirely new process that will require additional supplies, time, and procedure to be executed.
- It is crucial that the C-slide plastic cover slip maintains its functionality throughout transportation, storage, and preparation procedures. If the cover slip loses its functionality due to bending or excessive sliding, it is possible that the glass ampoule will remain in the first chamber with no route of transport to the second chamber.

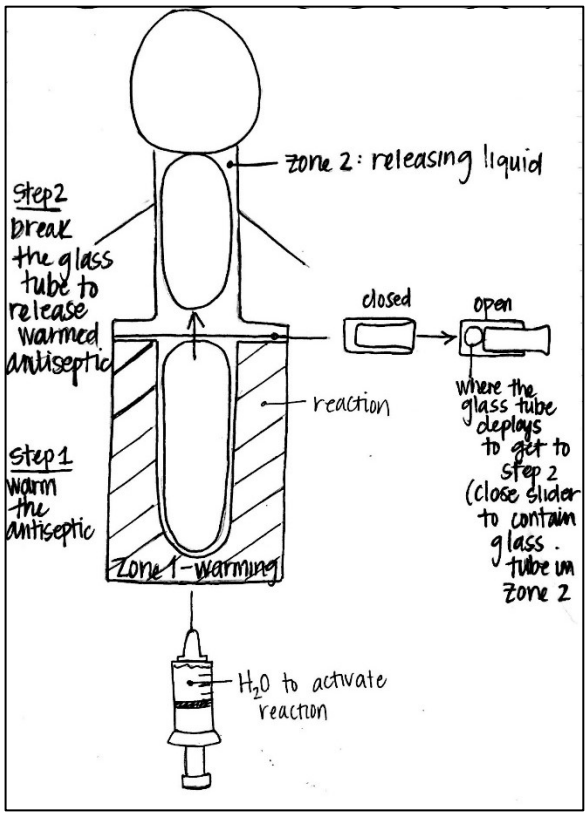


Figure IV. Illustration of dual chamber design

4.4.4.2 Internal Tube

An internal tube (containing the exothermic reaction) placed inside the glass ampoule (containing the antiseptic) would offer the best heat transfer to the solution because there is only one layer separating the reaction from the chlorhexidine solution (Figure V). The reaction tube would be made of plastic to ensure it does not break and mix with the antiseptic solution. To initiate the exothermic reaction, the reaction tube would contain the reactant and water separated by a breakable membrane. The membrane would be broken by shaking the tube vigorously. The dimensions of the original housing would need to change to accommodate the inner reaction tube. The complications of this design idea include manufacturing and ensuring proper breakage of the inner membrane without breaking the glass ampoule.

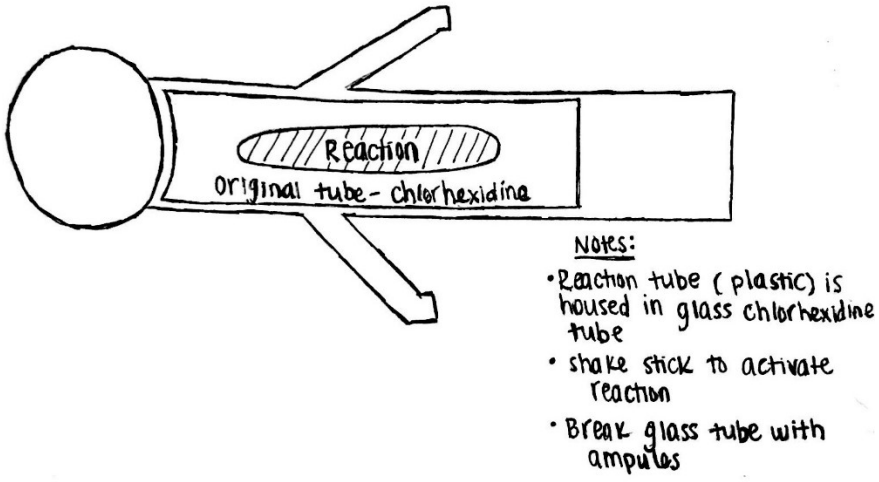


Figure V. Illustration of internal tube design.

4.4.4.3 Reusable Sleeve

The idea for the reusable sleeve prototype came from an environmentally friendly standpoint. The exothermic reaction would occur in a separate chamber from the application stick. While the reaction is producing heat, the user would slide on the chamber sleeve which would encase the long portion of the application stick (Figure VI). The heat would be transferred from the reaction, through the sleeve material, through the air in the tube and finally to the glass containing the chlorhexidine solution. This design would not change the existing mechanism and could be made to fit all applicator sizes, therefore eliminating the production of excess disposables. Once the reaction is completed, only the reactants would need to be changed while the housing could be kept and reused. The complications with this design come with sterilization and adequate heat transfer. For the sleeve to be reused, there must be a sterilization component between uses. Also, the mechanism of how to mix water with the reactant is unclear if the sleeve is enclosed. This design idea was ruled out because of the limited heat transfer between multiple layers of materials.

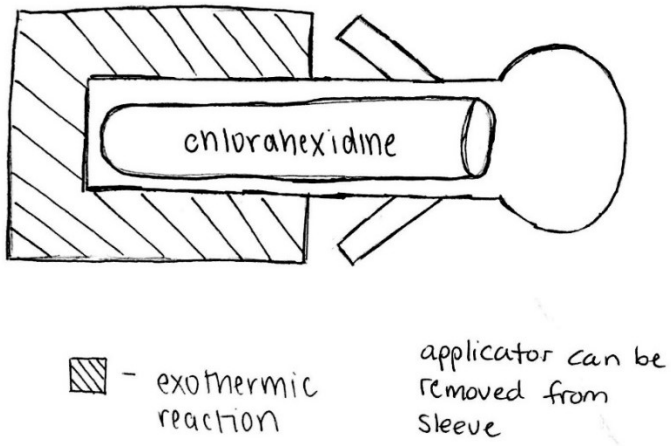


Figure VI. Illustration of reusable sleeve design.

4.4.5 Final Design

The final design that was selected features some components from previous design iterations that were discussed. This option will feature several chambers that will keep the various materials/components of the device separated until it is ready for use (Figure VII). The bottom-most chamber will hold the amount of water necessary to initiate the exothermic reaction. A pull tab will be separating this chamber from the chamber above, which will contain the salts necessary for the exothermic reaction. Once the tab has been removed, the water will mix with the salts, initiating the exothermic reaction. This will allow heat will transfer from the second most chamber (where the salts were originally stored) through the material containing the isopropyl alcohol solution. Ideally, the exothermic reaction will warm the third chamber filled with isopropyl alcohol to the desired temperature for a certain amount of time. Once the antiseptic has been sufficiently warmed, a second pull tab can be removed. The removal of this tab will cause the antiseptic to flow through the orange dye above it and proceed through the sponge for final application to the patient skin.

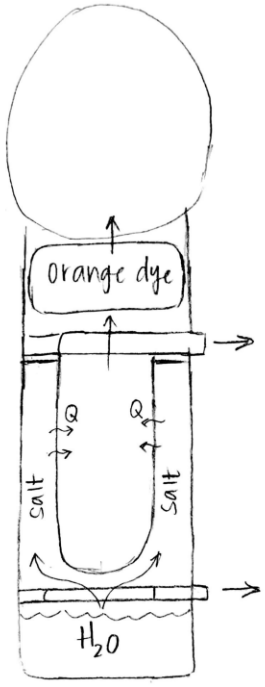


Figure VII. Illustration of final design.

4.5 Initial Testing

In order to aid redesign of the ChloraPrep™ applicator, the team executed various initial self-testing protocols in which each team member served as an experimental test subject. The primary objective of this protocol was to record skin temperature before and after application of ChloraPrep™ antiseptic solution at room temperature and after being warmed to 37-40°C. The secondary objective was to relate the temperature data obtained from the protocol to the theoretical heat loss calculations. In addition, it also allowed the team to qualitatively feel if there was a significant difference in comfort when the solution was warmed prior to application on the skin.

To limit the quantity of experimental variables, each protocol was completed in one-sitting under the same conditions (e.g. room temperature and humidity, location of application). The antiseptic solution was applied on the inside of the upper left arm with at an application site with an approximate 4-centimeter radius.

4.5.1 Initial Self-Testing

The first protocol that the team executed required the application of the ChloraPrep™ solution at room temperature. This test was performed in the GH007 MQP Lab and allowed the

team to qualitatively and quantitatively determine the heat loss of the skin when the solution was applied.

4.5.1.1 *Initial Self-Testing Protocol*

Objective:

- Record quantitative data regarding temperature of skin before and after application of ChloraPrep™ antiseptic solution
- Relate antiseptic application to theoretical heat loss calculations

Materials:

- Etekcity Laser Grip 774 infrared temperature gun
- 4 ChloraPrep™ 10.5 mL antiseptic applicators
- Thermometer and humidity detector
- Test subjects (ourselves)

Procedure: The following describes the protocol that will be used to test the ChloraPrep™ antiseptic on test subjects.

1. Record ambient room temperature and humidity.
2. Record the initial temperature of the testing area using the non-contact digital infrared thermometer.
    a. Following the instructions of this device, the thermometer should be held at a distance approximately 36 cm away from the surface of interest.
3. Open ChloraPrep™ antiseptic applicator and follow directions for application.
4. Apply to inside of bicep in a circular motion approximately 4 cm diameter for 30 seconds.
5. Record temperature using digital infrared thermometer at time 0s, 30s, 60s, 120s, 180s. Follow the same procedure as stated in Step 2a.
6. Repeat on each team member.

4.5.1.2 *Initial Self Testing Results*

Table XI below displays the skin surface temperature at various times. The "-30 seconds" time stamp refers to the initial skin temperature prior to antiseptic solution. The "0 seconds" time

stamp refers to the skin's temperature immediately after the antiseptic solution was applied to the skin. The remainder of the time stamps refer to skin's temperature while the antiseptic solution was drying on the skin. The skin's temperature was recorded for a total of 3 minutes, which is the recommended drying time for antiseptic solution applied on hairless skin. When analyzing the line graph (Figure VIII) it is evident that the largest drop in skin temperature was immediately after the completion of the antiseptic application with the skin's temperature dropping an average of 3.8 °C. This result reinforced the initial client problem statement the team received from Dr. Hussain as he stated that, "Patients are discomforted by the sudden chill of the antiseptic solution upon initial stages of application".

Table XI. Average Change in Skin Temperature after Application of Antiseptic at Room Temperature

Test Subject	Time (s)	Skin Surface Temperature (°C)	Average Change in Skin Temperature (Directly After Application) (°C)	Average Change in Skin Temperature (Overall) (°C)
A	-30	31.4	3.8	2.4
	0	27.6		
	30	26.8		
	60	27.2		
	120	28.3		
	180	29.0		
B	-30	32.1	2.9	3.1
	0	29.2		
	30	28.0		
	60	27.7		
	120	29.4		
	180	32.1		
C	-30	32.5	4.5	2.9
	0	28.0		
	30	27.5		
	60	29.0		
	120	29.2		
	180	32.5		
D	-30	29.0	4.0	2.9
	0	25.0		
	30	27.0		
	60	26.3		
	120	26.0		
	180	26.1		
Average Change in Skin Temperature (Directly After Application) (°C)				**3.8**
Average Change in Skin Temperature (Overall) (°C)				**2.8**

Note: the data in Table XI is the average of three testing trials

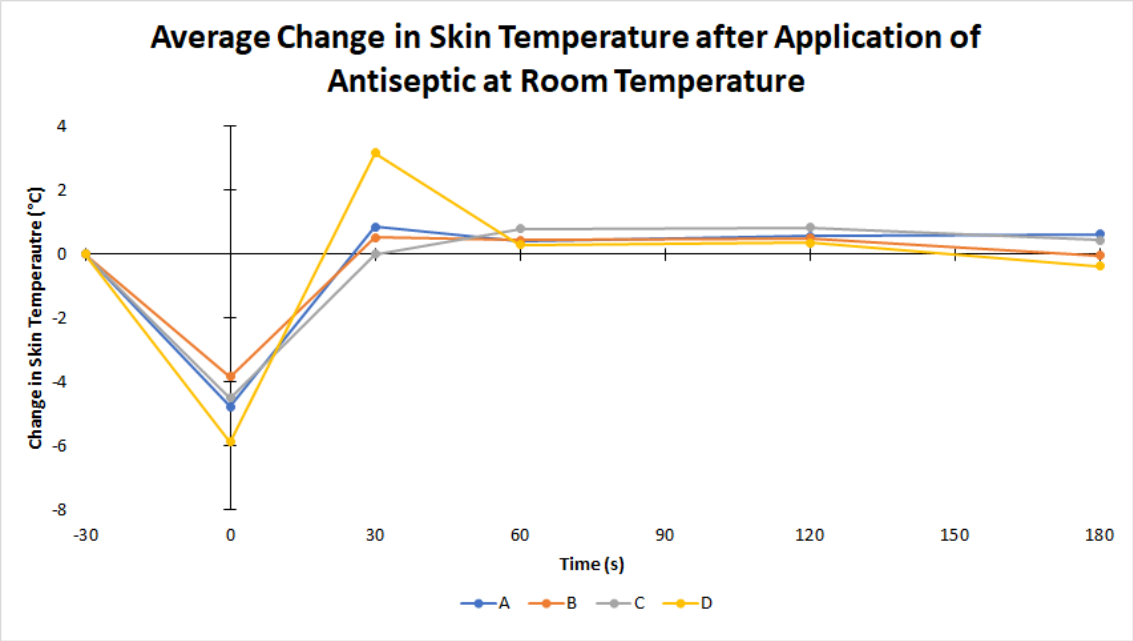


Figure VIII. Average change in skin temperature after the application of antiseptic at room temperature from three testing trails per test subject (n = 3). Skin temperature was measured for a duration of 3 minutes. The"-30" second time stamp represents initial skin temperature 30 seconds prior to application of ChloraPrep™. The standard deviation at time zero is ±0.85°C.

4.5.2 ChloraPrep™ Warming Testing

Following the initial testing performed, the team then tested the application of warmed ChloraPrep™ solution. This test was performed for the team to determine if applying warmed ChloraPrep™ solution would result in a more pleasant application experience.

4.5.2.1 *ChloraPrep™ Warming Testing Protocol*

Objective:

- To determine if warming the ChloraPrep™ applicator prior to application would result in a smaller decrease in temperature of the skin.

Materials:

- 4 ChloraPrep™ Applicators
- Water

- Hot water bath
- Etekcity Laser Grip 774 infrared temperature gun
- Thermometer and humidity detector
- Test subjects

Procedure:

1. Place sticks in a water bath of 37 °C for approximately 1 hour prior to the start of testing.
2. Record the initial temperature of the testing area using the non-contact digital infrared thermometer.
3. Following the instructions of this device, the thermometer should be held at a distance approximately 36 cm away from the surface of interest.
4. Open ChloraPrep™ antiseptic applicator and follow directions for application.
5. Apply to inside of bicep in a circular motion approximately 4 cm diameter for 30 seconds.
6. Record temperature using digital infrared thermometer at time 0s, 30s, 60s, 120s, 180s. Follow the same procedure as stated in Step 2a.
7. Repeat on each team member.

4.5.2.2 *ChloraPrep™ Warming Testing Results*

Unfortunately, this was a failed experiment where no real results were obtained. While the ChloraPrep™ applicators were warming in the water bath, the liquid from within them began to leak around the twenty-two-minute mark. The team believes this leakage was due to the sponge portion of the applicator getting wet. Although the sponges were wrapped in parafilm, a water-tight seal was not formed. Once the applicators began to leak, they became unusable for accurate testing results (Figure IX).

Figure IX. Image of the ChloraPrep™ applicators in a water bath at 37°C. After 22 minutes in the water bath, the applicators began to leak orange coloring from their sponge applicator.

4.5.3 Alcohol Warming Testing

As a result of the failed ChloraPrep™ warming testing, the team modified their plan and tested solely warmed 70% IPA. Without the applicators this experiment did not completely simulate the application process during a standard procedure, but it still allowed the team to observe the effects of warming the antiseptic.

4.5.3.1 *Alcohol Warming Testing Procedure*

Objective:

- Record quantitative data regarding the temperature of the skin before and after the application of warmed 70% isopropyl alcohol

Materials:

- 70% Isopropyl Alcohol
- 10mL Test tube
- Hot plate
- Beaker
- Stir bar
- Etekcity Laser Grip 774 Infrared Temperature Gun
- Thermometer and Humidity Detector
- Test Subjects (ourselves)

Procedure:

1. Place a test tube full of 70% Isopropyl alcohol in a beaker full of water on a hot plate
2. Heat until the Isopropyl alcohol reaches 35°C
3. Record the initial temperature of the testing area using the non-contact digital infrared thermometer.
4. Following the instructions of this device, the thermometer should be held at a distance approximately 36 cm away from the surface of interest.
5. Wet a paper towel with the warmed Isopropyl alcohol
6. Apply to inside of forearm in a circular motion approximately 4 cm diameter for 30 seconds.
7. Record temperature using digital infrared thermometer at time 0s, 30s, 60s, 120s, 180s. Follow the same procedure as stated in Step 2a.
8. Repeat on each team member.
9. Repeat entire testing protocol at 40°C.

4.5.3.2 *Alcohol Warming Testing Results*

As outlined in the procedure from the previous section, IPA was warmed to 35°C and 40°C and applied to the inner forearm of the test subjects. This testing was designed to guide the team in determining a target temperature for the antiseptic that felt most comfortable on the skin. The raw data from this testing can be seen in Tables XII and XIII below. In these tables, "-30 seconds" symbolizes the initial skin temperature prior to antiseptic solution. The "0 seconds" time

stamp refers to the skin's temperature immediately after the warm isopropyl alcohol was applied. The remainder of the recorded times refer to skin's temperature while the isopropyl alcohol was drying on the skin. The skin's temperature was recorded for a total of 3 minutes, which is the recommended drying time for antiseptic solution applied on hairless skin.

The temperature loss at application can best be observed in the graphical representation of the data shown in Figures X and XI. At 35°C, the average temperature loss at application for the team as a whole was 1.63°C. At 40°C, the average temperature loss was 1.70°C. For the application at both 35°C and 40°C, the largest drop in skin temperature occurs immediately after the application of the IPA. It is important to notes, however, that the overall decrease in temperature of the warmed IPA is significantly less than the testing with room temperature IPA. This shows that warming of isopropyl alcohol does in fact decrease the skin temperature drop felt by patients.

Table XII. Average Change in Skin Temperature after Application of Antiseptic at 35°C

Test Subject	Time (s)	Skin Surface Temperature (°C)	Average Change in Skin Temperature (Directly After Application) (°C)	Average Change in Skin Temperature (Overall) (°C)
A	-30	32.4	2.8	0.4
	0	29.6		
	30	27.9		
	60	28.4		
	120	29.3		
	180	30.0		
B	-30	32.0	2.0	0.4
	0	30.0		
	30	28.9		
	60	29.0		
	120	29.9		
	180	29.9		
C	-30	31.6	1.3	0.3
	0	30.3		
	30	28.9		
	60	29.0		
	120	29.9		
	180	29.9		
D	-30	28.9	0.4	0.1
	0	28.5		
	30	27.5		
	60	27.4		
	120	28.0		
	180	28.1		
Average Change in Skin Temperature (Directly After Application) (°C)				**2.5**
Average Change in Skin Temperature (Overall) (°C)				**1.2**

Note: the data in Table XI is the average of three testing trials

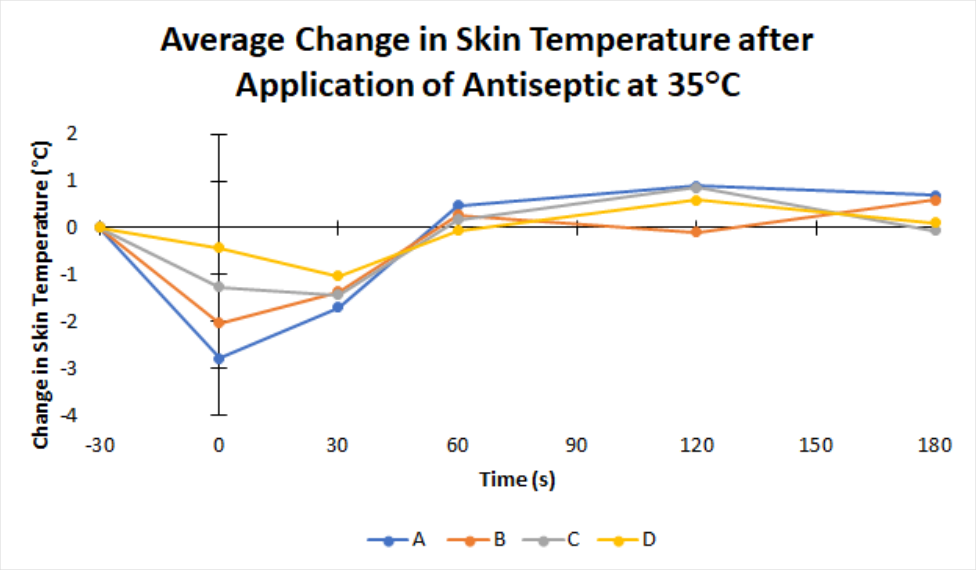


Figure X. Average change in skin temperature after the application of antiseptic at 35°C from three testing trails per test subject (n = 3). Skin temperature was measured for a duration of 3 minutes. The"-30" second time stamp represents initial skin temperature 30 seconds prior to application of ChloraPrepTM. The standard deviation at time zero is ±1.02°C.

Table XIII. Average Change in Skin Temperature after Application of Antiseptic at 40°C

Test Subject	Time (s)	Skin Surface Temperature (°C)	Average Change in Skin Temperature (Directly After Application) (°C)	Average Change in Skin Temperature (Overall) (°C)
A	-30	31.7	2.6	0.7
	0	29.1		
	30	30.1		
	60	30.7		
	120	31.0		
	180	31.0		
B	-30	31.4	2.8	1.9
	0	28.6		
	30	28.9		
	60	29.0		
	120	29.3		
	180	29.5		
C	-30	32.4	3.2	0.7
	0	29.2		
	30	29.7		
	60	30.4		
	120	30.9		
	180	31.1		
D	-30	31.8	1.2	1.0
	0	30.6		
	30	30.8		
	60	30.8		
	120	30.6		
	180	30.8		
Average Change in Skin Temperature (Directly After Application) (°C)				**2.5**
Average Change in Skin Temperature (Overall) (°C)				**1.2**

Note: the data in Table XII is the average of three testing trials

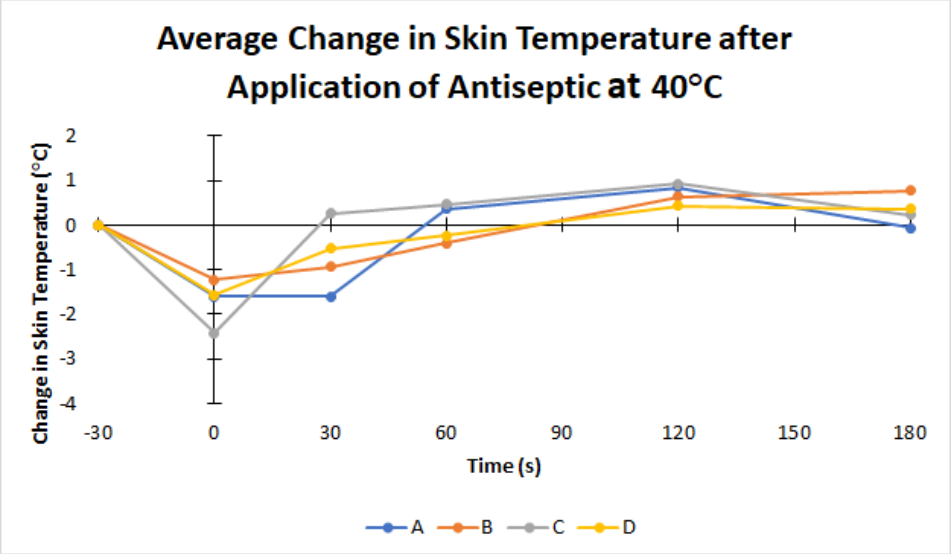


Figure XI. Average change in skin temperature after the application of antiseptic at 40°C from three testing trails per test subject (n = 3). Skin temperature was measured for a duration of 3 minutes. The "-30" second time stamp represents initial skin temperature 30 seconds prior to application of ChloraPrep™. The standard deviation at time zero is ±0.51°C.

A one-way ANOVA test was performed comparing the temperature changes at time zero for the unwarmed, 30°C, and 40°C self-testing trials. The p-value corresponding to the one-way ANOVA ($\alpha = 0.05$) is less than 0.05 which suggests that one or more treatments are significantly different. A post-hoc test will identify which pairs of treatments are significantly different from each other. Tukey's Honest Significant Difference (HSD) test is based on the studentized range distribution. With three groups and 9 degrees of freedom, the critical values of the studentized range Q statistic are compared resulting in a significant difference between unwarmed vs. 35°C and unwarmed vs. 40°C with Tukey HSD p-values 0.0012 and 0.0014 respectively. There is no significant difference between the 35°C and 40°C pair.

5 Design Verification

Design verification is a fundamental aspect of a design process. This chapter will focus on the verification completed for the team's final prototype. This will include the raw results from all testing completed with the final design. These tests include temperature changes during LiCl and water mixing, temperature changes of IPA from LiCl and water, and a second set of self-testing on the team's skin. The importance and meaning of these results will be discussed further on in the paper in the "Analysis and Discussion" section.

5.1 Lithium Chloride and Water Testing

Once the team decided to move forward with a LiCl and water warming mechanism, the first testing completed was to determine the amount of LiCl needed to warm the Chlorhexidine solution. The team began the testing with the amount of LiCl and water calculated previously in section 4.4.3 – 0.0898 g and 7 mL, respectively. However, more tests were also completed that used 7mL of water and increasing amounts of LiCl – 0.19 g, 0.5 g, 1 g, and finally 2 g. These were completed in order to find the correct ratio of LiCl to water for the temperature increase that was desired.

For each trial, the respective amount of LiCl was placed in a small beaker on a stir plate. The 7 mL of water was then added, and the temperature of the mixture was recorded for up to 120 seconds. The summarized results of the experiments can be seen in the Table XIV below:

Table XIV: Resulting Temperatures of Varying Amounts of LiCl in 7 mL of Water

Amount of LiCl in 7 mL of Water (g)	Largest Change in Temperature (°C)
0.0898	1.5
0.1900	0.5
0.5000	4.5
1.000	10
2.000	23
2.000	17

As seen in the table above, 2.000 g of LiCl in 7 mL of water was performed in duplicate. This is because only the initial 2.000 g test gave us a large enough increase in temperature for us to perform testing. The team's conclusion and analysis of these results will be discussed in section 7, "Analysis and Discussion".

5.2 Lithium Chloride, Water, and IPA Testing

Following the testing discussed in section 5.1, the team then decided to test the change in temperature of Isopropyl Alcohol during the mixing of LiCl and water. For this test, 7 mL of water and 3.000g of LiCl were placed in a graduated cylinder on a stir plate. A conical tube filled with 10.5 mL of Isopropyl alcohol was then placed within the graduated cylinder. Two thermometers were used to measure the temperature of the LiCl and water mixing, as well as the isopropyl alcohol over a 120 second period.

From three separate trials, the average highest temperature that the IPA reached was 40°C. These average results from the three testing trials can be seen in the Figure XII below.

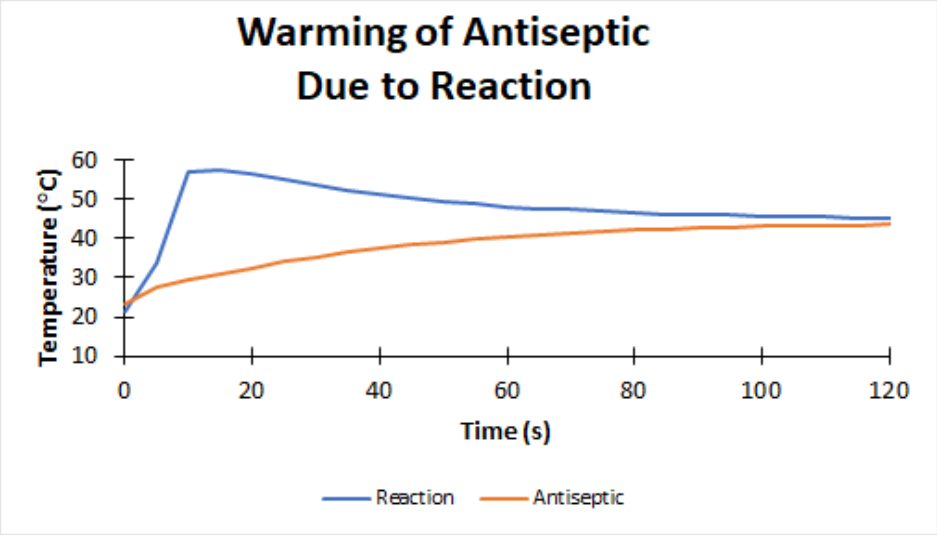


Figure XII. Average Results from 3 Testing Trials of IPA and Heat of Mixing Reaction

5.3 Antimicrobial Testing

Quantitative suspension antimicrobial testing was performed following the EN 1276 standard in order to ensure that ChloraPrep is still fully effective as a disinfectant even after being heated. The protocol for this standard can be found in Appendix D. The team performed 3 replicates for their testing. For each replicate, there were three groups: a sterile plate with culture broth, a growth place with 150 colony-forming units (CFU) of *Staphylococcus Aureus*, and an experimental plate 1.5 x 10^8 CFU of *Staphylococcus Aureus* suspended in Chlorhexidine Gluconate in IPA. The EN 1276 standard states that there must be a 4-log reduction in bacterial count after a 24-hour incubation period in order to be effective. The team had 6-log reduction for

all three replicates of plates with warmed chlorhexidine gluconate, meaning that the standard was met. This can be observed visually in Figure XIII below.

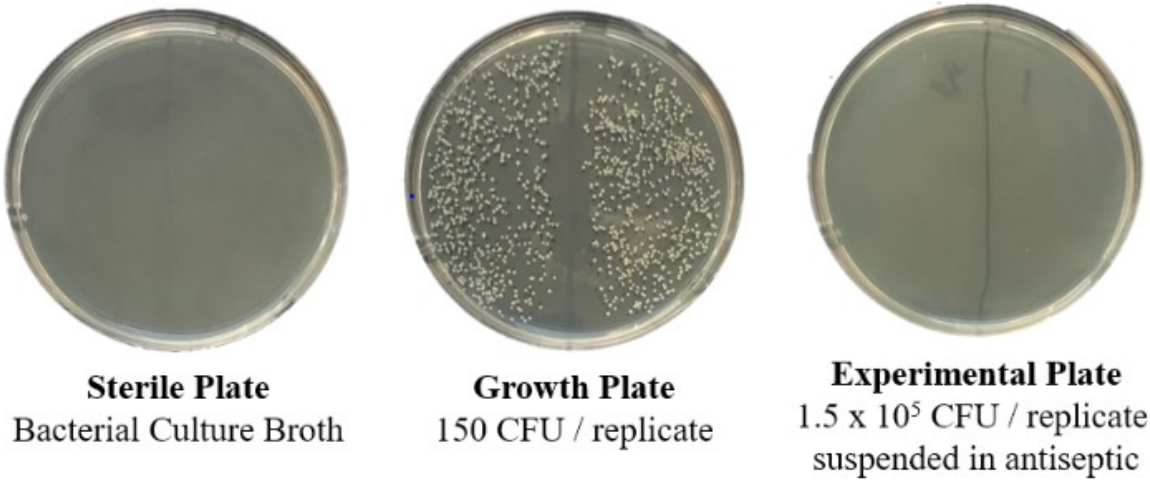


Figure XIII: Visual representation of antimicrobial testing results. Each plate is labeled with the name of its respective experimental group and the quantity of bacteria plated.

5.5 Rapid Prototyping and 3D Prototype Evaluations

Rapid prototyping is advantageous for design-based projects as research teams can conduct conceptual analyses, functionality testing, and design verification with 3D-printed models in a cost-effective and time-efficient manner. Over the course of the prototyping timeline, the team created a total of 3 prototypes using CAD modeling in SolidWorks, which also served as the modeling files for 3D printing. In the subsections below, each prototype design will be explained and evaluated.

After consulting with Dr. Erica Stults, the prototypes were printed using WPI's FormLabs Form 2 Stereolithography (SLA) 3D printer, which uses a liquid resin that is cured with a 405 nm violet laser. The primary benefit of this printer to is its ability to print small, intricate features with a smooth surface finish.

The main features the team wanted the devised prototypes to incorporate include the following: (a) a compartment to store 7 mL water, (b) compartment to store the ≥ 2g reactive salt, (c) a compartment to store 10mL antiseptic solution, (d) a barrier mechanism to separate the water from the reactive salt, (e) barrier mechanism to separate the salt-water reaction from the antiseptic, and (f) a barrier mechanism to separate the antiseptic from the dye pledget and application sponge.

Such features would allow the following processes to be executed when a patient is being prepared for procedure that requires antiseptic application:

When the rubber pull tab is released outward, the opening of the water-storing compartment is exposed and allow water to expel into the compartment containing the reactive salt. The heat that is generated from the thermogenic reaction, when the water meets the salt, will warm the antiseptic solution contained in the inner tube. Once the antiseptic solution is warm, the second pull tab can be released to allow the warm antiseptic to dispel into the dye pledget and the application sponge.

5.5.1 Prototype 1

The first prototype the team created consists of 2 concentric tubes: an inner tube to store the antiseptic and an outer tube to store the salt (Figure XIV and XV). The semi-circle openings on the ends of the tube are designed to hold the rubber tabs, which would serve as a physical barrier that separates the water from the salt and the antiseptic from the application sponge (not shown).

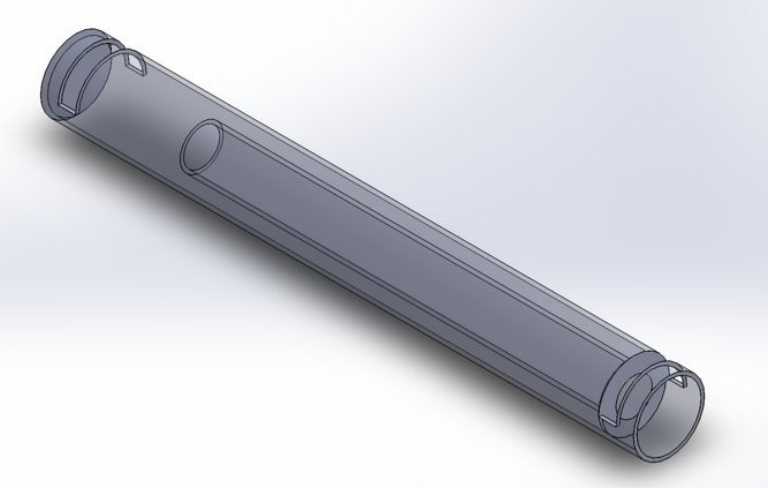


Figure XIV. Isometric view of prototype 1

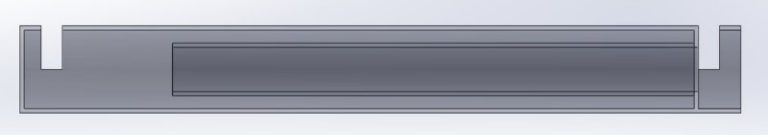


Figure XV. Front view of prototype 1

To generate a high-level tangible model of the tube, the team did not include the compartment to store water and the region to adhere the application sponge. This prototype served

as a baseline prototype that the team would gradually modify to improve functionality. Favorable and unfavorable design features are described in Table XV below.

Table XV. Prototype 1 Evaluation

Prototype 1	
Material: Rigid White Cost: $6.09	
Favorable Features	**Unfavorable Features**
• The prototype is ergonomically designed in that it is easy to hold with a comfortable grip. • The dimensions of the prototype yield a thin, cylindrical tube that has a streamlined profile.	• The outer tube's wall thickness of 1mm is fragile and too thin. When removing the supports, the one of the ends of the tube broke off (Figure XIII). • The semi-circle slots do not allow for the rubber tabs to be inserted and pulled out securely while preventing any water from leaking out of the device.

5.5.2 Prototype 2

Based on the evaluation of the first prototype, the team devised a second prototype shortly after. This prototype follows a design scheme that is similar to prototype 1 in that is features compartments for each material and two thin slots to separate the contents of the compartments (Figure XVI).

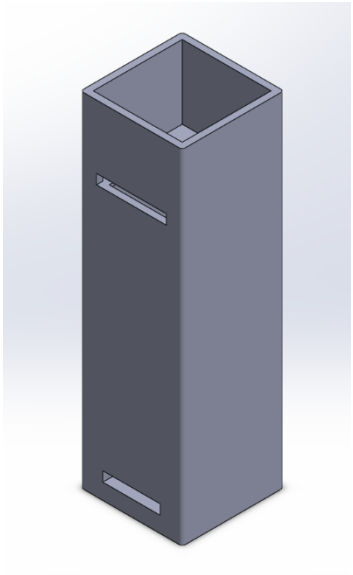


Figure XVI. Isometric View of Prototype 2

While evaluating the first prototype, the team noted that the fragility of the design was partially caused by the high length-to-width ratio. To better balance the tube's dimensions, the team opted for a square-shaped tube because with the same dimensions (length and width) can store more volume. Additionally, the outer wall thickness was doubled (from 1mm to 2mm) to increase the strength of the walls.

In prototype 1, where this system was not included, the pull tabs were easily bent and shifted and that encouraged undesired water leakage from the device. To resolve this design issue, the team incorporated a "ledge/shelf" system at the slot separating the water and salt compartments to allow the pull tab to rest between the rigid surfaces. Favorable and unfavorable design features are described in Table XVI below.

Table XVI. Prototype 2 Evaluation

Prototype 2	
Material: Rigid Clear Cost: $10.90	
Favorable Features	**Unfavorable Features**
• The prototype is ergonomically designed in that it is easy to hold with a comfortable grip. • The design includes a shelf system that will add stability to the pull tab and reduced unwanted movement. • The tube design is stronger as the dimension ratios are more balanced.	• Another pull tab is needed at the top of the tube to contain the antiseptic solution. • The inner tube is too short in length, which will result in inconsistent warming of antiseptic solution.

6 Final Design and Validation

Throughout the course of this project, the team has brainstormed, developed, and carried out various testing procedures in order to create a successful final design. A large portion of this project was also dedicated to brainstorming and executing various design solutions. The purpose of this report section is to give an overview of how the team's initial objectives were met with the final design. In addition, the team will briefly discuss industry standards relevant for the design, as well as various societal impacts the design might make.

6.1 Final Design Overview

This section will briefly outline the steps that were taken in order to achieve the final design. This will include an overview of the objectives the team was aiming to reach, and whether they were. Additionally, the team's experimental and data analysis methods will be summarized.

6.1.1 Final Design Objectives

When beginning this project, the team had five main objectives to achieve. The first objective was to develop a cost-effective device for pre-warming of antiseptics solutions. The team believes that this objective was ultimately achieved. With the use of a LiCl and water mixture, the ChloraPrepTM solution temperature was raised an average of 18 °C prior to application. 100 g of LiCl, enough for 50 applicators, can be bought for under $80 – meaning that the only additional cost to this device is under $2. Objective two was to improve overall patient experience. Although this objective cannot be quantified, the team believes that the successful warming of the ChloraPrep^{TM} solution will make patients more comfortable. The third objective was to create a universal design that could be applied to comparable skin preparation applicators on the market. Although the safety of warming different skin preparation solutions would need to be ensured, the team also believes this objective was achieved. With our three-chamber final design, the salt solution (LiCl and water) can remain constant. However, the inner chamber of the applicator can hold other types of disinfectants, as needed. The fourth objective was to ensure the safety of the patient and medical staff. Although antiseptic solutions can be flammable, the amount of LiCl and water used to heat the ChloraPrep^{TM} only allows it to reach a maximum temperature of 40°C. We strongly believe this temperature is not high enough to put the patient or medical team in danger. The fifth objective was maintaining the original functionality of the device. Through antimicrobial

testing with the EN 1276 standard, the team was able to meet this objective and maintain a 6-log bacterial reduction, meaning that the device remained fully effective.

6.1.2 Summary of Experimental Analysis

Overall, the team had two main groups of experimental methods: warming of the ChloraPrep™ solution and the effectiveness of a newly designed applicator. These two groups were initially tested independently, before being combined into one functioning device.

To begin the task of effectively warming ChloraPrep™, the team had to complete background research pertaining to the effectiveness of mixing solutions to give off heat. Factors such as cost and safety helped the team narrow this down to three different mixing reactions. From here, the team completed a series of calculations in order to determine the amount of each salt required to produce the desired amount of heat (enough to raise the ChloraPrep™ to a maximum of 40°C). LiCl was then chosen by the team to be experimentally tested, due to its relatively low price and the small amount needed. Although these calculations provided the team with an effective estimate, there were assumptions that were made – such as no loss of heat to the air, and heat transfer through our desired final material rather than the materials we had access to in the lab. Therefore, obtaining experimental results was the next step. The team began by testing various amount of LiCl in water until it reached our desired temperature of 40°C. Adjustments in the amount of LiCl used were made, despite the fact that this left the team with a higher amount than originally calculated.

Once the team determined that 2.00 g of LiCl in 7 mL of water was needed, the effects of this reaction on the temperature of IPA was tested. For these tests, LiCl and water were mixed in a graduated cylinder, and a conical tube of 10.5 mL of IPA was also placed in the graduated cylinder. The temperature of both solutions was measured over a period of about two minutes.

The testing performed in the previous paragraph demonstrated to the team the difficulty of warming IPA to 40°C. Although the LiCl and water mixture temperature exceeded this amount, due to various factors such as heat escaping to the air or poor heat transfer, the alcohol was not warmed as the team hoped. Therefore, the team performed self-testing in order to determine the effects of applying IPA at 35°C to the skin rather than 40°C. The team felt that this was a much more attainable result that would still reduce or eliminate the chilling sensation currently induced by ChloraPrep™ application.

In addition to the warming testing, the team simultaneously designed and created applicator prototypes. The design process for these prototypes began with brainstorming, from which we chose a few designs to further develop. After various discussions, the team's first attempted design was chosen, designed on SolidWorks, and rapid prototyped. After receiving the prototype, the team tested its capability to hold water and determined design changes to be made for the next version. From here, two more designs were prototyped and tested until the final design was created.

6.2 Applicable Engineering Standards

As discussed previously in this report, there are various standards that are applicable to the team's final design. The purpose of this section is to discuss whether these standards were met with our design, or if they must be incorporated into the design if the device were to be manufactured and marketed.

The first set of standards to be considered are AST Standards – specifically Standard of Practice II, III, and VIII. Standard of Practice II states that for pre-procedural skin preparation, healthcare facilities should use FDA-approved agents with immediate and persistent antimicrobial properties (AST Education and Professional Standard Committee, 2008). The team's final design will continue to incorporate the same Chlorhexidine Gluconate and IPA solution as current ChloraPrep^{TM}, which is FDA approved, and thus this standard is met by the new design. Standard III states that alcohol should not be used as a single agent for antiseptic purposes (AST Education and Professional Standards Committee, 2008). As previously mentioned, the Chlorhexidine Gluconate and IPA solution of the current ChloraPrep^{TM} will be used within the new design, and therefore this standard is also met. The final standard, Standard of Practice VIII, however, is not met by the team's design. This standard states that if a skin preparation solution is flammable, it must not be warmed, per manufacturer's instructions (AST Education and Professional Standards Committee, 2008). Seeing as warming the ChloraPrep^{TM} solution was one of the main objectives of this project, this standard was not met, and will continue to not be if it were to be manufactured and marketed. However, the team does not believe the level to which the solution is being warmed is harmful or will pose a threat to personal safety.

The next of standards to be considered are ISO standards. Standards of interest to the team are ISO 11737-2:2009, ISO 13485:2016, and ISO 15378:2017. In order for an ISO standard to be met, all activities must be completed within an ISO certified environment. None of the lab spaces

that were utilized for this project were ISO certified, and therefore, currently the team's design does not meet these standards. However, in the future, if this device is manufactured in the future, it should be ensured that the manufacturing facility is ISO certified for these specific standards.

In order to be marketed and used in medical facilities, the team's design must abide by current FDA regulations. Currently, antiseptic agents are regulated under the FDA's Over-the-Counter Drug Products division ("Safety and Effectiveness", 2017). These antiseptic agents must reduce transient microorganisms, possess a broad range of antimicrobial properties, be fast-acting with long-lasting activity, and not cause irritation to the skin. Seeing as ChloraPrep™ solution is currently FDA approved, by using the same solution, the team's design in theory would also be FDA approved. However, because the team modified a pre-existing skin preparation applicator that contains chlorhexidine-gluconate, a New Drug Application will need to be submitted for FDA approval ("Safety and Effectiveness", 2018). This is because in December 20, 2018, the FDA stated that chlorhexidine-gluconate and iodophors will not be general recognized as safe for use in antiseptics – individual approval is now required.

The final standards being considered are European Standards and Criteria. These standards confirm or reject that the redesigned device does not jeopardize the effectiveness of the antiseptic solution. ChloraPrep™ is currently compliant with standards EN 1040, EN 1275, EN 13727, and EN 13624. Antimicrobial testing was completed for this project according to standard 1276. However, all other applicable standards would need to be considered when manufacturing and marketing this device in the future.

6.3 Impact of Final Design

It is desired that the team's final design will someday be manufactured and marketed. With this, however, it is necessary to consider the impacts that the final design may have on the world. This is a design that will be in direct contact with both patients and healthcare professionals. In this section the team will briefly analyze the final design's impact on daily economics, manufacturability, health and safety, and the environment.

6.3.1 Economics

The goal of this project was to improve upon the current ChloraPrep™ design by reducing the chilling sensation that it causes when applied to the skin. Although the final design has not

undergone high-volume manufacturing with the team's recommended final materials, its prototype has been successfully manufactured with the team's resources. This involved utilizing the rapid prototyping, as well as other academic labs, on WPI's campus.

The final design developed closely models the current ChloraPrep™ applicator on the market. Therefore, the team does not believe that the economic impact of their design will be large. The device is about the same size as the current applicator, so the team expects the amount of resin required to injection or blow mold the product to stay the same. The only additional cost for the new design is the LiCl, which can be purchased for as little as $80 per 100 grams (Sigma Aldrich, n.d.). For reference, the new design only utilizes about 2 grams per applicator, meaning that at this price point, each applicator will have an increased cost of no more than $2.00. Although there are economic factors to consider when taking this design from the lab to full utilization in the clinic, the team believes the additional cost does not outweigh the design's benefits.

6.3.2 Manufacturability and Sustainability

Although the team believes the project design can be manufactured, there are still concerns regarding manufacturability. Currently, ChloraPrep™ applicators are injection- or blow-molded. Although the new design is also able to be molded in this manner, injection molding can be quite costly if the product is not being produced in a large volume. In order to be cost efficient, high volume manufacturing will be required. In order to manufacture this device in a sustainable manner, it would be beneficial to create it using recycled resins and plastics for molding. This would hopefully cause a smaller environmental impact than the use of new resins. The new design will also require additional manufacturing steps that will involve either an operator adding LiCl and water to their respective chambers within the device, or some type of automated system to do so. Although manufacturing is viable at this point in the project, if it were to be continued, the cost and lead time of such a process must be considered.

6.3.3 Ethical Concerns and Health and Safety Issues

It is imperative that the team consider the health and safety issues surrounding the device as its eventual intended use is in a medical/hospital setting on a frequent basis. Based on the research and data collected, the device that the team has design should pose no more risk than the current ChloraPrep™ sticks. Although the current ChloraPrep™ sticks bear a warning regarding

warming/heating of the device, the team has determined that the temperature to which the antiseptic is being warmed does not increase risk to the patient or user. The device does not reach a high enough temperature to pose risks of flammability or explosion. Furthermore, warming of the antiseptic solution does not affect its antimicrobial properties. Additionally, the solution will not reach a high enough temperature for thermal expansion to be a concern within ithe device.

Additional caution should be taken with the new device design to ensure that the mixture of LiCl and water does not mix with the antiseptic solution. The final design should incorporate a visual indicator (such as a color change) to show the user if the antiseptic mixes with the LiCl.

It is also important to consider ethics when introducing a new device into the market. It will be important that a patient's level or manner of treatment is in no way dictated by the type of antiseptic device they elect to have used. Additionally, all patients should be given the choice to decide between traditional antiseptic and the team's new warmed device, once it is on the market.

6.3.4 Environmental Impact

It is essential to consider potential environmental impacts of a new product to ensure that damage is not occurring to the world. Currently, the project is still being run and explored on a small scale. However, if large-scale manufacturing and marketing is a goal in the future, their environmental impact must be considered. As far as benchtop lab testing is concerned, the team utilized items such as IPA, glass labware, and items such as hotplates – all of which are not regularly discarded or do not cause concern when discarded. In the future, considerations will include the disposal of the finished device due to the LiCl held in it. The new design cannot be disposed in the same manner as current ChloraPrep^{TM} sticks due to this reason. It is necessary to keep LiCl out of drains, sewers, and waterways ("Safety Datasheet for LiCl Solution", 2016). Additionally, it is advised that LiCl is dissolved in a combustible solvent or absorbed into a combustible material and burned by a chemical incinerator. Any empty containers that once held LiCl, such as the final project design, must also be triple rinsed prior to disposal ("Safety Datasheet for LiCl Solution", 2016). Although there are ways in which to safely dispose of LiCl, before producing this product on a large scale, they must be determined and advised to all that utilize the design. If a safe disposal protocol is determined, the team's design should have little negative impact on the environment.

6.3.5 Societal Impact and Political Ramification

It is hoped that the new design will help patients feel more comfortable during medical procedures and willing to return for more in the future, and thus will have a positive societal impact. The team does not believe that there will be political ramification in the United States from this product. However, it is important to consider that any increase in price from standard antiseptic applicators may be too expensive for some patients in other communities to take advantage of. The team expects that in some other communities, the device will have a neutral impact rather than a positive one.

7 Discussion

The goal of this chapter is to discuss the results presented in previous sections of this report. This will include a discussion of the warming results achieved by the new design. Additionally, the antimicrobial activity of the team's design will be discussed and compared to that of the required standards and the current ChloraPrep™ applicator and solution. The team will also discuss limitations encountered during the course of the project, and how they were not critical to designing a successful product in the end.

7.1 Final Design

The final design, as seen in Figure XVII, is comprised of one solid part made of resin with multiple rubber parts. The open end has the function of holding the 10.5 mL of water needed for the reaction. A rubber top will be cut to size and glued into place. There is a square space for a rubber tab to act as a physical separation between the water and LiCl. The ledges above and below the tab space have the function of holding the rubber tab in place. The inner tube will hold the 10.5 mL isopropyl alcohol and ChloraPrep™ solution. This tube is closed off by another physical separation tab made of rubber. The outside of this inner tube will hold the 7 g LiCl. The angled edge is where the sponge applicator will be secured. To use, pull the first tab that separates the water from the LiCl. When the water rushes in, the reaction will start and produce heat to warm the ChloraPrep™ solution. Then, the second tab can be pulled and cause the ChloraPrep™ solution to soak the sponge. The applied solution should feel warm on the patient's skin.

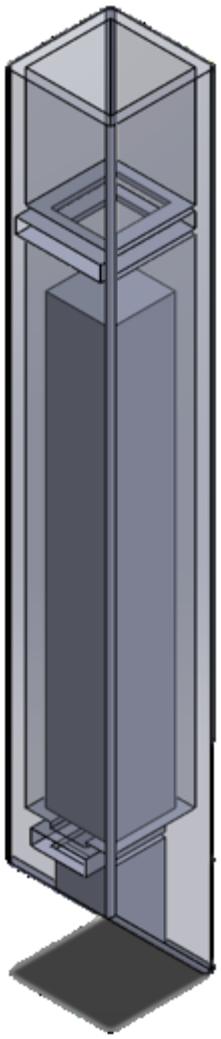


Figure XVII – Final Design Model

7.2 Warming Results Achieved

The results from testing the temperature of the LiCl and water reaction and temperature of IPA showed that as the reaction increased temperature, so did the IPA.

When the team self-tested with IPA warmed to 35°C, there was a clear drop in temperature of the skin immediately after application, but the initial shocking cold sensation was less. After 180 seconds, the temperature of the skin dropped 2.8, 2.0, 1.3, and 0.43°C for Costi, Kaur, Kolaya and Ricciuti, respectively. These results compared to IPA at room temperature can be seen in Table XVI. The warmed self-testing made it clear to the team that the minimum temperature that the antiseptic solution should be warmed to is 35°C. Although a warmer temperature would also

increase patient comfort, the team believes that 35°C is the minimum required to reduce the chilling sensation.

The team then self-tested with IPA warmed to 40°C. The results from this testing can also be seen below in Table XVII. Although numerically the results are not very different than the 35°C testing, the team agreed that this round of testing felt much more pleasant, and that 40°C should be the target temperature to warm the antiseptic to.

Table XVII – Change in Skin Temperature Upon Application of Isopropyl Alcohol

Change in Skin Temperature Upon Application				
	A	B	C	D
IPA at Room Temperature	3.8	2.9	4.5	4.0
IPA Warmed to 35°C	2.8	2.0	1.3	0.43
IPA Warmed to 40°C	1.6	1.2	2.4	1.6

7.3 Antimicrobial Properties Maintained

The team completed antimicrobial testing with warmed ChloraPrep solution in order to ensure that its original functionality is still maintained even after being warmed to 40°C. In order to determine if this was the case, the team followed EN standard 1276 and performed quantitative suspension tests with *Staphylococcus Aureus* and three tests groups – a sterile plate, a growth plate, and an experimental plate that was exposed to the warmed ChloraPrep. In order to be considered successful, the team needed to see a 4-log reduction in bacteria count on the experimental plate. After performing three replicates and counting the bacteria on all plates, the team calculated and determined that all experimental plates had a 6-log bacterial reduction. This means that the team's results surpassed the accepted standards. The team feels confident from these results that warming ChloraPrep to the target temperature of 40°C will have no effect on its antimicrobial properties.

7.4 Project Limitations

While the team would consider this a successful project, there were many obstacles faced along the way that are worth discussing.

The project was limited by time as the team only had one academic year to complete the project. As this year marked the proposal of the project, the team had to begin the design process from the begin, which made time an even greater limiting factor. It was not possible to for the team to create a prototype that would resemble the product the team would hope to one day see on the market. More time would certainly be necessary to see this device to market as the team sponsor had originally intended.

One of the biggest limitations of this project was resources, particularly the resources available to the team in the laboratory. One challenge was a lack of autoclaved glass beakers in the lab. This introduced possible contamination to the antiseptic solution that the team prepped. While the likelihood of this solution being contaminated is very low due to its antiseptic properties, it would have been beneficial to work with sterile equipment regardless. Additionally, the lab lacked a lot of basic equipment that the team required for testing such as electronic/automated thermometers, calipers and glass test tubes. This was limiting as the team often had to acquire these materials, which would delay testing that could have otherwise been very simple. Another limitation was the space available to the team in the laboratory. Each MQP is allotted one bench, which was sufficient in terms of storage. When the team ran testing protocols, however, more space than just one bench was often required. This was problematic when teams on nearby benches were also in the laboratory because there was often not enough space for both teams to conduct testing simultaneously.

In addition to resources, the team was limited in their testing due to a lack of test subjects. The self-testing was conducted on the team members. While this was sufficient, the team recognizes that skin temperature can vary to a certain degree depending on several conditions. The team would have liked to test a larger number of subjects to validate the data further and obtain more statistically significant data. Unfortunately, this would have required additional IRB approval, which was not feasible for the scope of this project.

Another minor limitation was lack of direction and input from the sponsor at UMass. While this gave the team the freedom to be creative and independent, it was limiting when the team needed feedback or information. For example, the survey that the team distributed at the hospital took much longer than expected due to difficulty in communication with the contacts there.

The final limitation of this project was that a lot of the subject matter and background knowledge required for this project was not within the areas of expertise of the team members. For

example, a better understanding of the principles of heat transfer would have been desirable to make the heat transfer components of this project more straightforward. Furthermore, the team had limited knowledge in cell and bacteria culture and had to outsource to an additional person to help with this validation testing.

8 Conclusion and Recommendations

8.1 Project Conclusions

The team was able draw several conclusions upon the completion of this project. To begin, through heat loss testing with non-warmed ChloraPrep™, it was determined that the application process is indeed an uncomfortable sensation. With this being determined, testing with warmed ChloraPrep™ led the team to decide that ChloraPrep™ warmed to 40°C both felt more pleasant, and caused a smaller heat loss from the skin during application. Additionally, the team was able to successfully use a lithium chloride and water heat of mixing reaction in order to warm antiseptic solution to this target temperature, meaning that we hit our target objective of making ChloraPrep™ more comfortable. The team also concluded that warmed ChloraPrep™ remains as effective as an antimicrobial agent than non-warmed ChloraPrep™, through our antimicrobial testing. The team concludes this project to overall be successful and hopes that in the future the design can be continued to be perfected, and hopefully used in hospitals in the future.

8.2 Future Recommendations

Throughout the course of this project, the team has developed recommendations for the continuation of the device design in the future. These recommendations mainly stem from the project limitations, specifically time and resources. The team hopes that with these recommendations, this project can be continued and improved upon in the future.

8.2.1 Recommended Applicator Materials

Moving forward from the end of this project, the team has recommendations for the continuation and improvement of the skin preparation applicator design. The first recommendation is regarding the material of the applicator. Due to manufacturing limitations, the team did not get to utilize what they recommend being the final material for their applicator. The team was limited to 3D printing in a rapid prototyping lab, and thus all prototypes were printed with varying materials. However, it is important to carefully select a final material for mass manufacturing, because the device will contain isopropyl alcohol, which is known to degrade certain plastics. The team recommends future versions of this device to be manufactured using HDPE or LDPE. Based on compatibility charts found during our research, HDPE shows no damage after 30 days of exposure of IPA (“Chemical Compatibility Chart”, n.d.). This means that even if the applicators

were stored in a medical facility for up to a month, degradation of the applicator material will not be a concern. LDPE is also a recommended material for the applicator because it is commonly used to make IPA storage containers. If possible, creating the applicator out of this material will ensure no degradation from IPA occurs (US Plastics Corp., n.d.).

When selecting a material to be used in the final applicator design, it is also important to ensure adherence to industry standards. Although not as strict as materials being placed in the body, there are still standards in place for any materials regarding medical devices and entering operating rooms. The first standard to adhere to is "ASTM F619-14: Standard Practice for Extraction of Medical Plastics". ASTM is the American Society for Testing and Materials – a group that publishes voluntary technical standards (ASTM International, 2014). This standard is used for the evaluation of raw materials, auditing materials within the manufacturing process, and testing of final products. The team recommends that this standard, although voluntary, be adhered to during the manufacturing process in order to ensure the use of high quality, safe materials.

An additional standard to follow regarding materials is "USP 661.2 Plastic Packaging Systems for Pharmaceutical Use" (USP, n.d.). USP is the United States Pharmacopeia, a yearly publication by the United States Pharmacopeial Convention. This standard considers safety aspects of a product's packaging system based on chemical structures (USP, n.d.). USP Performs extractables and leachable testing, both which will be essential for our product. Following this standard and testing procedure, it can be ensured that there are no leachables from isopropyl alcohol, which would make the device unsafe for use.

8.2.2 Future Testing

Due to time constraints, the team was unable to complete all of the testing that was initially planned. In the future, the team recommends that the effectiveness of the antiseptic solution be tested on additional strains of bacteria including *Escherichia coli and Pseudomonas fluorescens*. The team was able to successfully test with *Staphylococcus Aureus,* a common skin bacterium, but it would be beneficial to complete testing with additional bacteria strains. Furthermore, the team would recommend warming the antiseptic solution to various temperatures

to determine at what temperature the antiseptic becomes ineffective. These varying degrees of warmed antiseptic should then be utilized in the antimicrobial testing.

Additionally, the physical antiseptic applicator design needs future development. As previously stated, the team recommends that the body of the device is manufactured via blow molding or injection molding with HDPE or LDPE. However, the pull tabs are currently made from rubber. These rubber tabs were not fully leak proof – additional testing will be required to determine if it was the rubber material or tab shape that caused the leaking. A cap will also need to be designed in order to hold the contents of the applicator fully in the device. Currently, there is an open end to the applicator, meaning that it has not yet be fully designed.

Finally, the team recommends testing of the heat of mixing reaction and warming of the antiseptic within the device. The team was only able to measure the heat of mixing in an open beaker, rather than in the device, and it was difficult to account for heat loss to the open air. It will be critical to test the reaction within the closed device in order to ensure that heat transfer can occur through the final chosen device material.

References

About AORN. Retrieved from https://www.aorn.org/about-aorn

About chlorhexidine: Mechanism of action. Retrieved from https://chlorhexidinefacts.com/mechanism-of-action.html

Ambulatory surgery data from hospitals and ambulatory surgery centers: United states, 2010. (2017). Retrieved from https://www.cdc.gov/nchs/data/nhsr/nhsr102.pdf

Apelblat, A., & Tamir, A. (1986). Enthalpy of solution of lithium bromide, lithium bromide monohydrate, and lithium bromide dihydrate, in water at 298.15 K. *The Journal of Chemical Thermodynamics, 18*(3), 201-212. doi:10.1016/0021-9614(86)90048-0

Apelblat, A., Weintraub, R., & Tamir, A. (1984). Enthalpy of solution of lithium chloride and of lithium chloride monohydrate in water. *The Journal of Chemical Thermodynamics, 16*(10), 935-941. doi:10.1016/0021-9614(84)90161-7

Apellaniz, R., & Belgium, L. *United States Patent Number PCT/BE1986/000009.* Retrieved from https://patentscope.wipo.int/search/en/detail.jsf?docId=WO1986005671

Association of surgical technologists. Retrieved from http://www.ast.org/

AST standards of practice for skin prep of the surgical patients. Retrieved from http://www.ast.org/uploadedFiles/Main_Site/Content/About_Us/Standard_Creating_Sterile_Field.pdf

ASTM international. Retrieved from https://www.astm.org/

Bergman, T. L., Lavine, A. S., Incropera, F. P., & Dewitt, D. P. (2011). *Fundamentals of heat and mass trasnfer* (Seventh ed.). Hobkone, New Jersey: John Wiley & Sons, Inc.

Betadine compound summary. Retrieved from https://pubchem.ncbi.nlm.nih.gov/compound/Povidone-iodine#section=Top

Burks, R. I. (1998). Povidone-iodine solution in wound treatment. *Physical Therapy, 78*(2), 212-218. doi:10.1093/ptj/78.2.212

Chemical compatibility chart. Retrieved from http://sevierlab.vet.cornell.edu/resources/Chemical-Resistance-Chart-Detail.pdf

ChloraPrep® summary of product characteristics. (2016). (n.d.) BD.

Chlorhexidine. Retrieved from https://www.drugbank.ca/drugs/DB00878

Compound summary - isopropyl alcohol. (2019). Retrieved from https://pubchem.ncbi.nlm.nih.gov/compound/isopropanol

Denaturation of proteins. Retrieved from http://chemistry.elmhurst.edu/vchembook/568denaturation.html

Ebnesajjad,S. (2015). Injection molding. *Fluroplastics. 2*, 236-281. doi:10.1016/0021-9614(84)90161-7.

Ehwerhemuepha, L., Schultz, S., & Feaster, W. (2018). Clinical and psychosocial factors associated with patient experience in pediatrics. *Clin Pediatr (Phila), 57*(8), 937-944. doi:10.1177/0009922817737078

Dean, James B. (1994). *United States patent number US5483949A.* Retrieved from https://patents.google.com/patent/US5483949/en

Hansen, M. (2005). Gas-assist injection molding: An innovative medical technology. *Medical Device and Diagnostics Industry,* Retrieved from https://www.mddionline.com/gas-assist-injection-molding-innovative-medical-technology

Hemani, M., & Lepor, H. (2009). Skin preparation for the prevention of surgical site infection: Which agent is best? *Reviews in Urology, 11*(4), 190-195.

ISO 10933-1:2018. (2018). Retrieved from https://www.iso.org/standard/68936.html

ISO 11737-2:2009. (2015). Retrieved from https://www.iso.org/standard/44955.html

ISO 13485 - medical devices. (2016). Retrieved from https://www.iso.org/iso-13485-medical-devices.html

ISO 15378:2017 (2017). Retrieved from https://www.iso.org/standard/70729.html

Isopropyl and ethyl alcohol explained. Retrieved from http://kohlindustries.com/kohl-tips/isopropyl-and-ethyl-alcohol-explained/

Jackson, J. L., Chamberlin, J., & Kroenke, K. (2001). *Predictors of patient satisfaction,* 52(4), 609-620. doi://doi.org/10.1016/S0277-9536(00)00164-7

Jha, A. K., Orav, E. J., Zheng, J., & Epstein, A. M. (2008). Patients' perception of hospital care in the united states. *New England Journal of Medicine, 359*(18), 1921-1931. doi:10.1056/NEJMsa0804116

John, M., Ford, J., & Harper, M. (2014). Peri-operative warming devices: Performance and clinical application. *Journal of the Association of Anesthetists, 69*(6), 527-654. doi: 10.1111/anae.12626

Kirkham, M. B. (2014). In Kirkham M. B. (Ed.), *Chapter 3 - structure and properties of water*. Boston: Academic Press.

Kurz, A., Sessler, D. I., & Lenhardt, R. (1996). Perioperative normothermia to reduce the incidence of surgical-wound infection and shorten hospitalization. *New England Journal of Medicine, 334*(19), 1209-1216. doi:10.1056/NEJM199605093341901

L.H.H. (1936). The temperature of the skin surface. *Bierman,* 106, 1158-1936. . doi:10.1016/S0002-8703(36)90516-1

Lee, N. C. (2000). *Understanding blow molding*. Cincinnati, Ohio: Hanser.

Lithium chloride. Retrieved from https://www.sigmaaldrich.com/catalog/product/sigma/62476?lang=en&region=US

Lohner, S. (2017). Chilling science: Evaporative cooling with liquids. Retrieved from https://www.scientificamerican.com/article/chilling-science-evaporative-cooling-with-liquids/

McDonnell, G., & Russell, A. D. (1999). Antiseptics and disinfectants: Activity, action, and resistance. *Clinical Microbiology Reviews, 12*(1), 147-179. doi:10.1128/CMR.12.1.147

Medline. (2017). ChloraPrepTM solutions safety data sheet. Retrieved from https://www.medline.com/media/catalog/Docs/MSDS/MSD_SDSD14678.pdf

National Institute of Standards and Technology, (NIST). (2018). Isopropyl alcohol. Retrieved from https://webbook.nist.gov/cgi/cbook.cgi?ID=C67630&Mask=4

No water needed in new army MRE heaters. (2015). Retrieved from http://link.galegroup.com/apps/doc/A398953369/PPMI?u=mlin_c_worpoly&sid=PPMI&xid=01335476

Oppel, E., & Young, G. J. (2018, Nurse staffing patterns and patient experience of care: An empirical analysis of U.S. hospitals.*53*, 1799+. Retrieved from http://link.galegroup.com/apps/doc/A543612827/AONE?u=mlin_c_worpoly&sid=AONE&xid=29a5a403

Povidone iodine compound summary. Retrieved from https://pubchem.ncbi.nlm.nih.gov/compound/Povidone-iodine#section=Top

Povidone-iodine. (a). Retrieved from https://www.drugbank.ca/drugs/DB06812

Povidone-iodine. (b). Retrieved from https://www.sciencedirect.com/topics/pharmacology-toxicology-and-pharmaceutical-science/povidone-iodine

AORN. *Recommended practices for preoperative patient skin antisepsis.* (2013). Retrieved from https://www.hqinstitute.org/sites/main/files/file-attachments/skin_antisepsis_0.pdf

Reichman, D. E., & Greenberg, J. A. (2009). Reducing surgical site infections: A review. *Reviews in Obstetrics & Gynecology, 2*(4), 212-221. PMC2812878

Researchers submit patent application, "porous oxygen activated heater", for approval. (2013). *Life Science Weekly.* Retrieved from http://link.galegroup.com/apps/doc/A338936901/AONE?u=mlin_c_worpoly&sid=AONE&xid=57c6c41b

Rose, G., & McLarney, T. (2013). *Anesthesia equipment simplified.* McGraw Hill Professional.

Rüegg, P. (2017). Rare proteins collapse earlier. Retrieved from https://phys.org/news/2017-02-rare-proteins-collapse-earlier.html

Safety and effectiveness of health care antiseptics: topical antimicrobial drug products for over-the-counter human use. (2017). Retrieved from https://www.federalregister.gov/documents/2017/12/20/2017-27317/safety-and-effectiveness-of-health-care-antiseptics-topical-antimicrobial-drug-products-for

Safety data sheet for LiCl solution. (2016). Retrieved from https://www.neb.com/-/media/dcdb9d7421b3439792ab0201565dc36a.pdf

Seow, L. W., & Lam, Y. C. (1997). Optimizing flow in plastic injection molding. *Journal of Materials Processing Tech, 72*(3), 333-341. doi:10.1016/S0924-0136(97)00188-X

Shin, K. M., et al. (2015). The efficacy of pre-warming on reducing intraprocedural hypothermia in endovascular coiling of cerebral aneurysms. *BMC Anesthesiology, 15*(1), 8. doi:10.1186/1471-2253-15-8

Sigma-Aldrich. (2018). Isopropyl alcohol product information. Retrieved from https://www.sigmaaldrich.com/content/dam/sigma-aldrich/docs/Sigma-Aldrich/Product_Information_Sheet/190764pis.pdf

Singh, R., Asthana, V., Sharma, J. P., & Lal, S. (2014). Effect of irrigation fluid temperature on core temperature and hemodynamic changes in transurethral resection of prostate under spinal anesthesia. *Anesthesia Essays and Researchers, 8*(2), 209-215. doi:10.4103/0259-1162.134508

Stockmen's Supply. (2018). Material safety data sheet - isopropyl alcohol 70%. Retrieved from http://www.stockmens.com/images/PDF/195529.pdf

Supersaturated solution. (2013). Retrieved from https://www.stevespanglerscience.com/lab/experiments/instant-hot-ice/

Sykes, J. E., & Weese, J. S. (2014). Chapter 11 - infection control programs for dogs and cats. *Canine and feline infectious diseases* (pp. 105-118) Elsevier Inc. doi:10.1016/B978-1-4377-0795-3.00011-9

Szolcsányi, J. (2015). Effect of capsaicin on thermoregulation: An update with new aspects. *Temperature: Medical Physiology and Beyond, 2*(2), 277-296. doi: 10.1080/23328940.2015.1048928

Toomey, M. (2013). Preoperative chlorhexidine anaphylaxis in a patient scheduled for coronary artery bypass graft: A case report. *Aana, 81*(3). doi: 10.5704/MOJ.1707.008

Usp. (a). Retrieved from http://www.usp.org/

Usp. (b). Retrieved from https://www.usplastic.com/catalog/item.aspx?itemid=30899

Vandyshev, V. N. (2003). Enthalpy characteristics of solution and solvation of CuCl2 in water-acetonitrile mixtures at 298.15 K. *Russian Journal of General Chemistry, 73*(6), 855-859. doi:1026380113367

Warming cabinets. Retrieved from https://www.universalmedicalinc.com/all-products/clinical-equipment/warming-cabinets.html

Weiser, T., Regenbogen, S., Thompson, K., Haynes, A., Lipsitz, S., Berry, W., & Gawande, A. (2018). An estimation of the global volume of surgery: A modelling strategy based on available data. *The Lancet,* 372, 139-144. doi:10.1016/S0140-6736(08)60878-8

What is a european standard (EN)? (2019). Retrieved from https://www.cencenelec.eu/standards/DefEN/Pages/default.aspx

WHO guidelines on hand hygiene in health care. (2009). (). Geneva: World Health Organization. Retrieved from http://apps.who.int/iris/bitstream/handle/10665/44102/9789241597906_eng.pdf;jsessionid=FC9B945E9DCE4A8F96226DD9CA3A2B0A?sequence=1

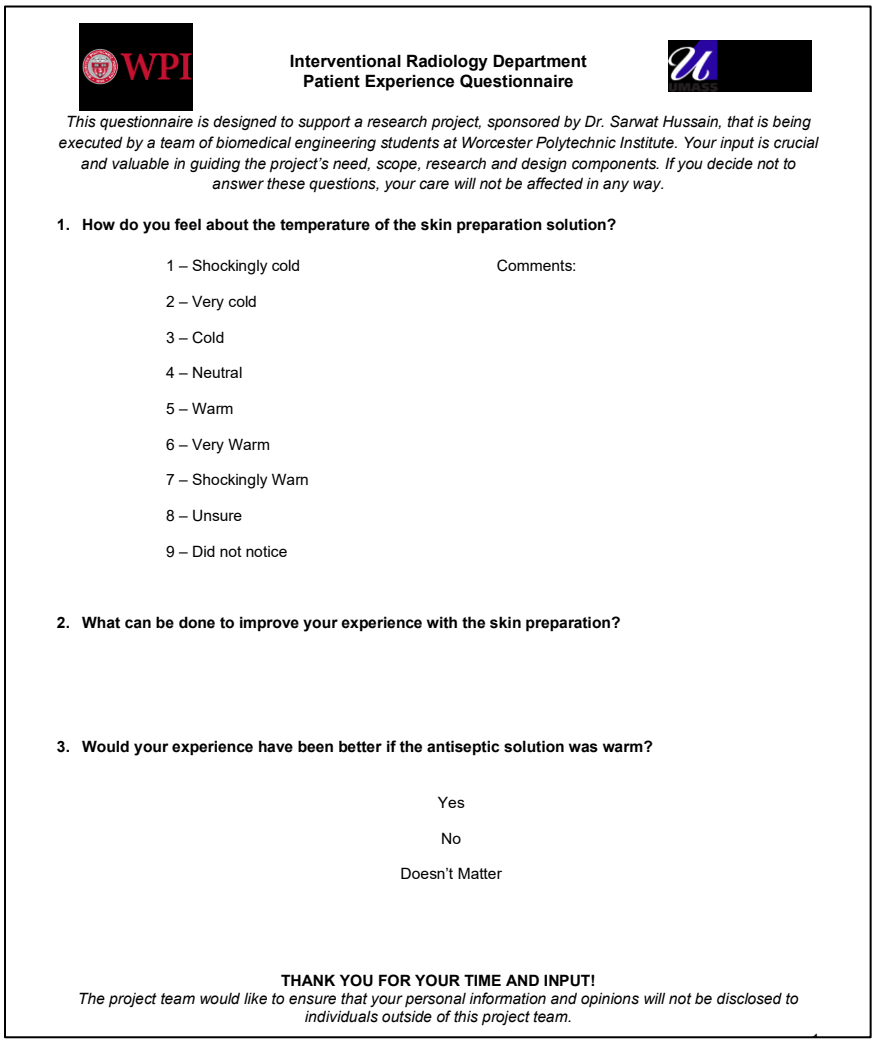
Why does rubbing alcohol evaporate quicker than water? Retrieved from http://scienceline.ucsb.edu/getkey.php?key=4875

X. Liang, & S. A. Boppart. (2010). Biomechanical properties of *in vivo* human skin from dynamic optical coherence elastography. *IEEE Transactions on Biomedical Engineering, 57*(4), 953-959. doi:10.1109/TBME.2009.2033464

Appendices

Appendix A

Appendix A includes the patient experience questionnaire that was given to Interventional Radiology department at UMMS.



Interventional Radiology Department
Patient Experience Questionnaire

This questionnaire is designed to support a research project, sponsored by Dr. Sarwat Hussain, that is being executed by a team of biomedical engineering students at Worcester Polytechnic Institute. Your input is crucial and valuable in guiding the project's need, scope, research and design components. If you decide not to answer these questions, your care will not be affected in any way.

1. **How do you feel about the temperature of the skin preparation solution?**

   1 – Shockingly cold — Comments:
   2 – Very cold
   3 – Cold
   4 – Neutral
   5 – Warm
   6 – Very Warm
   7 – Shockingly Warn
   8 – Unsure
   9 – Did not notice

2. **What can be done to improve your experience with the skin preparation?**

3. **Would your experience have been better if the antiseptic solution was warm?**

   Yes
   No
   Doesn't Matter

THANK YOU FOR YOUR TIME AND INPUT!
The project team would like to ensure that your personal information and opinions will not be disclosed to individuals outside of this project team.

MEDICAL PERSONNEL ONLY

---

1. **Which bodily region required skin preparation for the procedure? What procedure was performed?**

2. **How important is warming the skin preparation stick to the overall patient experience? Please circle an option below!**

   1 - very unimportant — Comments:
   2 - somewhat unimportant
   3 - neutral
   4 - somewhat important
   5 - very important

Appendix B

Appendix B include the WPI IRB Approval for the patient questionnaire in Appendix A.

WORCESTER POLYTECHNIC INSTITUTE

100 INSTITUTE ROAD, WORCESTER MA 01609 USA

Institutional Review Board
FWA #00015024 - HHS #00007374

Notification of IRB Approval

Date:	29-Nov-2018
PI:	Coburn, Jeannine M
Protocol Number:	IRB-19-0247
Protocol Title:	Redesigning Preoperative Skin Preparation Applicators to Enhance Patient Comfort
Approved Study Personnel:	Costi, Alicia~Kolaya, Emily~Ricciuti, Kalyn~Kaur, Ravneet~Coburn, Jeannine M~
Effective Date:	
Exemption Category:	2
Sponsor*:	

The WPI Institutional Review Board (IRB) has reviewed the materials submitted with regard to the above-mentioned protocol. We have determined that this research is exempt from further IRB review under 45 CFR § 46.101 (b) (2), which applies to

Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless: (i) information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and (ii) any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.

The study is approved indefinitely unless terminated sooner (in writing) by yourself or the WPI IRB. Amendments or changes to the research that might alter this specific approval must be submitted to the WPI IRB for review and may require a full IRB application in order for the research to continue. You are also required to report any adverse events with regard to your study subjects or their data.

Changes to the research which might affect its exempt status must be submitted to the WPI IRB for review and approval before such changes are put into practice. A full IRB application may be required in order for the research to continue.

Please contact the IRB at irb@wpi.edu if you have any questions.

*if blank, the IRB has not reviewed any funding proposal for this protocol

Appendix C

Appendix C includes results from the patient questionnaire in Appendix A.

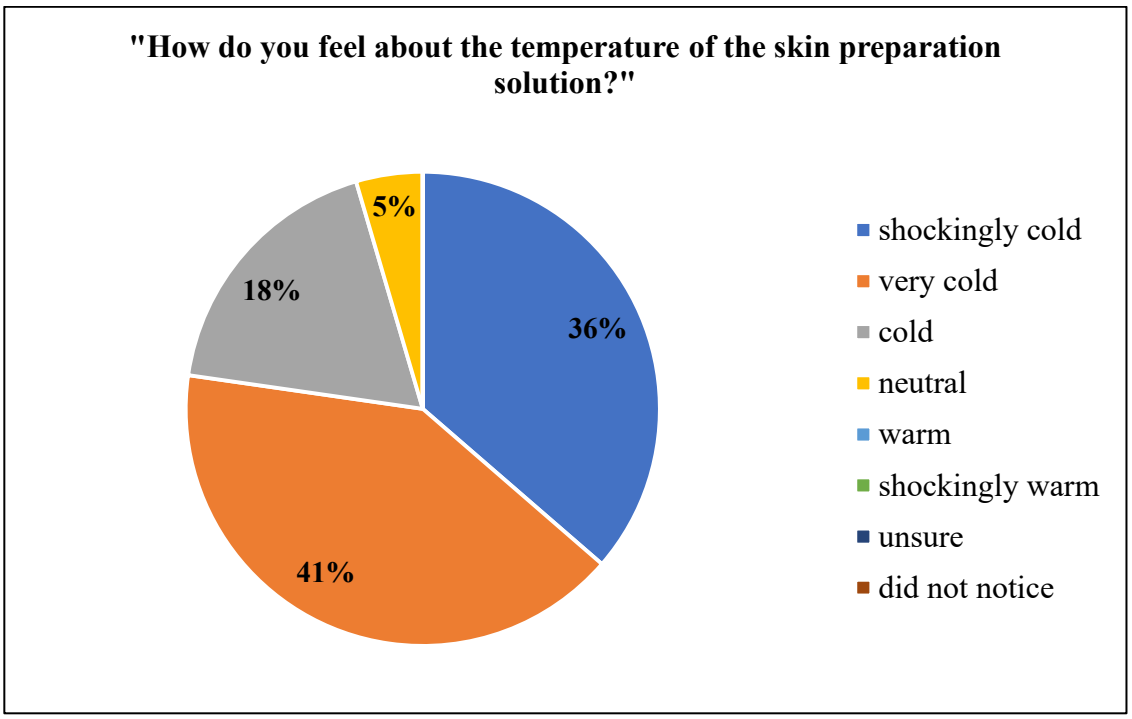


Figure C1. Responses to Question 1: "How do you feel about the temperature of the skin preparation solution?"

"What can be done to improve your experience with the skin preparation?"				
Patient did not answer question	"to be warmed"	"warm"	"make it warmer"	"hot"
"warming could benefit some patients"	"warm"	"warm"	"warmer"	"warmer"
"warmer"	"warmer"	"to be warm	"warmer"	
"hot"	"warming"	"warmer"	"to be warm"	
Patient did not answer question	"nothing"	"warmer"	"to be warm"	

Figure C2. Responses to Question 2: "What can be done to improve your experience with the skin preparation?"

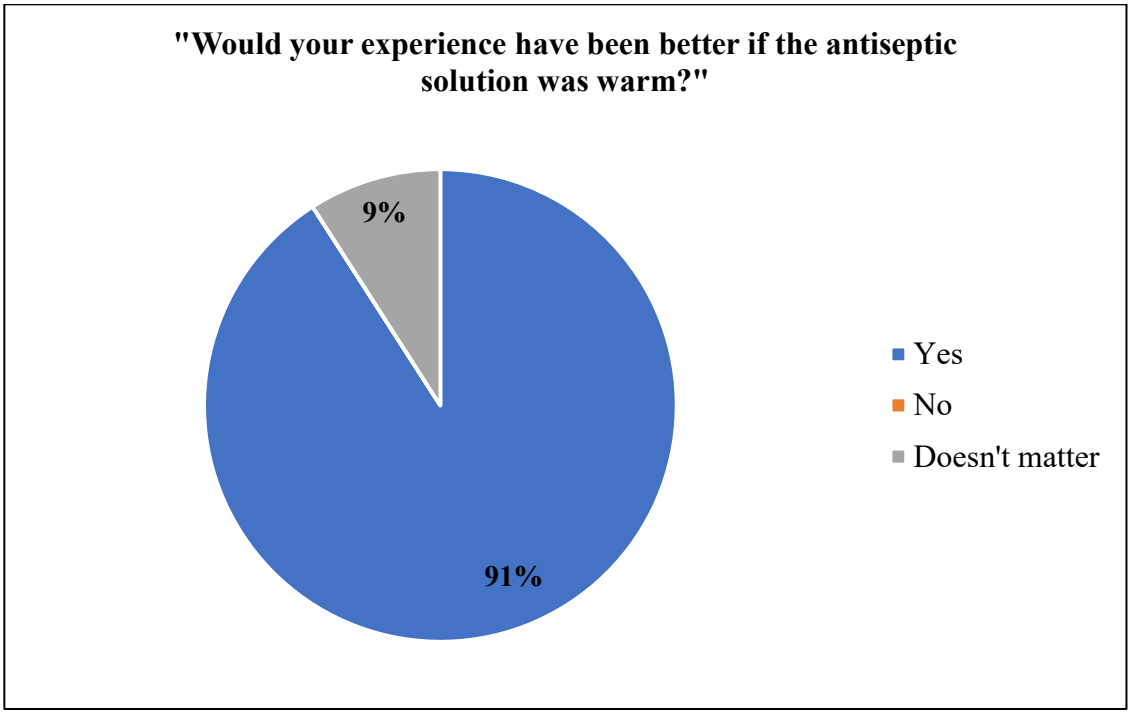


Figure C3. Responses to Question 3: "Would your experience have been better if the antiseptic solution was warm?"

Appendix D

Appendix D contains the EN Standard Protocol for the antimicrobial testing that was performed.

Requirements:

The product, when tested in accordance with the test protocol described above, shall demonstrate at least a 10^4 log reduction in viable counts when the test organisms are Pseudomonas aeruginosa, Staphylococcus aureus, Escherichia coli and Enterococcus hirae.

Test Method:

Prep

1. Subculture culture from the stock culture by streaking onto TSA agar and incubate overnight.
2. Make a second subculture and incubate as earlier.
3. The second subculture is the working culture. Bacterial test suspensions are prepared by taking 10 ml of diluent (Tryptone Sodium Chloride solution) in a 100 ml flask with 5g of glass beads.
4. From the working culture a loopful of bacterial cells is transferred into the diluent and suspended. Flask is shaken 3 minutes using a mechanical shaker

Test

1. Pipette 8 ml of the test products in to container of suitable capacity and add 1ml of water.
2. Add 1ml bacterial suspension containing 1.5x108 cfu/ml to 5 x108 cfu/ml and 1ml of interfering substance (0.3/3g/l BSA) after incubating these two 2 minutes.
3. Immediately start the stopwatch, mix and place the container in the water bath at 20°C.
4. The activity of the product shall be determined for a contact time chosen from one of the following: 1min, 5min, 15min, 30min, 45min, 60min.
5. At the chosen contact time, pipette 1ml of the test mixture into a tube containing 8ml neutralizer (30g/l polysorbate 80 + 3g/l lecithine) and 1ml of water. Mix and incubate in the water bath for 5 minutes.
6. After neutralization take a 1ml sample in duplicate and transfer on TSA plates.
7. Incubate the plates in 36°C for 24 hours. Count the plates and determine the number of colony forming units for each plate.

Results:

For each test organism record the number of cfu/ml in the bactericidal test suspension (N) and after the test procedure for bactericidal activity of the product (Na).

Conclusion:

The product shall be deemed to have passed the test if it demonstrates a 10^4 or more reduction in viability of test organism within 60 min or less at 23°C.