REDUCING LEVELS OF MEDICAL DEVICE CONTAMINATION THROUGH PACKAGE REDESIGN, SEAL GEOMETRY AND OPENING TECHNIQUE

By

Paula Perez

A DISSERTATION

Submitted to
Michigan State University
in partial fulfillment of the requirements
for the degree of

Packaging – Doctor of Philosophy

2018

ABSTRACT

REDUCING LEVELS OF MEDICAL DEVICE CONTAMINATION THROUGH PACKAGE REDESIGN, SEAL GEOMETRY AND OPENING TECHNIQUE

By

Paula Perez

Healthcare Acquired Infections (HAIs) are the cause of substantial pain and emotional stress. On any given day, 1 in every 25 patients in the US has an HAI. This has serious economic ramifications. Although the incidence of HAIs has been reduced through the implementation of varied prevention projects, work remains. Limited work has focused on indirect routes of contamination, and even fewer on packaging and handling as potential contributors.

The presented work is among the first objectively investigating how package design and provider technique impact the sterile transfer of medical devices. Specific research goals were:

1. To evaluate how package design features (inward curl, outward curl, tab design compared to a traditional, commercial pouch design) affect the likelihood of a device contacting non-sterile surfaces (the outside of the package or the hands of the provider).
2. To characterize how aseptic technique (traditional vs. a modified approach) contributes to the likelihood of contact between medical devices and non-sterile surfaces during sterile transfer.
3. To develop a reliable, relatively easy and cost effective methodology that can be used to design and prototype new styles of flexible packages.
4. To evaluate how peel geometry (using pouches created with the new prototyping method) impacts rates of contact between transferred devices and non-sterile surfaces.

To explore goals 1, 2 and 4, a total of 136 healthcare providers were asked to present devices to a simulated sterile field. Participants' gloved hands and the outside of test pouches were coated with a contamination simulant and participants were asked to present the contents of different pouch designs using two transfer techniques: "standard technique" where participants presented using their typical approach and a "modified technique" where participants were instructed to grab the package at the top center and transfer contents to the field using a single, fluid motion. Transferred devices were examined to verify the presence of the analyte and data was recorded in a binary fashion (yes/no) and analyzed using a generalized linear mixed model.

Results indicated significant main effects of pouch design ($p<0.001$) and aseptic technique ($P=0.0189$) on rates of contact with non-sterile surfaces. Pouches designed to curl outward resulted in less contact than all other designs, this was true for both opening techniques: standard technique: (outward vs. commercial, inward and tab pouch) (14±2.5% vs. 26±3.5% ($P <0.0047$), 25±3.4% ($P <0.0140$) and 23±3.3% ($P <0.0418$), respectively) and modified technique (outward vs. commercial, inward and tab pouch) (8±1.8% vs. 22±3.2%, 25±3.5% and 25±3.5% respectively; all comparisons $P = <0.0001$) (goal 2).

In support of goal 4, two geometries were created using a novel prototyping method we developed (goal 3-described within): one geometry represented a chevron pouch while the second was a rounded shape. Each of the two base geometries was modified with the addition of an extra seal intended to result in abrupt force differentials. A significant effect of geometry was indicated ($P =0.0108$). Specifically, the chevron geometry resulted in a higher rate of contact with non-sterile surfaces (42%±3%) than the round shaped geometry (35%±2%). Data did not support the idea that the addition of the bar intended to induce abrupt transitions in force profile had an effect on device contamination ($P=0.1002$).

This dissertation is dedicated to my family, especially to my father who always encourages me to pursue higher education and who suggested the idea of pursuing a PhD. To my mother and nephew, for keeping the balance and bringing joy to my life through long distance calls. To my sister in law and brother for being a long distance support during difficult moments. I also want to dedicate this dissertation to Chris Wilson, my partner, friend, co-adventurer and strong support during this journey. I will be eternally grateful for all the blissful memories, support and love.

ACKNOWLEDGMENTS

I would like to express my deep gratitude to my advisor Dr. Laura Bix for your patience, guidance, enthusiastic encouragement and for allowing me to explore and understand the world of academia. Thank you for teaching me to be brave and inspire me to become an expert on my field. I would also like to thank the rest of my committee (Dr. Tamara Bush, Dr. Maria Rubino, Dr. Gary Burgess, and Dr. Selke) for providing valuable and constructive suggestions during the planning and execution of this research.

I would also like to thank a series of contributors to the work of this dissertation. First, to the Blue Cross Blue Shield of Michigan Foundation who provided the funding for the execution of this project through the Investigator Initiated Grant program. Second, to Dhuanne Dodrill at Rollprint, LLC, Kent Hevenor at Sencorp White, Chris Sarantos at Steripackgroup and Dan Penny at Cardinal Health for providing the resources necessary to execute this project.

Third, to Nancy Miller, Shelia Cotten, Ted Glyn, Sharon Baer (affiliated with the MSU/Sparrow Center for Innovation and Research) and Sparrow Hospital, Mary Jo Nowicki, Program Director of Surgical Technology in Clinton Township and Baker College and Meri Goehring and Dan Vaughn at Grand Valley State University for providing assistance with subject recruitment and the provision of a testing space for the same.

A special thanks to Daewoo Pak from CSTAT, Tony Trier, and all graduate and undergraduate student workers who participated on this journey: Katie Cwiakala, Josh Drost, Alyssa Harben, Madison Hardy, Jiyon Lee, Yanfeng Miao, Chancy Zhang, Eric

Estrada, Lindsay Jessmore, Mazzella, Jack Michalski, Justin Scott, Michael Drost, Kelly Patterson, Tyler Tuttle, Megan Luzenski, Lindsay Hoard, Qiren Gao, Lindsay Nault, Zachary Sadler.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

CHAPTER I

INTRODUCTION

Healthcare acquired infections (HAIs) are defined as infections acquired during hospitalization that were neither present nor incubating in the patient prior to receiving services in the hospital (Collins, 2008). These infections not only cause patients extensive illness and suffering, they impose an economic burden that drains the health care system; patients with HAIs require more treatment, care and medication compared to other patients. It was estimated that in 2011, there were 722,000 HAIs in U.S. acute care (Magill et al., 2014). Although significant progress has been made in preventing HAIs, there is more work to be done.

Recognizing the paramount role of the sterile field in preventing surgical site infections, the Association of peri-Operative Registered Nurses (AORN)[1] and the Association of Surgical Technologists (AST)[2] have developed standards regarding its creation and maintenance. These standards include guidelines on how packaging should be handled, opened and transferred to the sterile field in the operating room (a process termed "aseptic presentation"). However, when each of the Associations' requirements are chased to their seminal sources, it is evident that many aspects of the requirements are based on traditional practice as opposed to being evidence-based (T. Trier, 2016).

Recent years have seen increasing interest in user-centered design for healthcare to improve healthcare quality and patient safety (Carayon et al., 2013; Parush, Parush, & Ilan, 2017). Among these initiatives, the US Food and Drug Administration (FDA) released a guidance document intended to assist the medical device industry when designing and evaluating

[1] Recommended practices for maintaining a sterile field
[2] Standards of practice for creating the sterile field

device designs for usability; ultimately, the goal of the document is to minimize potential use errors by understanding the environment, user needs, and devices application. The document focuses on all points of interaction between the user and products, including: packaging, labeling, and instructions for use (IFUs), etc. (FDA, 2011).

The ability of the package to support and maintain a medical device's sterility throughout distribution and to facilitate sterile transfer, or aseptic presentation, at the point of use, is critical. The packaging of medical devices accomplishes these responsibilities through the use of a "Sterile Barrier System," or SBS. A SBS is defined as the "minimum package that prevents ingress of microorganisms and allows aseptic presentation of the product at the point of use" (Technical Committee ISO/TC 198, 2006a). The medical device industry is guided by ISO 11607, a standard that provides requirements to validate SBS for terminally sterilized medical devices, making reference to the necessity that sterile barrier systems facilitate aseptic presentation. However, the standard provides limited information about aseptic presentation and does not specify procedures/methods to validate how effective a package design is in this regard.

A very limited number of studies have investigated the role of packaging as a potential route of microbe transmission (Minckley, 1969, Crick et al., 2008; Smith et al., 2009; Trier, 2012; Trier et al.,2014;, Trier, 2016). Critical information regarding the relationship of specific aspects of package design features and biomechanical approaches to aseptic technique are lacking in the published literature.

The research proposed herein has four major goals:

1. To evaluate how opening design features (inward curl, outward curl, tab design compare to a traditional, commercial pouch design) affects the likelihood of a device contacting non-sterile surfaces (the package or the hands of the provider),

2. To characterize how aseptic technique (traditional vs. a modified approach) contributes to the likelihood of contact between medical devices and non-sterile surfaces during aseptic transfer.
3. To develop a prototyping methodology capable of rapidly prototyping pouch designs with varying peel geometries using existing equipment.
4. To evaluate how peel geometry (using pouches crated with the new prototyping method) impact rates of contact between transferred devices and non-sterile surfaces.

CHAPTER II

LITERATURE REVIEW

2.1 Medical Devices

The U.S. Food and Drug Administration defines a medical device as:

> "An instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is:
>
> - recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them,
> - intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or
> - intended to affect the structure or any function of the body of man or other animals, and which does not achieve any of its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes." (Food and Drug Administration, 2014)

Medical devices are categorized into four different classes depending on its criticality or risk level. Class A devices are considered a low risk (e.g. tongue depressors), Class B posses a risk level low to moderate (e.g. suction equipment), Class C has a risk level moderate to high (e.g. lung ventilators), and Class D devices are considered high risk (e.g. heart valves) (Bix & de la Fuente, 2010)

2.1.1 Sterilization

Many medical devices are terminally sterilized. When terminally sterilized, the device is sealed in the package and then sterilization occurs. The sterilization process is, by necessity, a hostile process intended to result in the exponential death of microorganisms. Terminal sterilization renders the entire sterile barrier system (SBS) sterile, although its outside is later

contaminated through handling and environmental exposure. Terminal sterilization processes include: steam, ethylene oxide (EtO) gas, gamma radiation, and electron-beam (e-beam) radiation (Yambrach, 2010).

Steam sterilization combines heat and moisture to kill microorganisms. It requires a temperature of 121°C, however, this temperature has the potential to weaken the seals and package materials. EtO sterilization uses cycles that involve pressure differentials to drive ethylene oxide gas into filled, sealed packages in order to disrupt certain cellular activities within the microorganisms, resulting in their death; pressure differentials are also employed to evacuate the noxious fumes from within the package (Yambrach, 2010).

These processes, designed to induce stresses on microorganisms also have the potential to cause stresses within the SBS, potentially impacting its performance (Plester, 1973). These effects may not be totally apparent until products are exposed to further stress during handling and distribution. In contrast with steam and EtO sterilization, radiation sterilization does not expose the packages to high temperatures that might weaken seals. However, materials exposed to radiation can become brittle. Gamma sterilization uses cobalt-60 as a method to kill microorganisms while E- beam sterilization consists of the excitation of electrons that bombards the package and product causing biological damage. Embrittlement has the potential to affect SBS integrity because cracking can occur when materials are flexed, resulting in breaches with the potential to compromise package integrity. The issue is amplified during distribution as packages experience physical hazards. (Yambrach, 2010)

2.2 Packaging

ISO 11607 defines “product” as the contents (i.e. medical device) and the preformed sterile barrier system, suggesting that you do not have a product without the packaging. Packaging is an

integral part of medical device development; it must assure microbial integrity of the product (through the SBS) and, as mentioned previously, assist with aseptic transfer of the device to the field.

Packaging broadly performs three main functions: protection, provision of utility and communication (Bix & de la Fuente, 2010). In the medical device industry, protection is primarily associated with preventing any contact between a medical device and microbes in the environment (Bix & de la Fuente, 2010). Medical packaging can be classified into two broad categories: thermoformed trays, commonly used for surgical kits, and flexible non-formed pouches, commonly used for single-use disposable devices (Bix & de la Fuente, 2010)(see Figure 1).

Figure 1. (a) Flexible Non-Formed Pouch (b) Thermoformed Tray

Thermoformed trays can be classified as semi-rigid (semi rigid pictured in Figure 1b) or flexible. Semi-rigid trays contain a rigid component, which provides structural support and protection to the device, and a flexible lid. In contrast, flexible thermoformed trays are similarly

formed, but do not provide the same level of protection and support, making them appropriate for low cost medical devices. Flexible non-formed pouches are flat pouches made of two webs, usually film and Tyvek®, sealed along the perimeter (Bix & de la Fuente, 2010).

2.2.1 Chevron Pouches

Work presented herein employs the use of chevron pouches (see Figure 2) to investigate the study objectives. This type of pouch was chosen because it is the most common pouch used in the medical device industry and it is known because of its "peak-shaped seal" at the top center of the package (Sherman, 1998). Chevrons were designed to "distribute peel forces along the relatively narrow seal lines rather than across the entire seal as would be with the case of a rectangular seal and can be modified to better suit opening needs by configuring its angle." (Sherman, 1998). Even force distribution occurs when pouches are opened from the top center in with a straight motion of travel, parallel to the length of the package. However, research suggests that users frequently grip the corners of these pouches because they provide sufficient material to enable a stronger grip than the smaller amount available at the top center. This behavior has been suggested to be associated with higher rates of contamination than when these packages are opened as intended (T. Trier, 2016).

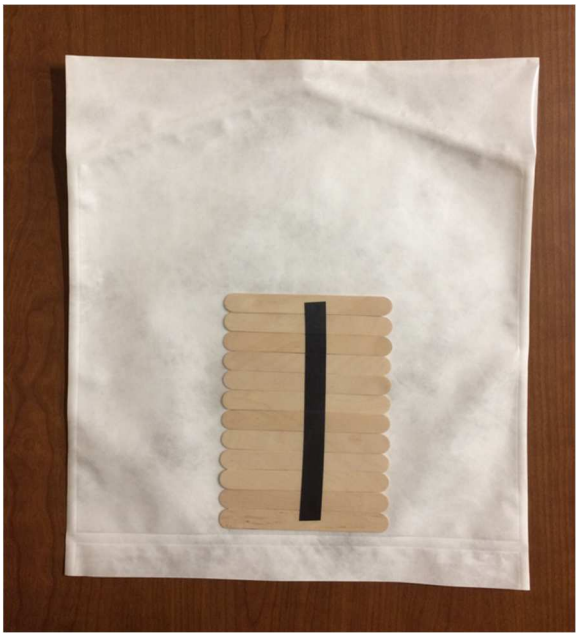


Figure 2. Chevron pouch

A post-hoc video review of a series of openings with chevron pouches by researchers in our lab investigating the biomechanical factors associated with opening suggested that users were better able to secure package corners in smaller sized packages. In fact, 100% of the small pouch openings had the corners secured with the hands, while only 31% of the trials comprised of large pouches were reported as having the corners secured. The research team observed that corners curled during 56% of the opening trials involving the large pouches, with 47% of the total number of trials curling inward and 9% curling out.

Although knowledge of the impact that material curl has on contact with non-sterile surfaces is very limited, several researchers have investigated how material properties, packaging composition, and processing result in material curling.

Morris (2003) used a cereal liner film to develop a model, which describes the curl of films as a function of shrinkage, modulus, and thickness of each layer. The author hypothesized

that curling is the result of residual stresses formed during processing since different layers shrink differently in the quenching process due to differences in freezing points, crystallinity and coefficients of thermal expansion. Residual stresses from processing are countered by a resisting force related to the stiffness and thickness of the layers that compose the whole structure. As a result, the film will experience curling when the residual stress is higher than the resisting force, that is, it is large enough to overcome it. In his study, pressure, volume, and temperature data were investigated to understand the effect of differential shrinkage between the layers. An experiment was conducted on a two-layer film; the author indicates that structures containing ethylene vinyl alcohol (EVOH) and nylon curl tightly, whereas structures utilizing polymers with lower crystallinity curled more loosely.

A second study was performed to understand the relative impact of factors related to curling. Different structures were processed to understand the variables affecting curling. Structures included in the study were: high-density polyethylene –ethylene-vinyl acetate (HDPE-EVA), HDPE-ionomer, ionomer-EVA, HDPE-EVOH, and HDPE-nylon. Crystallinity was found to most significantly impact curling, followed by blow up ratio (BUR), defined as the final film diameter divided by the die diameter, (Morris, 2016) and the thickness ratios of the materials. It was found that decreasing crystallinity of the polyolefin layer could reduce curling, followed by increasing the process time, reducing the BUR and decreasing the polyolefin/EVOH thickness ratio (Morris, 2003).

Goetz reinforces Morris' assertion of the important role that crystallinity plays in inducing material curl. Curling "is not due to different coefficient of thermal contraction of the polymers but to their different crystallization kinetics." (Goetz, 2003). The author explains that when a multilayer structure of polyamide (PA) /tie resin/polyethylene (PE) is in the molten stage,

the polymer chains are arranged in a random pattern. When the films start the cooling process following extrusion, the PA layer is the first to begin recrystallization because it has a higher crystallization temperature (the temperature where it starts to form a regular pattern of crystalline domains). Since the crystalline domain has high density, the crystallization causes shrinkage. While this happens in the PA layer, the PE layer is still molten and will adjust dimensionally with PA. Upon further cooling, PE will eventually reach its crystallization temperature and also shrink. The film will curl toward the PE layer since the PA has already solidified and cannot shrink (Goetz, 2003).

Given the established, discussed importance of the SBS in enabling and maintaining the sterility of many medical devices in perioperative environments, and the fact that packaging, through its exposure to distribution and handling, is only sterile internally, we believe that curling has the potential to play a significant and important role if packaging serves as an indirect route of contamination for microbes, and a potential source for Healthcare Acquired Infections (HAIs).

2.3 Healthcare Acquired Infections

A healthcare acquired infection (HAI), is defined as "an infection that is acquired while an individual is a patient at a hospital and was neither present nor incubating in the patient prior to receiving services in the hospital." (*Food and Drug Administration Amendments Act of 2007*, 2007) Also referred to as nosocomial infections or hospital acquired infections, HAIs have being categorized among the 10 leading causes of morbidity and mortality in the United States (Johnson, Hayes, Brown, Hoo, & Ethier, 2014). In 2011, there were an estimated 722,000 HAIs in U.S. acute care hospitals with 75,000 patients dying during hospitalization (Magill et al.,

2014). It has been indicated that on any given day, 1 in every 25 U.S. patients has an HAI (Magill et al., 2014).

HAIs not only result in illness and suffering, they also impose an economic burden on the healthcare system due to extended lengths of stay, costs associated with patients' medical treatments and patient readmission (Emerson et al., 2012). Although it is difficult to estimate the exact costs associated with HAIs, the U.S. Centers for Disease Control and Prevention (CDC) estimated that in 2007 associated costs were between $35.7 billion and $45 billion (Scott, 2009). A major concern within the healthcare system is who should bear these costs, a question that was confronted within the Medicare and Medicaid systems. It was estimated that overall, in 2004, approximately 20% of Medicare beneficiaries were re-hospitalized within 30 days of release and 34% were re-hospitalized within 90 days. Postoperative infections were included on the second most frequent reasons for rehospitalizations. The costs associated with readmissions were estimated at approximately $17.4 billion (Jencks, Williams, & Coleman, 2009). In cardiac surgery patients, it was estimated that among 4,320 patients, there were 849 readmissions where 137 (16.1%) were infection related (including major and minor infections) and 8.7% attributed to major HAIs. Readmission due to major HAIs had 2.6-fold higher costs readmissions due to other causes (Greco et al., 2015). In 2008, the Centers for Medicare and Medicaid Services (CMS) announced a new coverage and payment rule as an incentive for hospitals to develop proactive strategies intended to prevent HAIs. As part of this, Medicare and the patient no longer pay for additional costs resulting from hospitalizations due to surgical site infections (Hopper & Moss, 2010; Stone, 2009); hospitals are now responsible for covering these additional costs.

Recent reports suggest improvements in the rates of HAIs due, in large part, to programs incorporated by the US Centers for Disease Control and Prevention (CDC) and the World Health

Organization (WHO), which include tracking infections by the implementation of a surveillance system, laboratory research that improves understanding of HAIs and how to prevent them (through programs such as Prevention Epicenter Program, Developing Healthcare Safety Research organizations that conduct innovative infection control and prevention research), creating new strategies to prevent future infections (by conducting roundtable discussion focused on environmental Hygiene in Healthcare that discusses how germs spreads from different sources), and by providing infection prevention guidelines and tools regarding those infections (such as the Infection control Assessment Tools to assist healthcare departments in assessing prevention practices) (Centers for Disease Control and Prevention, 2016). Other interventions include research focusing on appropriate hand hygiene practices (Allegranzi & Pittet, 2009; Boyce & Pittet, 2002) and efficacious decontamination of hospital surfaces such as bed rails, bedside tables, and medical charts (Bhalla et al., 2004; Chen, Chen, & Wang, 2014; Kramer, Schwebke, & Kampf, 2006). A recent report suggested a 50% decrease in central-line associated bloodstream infections between 2008 and 2014, an 8% decrease in hospital-onset *Clostridium difficile* between 2011 and 2014, as well as a 13% decrease in hospital-onset methicillin-resistant *Staphylococcus aureus* during this same period (Centers for Disease Control and Prevention, 2016)

2.3.1 HAI Transmission

During hospitalization, patients are exposed, directly or indirectly, to a variety of microorganisms. These microorganisms can be transferred from other patients, healthcare providers, contaminated equipment, or the hospital environment itself (Collins, 2008). Two modes of transmission are described in the *2007 Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings*:

1. *direct contact transmission* occurs when an infection is transferred from one person to another and
2. *indirect contact contamination*, involves the transmission of an infection through an intermediate object or person (Siegel, Rhinehart, Jackson, Chiarello, & the Healthcare Infection Control Practices Advisory Committee, 2007).

2.3.1.1 Direct Transmission

The majority of interventions intended to reduce infection rates target reducing rates of contaminations that occur directly, that is, directly from a single person (e.g., healthcare providers, visitors, etc.) to a patient. Surgical gloves are widely used during hospital care to provide a barrier to protect patients (and providers) against infection. Guo et al. (2012) examined the barrier between patient and provider performed by gloves during surgery to evaluate the effectiveness of the practice of "double gloving." The authors reported that glove perforation was detected in 10 out of 112 sets of single layered gloves and 12 out of 106 sets of outer gloves in the group that wore double gloves; as a result, authors suggest double gloving as a good practice to reduce inner glove preformation and prevent contact with blood-borne pathogens as well as patient's risk of contamination.

A similar study was conducted to evaluate glove integrity during surgery. Gloves used by healthcare providers were examined after surgery to identify perforations. Results suggested that 131 out 1,090 gloves used by medical professionals had perforations after surgery. When double gloves were used 76.9% of the outer gloves presented perforations, 15.4% had perforation on both inner and outer glove, and only 7.7% had a perforation on the inner glove only, reaffirming the importance of using double gloves during surgery. The author suggested that the high rates of glove perforation when using double gloves could be attributed to the higher frequency of

exchanges between users of single glove (De Oliveira & Gama, 2014). Han et al. (2013) examined not only the perforation rate, but also tactile sensitivity when thick and conventional gloves were used. Both types of gloves were used in 70 knee surgeries. Glove perforation was detected after 27 surgeries in 48 gloves for all staff members and in 38 for the surgeon. Results suggested that thicker gloves resulted in less tactile sensitivity with no improvement in terms of protection from perforation.

Like the glove studies, interventions targeting hand hygiene attempt to reduce the likelihood of HAIs that are the result of direct contact transmission occurring from interactions with healthcare providers. Targeted strategies and interventions that involve effective hand hygiene are among the most common interventions. Chun et al. reported that the prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) cases decreased from 11.1% to 0% after conducting hand hygiene education that incorporated individual feedback. The study consisted of educating nurses on hand washing practices. Observations on hand washing behavior were made before education, and at 1 week and 6 weeks after the education session (Chun, Kim, & Park, 2015).

An observational study of different hospital staff suggested that surgical antisepsis knowledge and adherence to local hand hygiene protocol was low. Results concluded that almost 74% never used a brush during hand washing while 17% used it for nails only. Initial hand washing time was recorded as an overall mean of 69.1 seconds with time differences between populations (academic staff, attending staff, residents and nurses). However, according to a questionnaire administered by researchers, surgeons believed proper hand washing should take 4.2 minutes, suggesting their behavior in the operating room did not match their knowledge. This same pattern was observed in the use of a brush; interviews suggested that 70% of participants

believed brushes should be used for proper hand hygiene (Umit et al., 2014); yet 74% never used a brush during the observational portion of the work.

A similar study utilizing video review focused on observing anesthesia provider patterns of hand contact with work environment surfaces and compliance with hand hygiene standards (Rowlands et al., 2017). Authors suggested that anesthesia providers had low rates of hand washing, with abundant opportunities for improvement related to practice and policy involving hand washing.

2.3.1.2 Indirect Transmission

Strategies that are intended to reduce transmission of microbes through indirect routes, where the microbe is transferred through an intermediate object, such as a medical device, or a secondary person, to the patient have investigated the role of operating room traffic (Pokrywka & Byers, 2013; E. B. Smith et al., 2013), and hospital surfaces (Dalstrom, 2008; Kramer et al., 2006). As indicated previously, a limited number of studies investigated the sterile barrier system (SBS) as a potential indirect route for the transfer of microbes. The SBS as a transfer vehicle has been investigated in two ways: (1) as a failed package barrier system (Kassarjian, 2011; Moghimi, Kim, & Park, 2016; J. E. Severin, 2006) and (2) with regard to its performance in the hands of the provider (Crick et al., 2008.; G. Smith et al., 2009; T. Trier, 2016; T. Trier et al., 2014).

Invasive devices are introduced into the body either through a body orifice or through the surface of the skin (European Commission, 2010). Because invasive devices are frequently presented into delicate systems (e.g., pulmonary, cardiac, neurologic), penetrating the body, generally in the context of a surgical operation (European Commission, 2010), they can be associated with HAIs. Such infections include: central line-associated bloodstream, catheter-

associated urinary tract, surgical site infection, and ventilator-associated pneumonia (Rutala & Weber, 2008). Richards et al. suggested that HAIs such as bloodstream, urinary track and respiratory infections occurring in medical-surgical intensive care units were associated with the use of invasive devices (Richards et al., 2000). Although invasive devices are associated with HAIs as a mode of transmission and as a vehicle to harbor microorganisms (Percival et al.,, 2015; Safdar, Crnich, & Maki, 2001), the source of the contamination of the devices is not widely studied.

Proper operating room ventilation is a requirement for healthcare facilities and guidelines are provided by the CDC (Centers for Disease Control and Prevention, 2003). Pokrywka & Byers suggest that surgical site infections can be associated with a disruption in the airflow in the operating room when personnel enter or exit the room. Laminar airflow is used in hospitals to prevent airborne contamination. Unnecessary foot traffic by surgical personnel can cause a disruption of the laminar air flow leading to the potential for airborne contamination (Pokrywka & Byers, 2013). Smith et al. (2013) evaluated the association of door opening and operating room contamination. To determine the presence of microorganisms during different medical procedures, two basins were used to test surfaces within the surgical theater. One basin was placed next to the OR table within the laminar airflow and the other one was placed along an OR wall, located outside the laminar flow curtain. A total of 642 samples were collected from the basins. The authors used Replicate Organism Detection and Counting plates designed to detect bacterial presence on surfaces. Samples were taken from the plates at 30-minutes intervals until the end of the procedure. The authors found that any door opening increased the number of contaminated plates by approximately 70%. When a door is opened it creates air turbulence (non-laminar pattern) leading to faster spread of bacteria.

Dalstrom (2008) investigated the influence of OR traffic on contamination rates of sterile trays that had been opened in the operating room. The intention was that they serve as a proxy for contamination for devices contained within, which can serve as a vector for indirect contamination. Trays were divided into three groups: group 1 consisted of a series of trays that were left in a locked room with no traffic; group 2 was similar to group 1, except a single person entered and exited the operating room every ten minutes; and group 3 was comprised of a series of trays that were opened and immediately covered using a sterile, surgical towel. The authors concluded that rates of contamination of uncovered trays increased as time increased. Trays that were covered resulted in zero reports of contamination. The light traffic setting suggested no evidence of impacting contamination rates while covering trays with a sterile surgical towel reduced the potential risk of contamination (Dalstrom, 2008).

Clearly, even with careful strategies for managing hygiene, airflow, etc., microbes are present in the hospital. In fact, Kramer et al. found that most pathogens associated with HAIs, such as *Enterococcus spp*. (including VRE), *Staphylococcus aureus* (including MRSA), and *Streptococcus pyogenes*, can survive for months on dry surfaces and are associated with infection transmission if the appropriate disinfecting procedure is not followed (Kramer et al., 2006). As a result, it is not surprising that healthcare providers' hands are considered a potential major source of HAIs (Collins, 2008). The constant, direct contact between providers and patients coupled with the possibility of contact with contaminated surfaces (e.g., touch screens, counters, exam tables, etc.), where it has been suggested that microbes can survive for quite some time, creates ample opportunity for both direct and indirect transmission.

Weinstein (1991) suggested that 20% to 40% of HAIs are attributed to healthcare providers' hands which have become contaminated through contact with other patients or

contaminated surfaces. Similarly, Bhalla et al. (2004) found that investigators acquired HAI pathogens on their hands after having contact with hospital room surfaces, including rooms cleaned after patient discharge.

Published work investigating packaging as a route for indirect transmission typically focuses on the ability of the package to maintain its integrity as a barrier to microbes. ASTM F17 defines package integrity as "the physical capability of a given package to protect its contents with the desired level of protection over a defined period of service; for example, as a barrier to physical, microbiological, or chemical challenges" (ASTM, 2017). Packaging integrity is a major concern for sterile devices as a break could enable microorganisms to enter the package and contaminate the contents, allowing the potential for indirect transmission of microbes when a contaminated device is used during a procedure.

J. Severin et al. (2007) developed a new whole-package, microbial challenge test using medical device trays. By employing aseptic introduction of the growth medium into sterile trays, eliminating the need to open trays which had been exposed to microbes, the method no longer required trays to be disinfected prior to culturing, decreasing the potential of false positives. Medical device trays were sealed and sterilized using ethylene oxide (ETO) and divided into four groups; three groups were challenged with *Escherichia coli* K-12 and a fourth group was labeled as control. Trays were aseptically filled with growth medium and then exposed to aerosolized microbes in varied concentrations (0, 10^2, 10^4, 10^4,10^8 CFU/mL). Tray samples were incubated and inspected for growth and colony-forming units were counted.

Severin (2006) also examined the effect of pressure differential (0, -3.78psi) and hole size on microbial ingress in trays. Before sealing, trays were ablated with 100 or 10-micron holes located at the center bottom. Sealed, sterile trays were aseptically filled with sterile agar which

would support microbe growth using a port and syringe. Filled, sealed trays were then exposed to an aerosolized microbial challenge; samples varied in terms of the breaches (hole size) present, and pressure differentials (present and absent of microbes at levels previously indicated). After the prescribed exposures, packages were incubated and inspected for growth. The author concluded that the presence of a pressure differential has a significant effect on microbial ingress into trays.

Kassarjian investigated the effect of hole size (10 and 100 μm) and pressure differential (0 and -3.78 psi), and examined the efficacy of secondary packaging (folding carton vs. pouches) on packaging integrity of medical device trays. The author also validated Severin's methodology for microbial testing and suggested a significant effect of hole size, pressure differential and secondary packaging on microbial penetration. The author reported that none of the unlidded trays in pouches exhibited microbial growth, however, microbial penetration was more likely for unlidded trays packaged on folding cartons. The presence or absence of a lid resulted in a significant effect; microbial penetration on trays inside cartons was more likely with unlidded trays than with lidded trays (Kassarjian, 2011).

A similar study of flexible packages investigated how seal integrity impacted rates of contamination. Specifically, Moghimi et al. (2016) studied the effect of micro-channels in seals on package integrity. The authors used aerosols generated by a nebulizer to spread MRSA and *E. coli* over the package. Flexible pouches were sealed with 100, 50, 25, and 15 μm micro-channels 5 mm in length. Results suggested that defective packages with channels 25 μm and larger were incapable of maintaining package integrity.

But even if the packaging does successfully maintain its integrity as it traverses distribution and handling, arriving in the OR fully intact, the outside surface has been exposed to

microbes, it is being handled by stocking personnel as well as providers who have touched multiple surfaces within the care environment. As such, the sterile contents must be (sterilely) transferred to the field. To understand the role of packaging within this context, in the next section we cover aseptic technique.

2.4 Aseptic Technique

During surgery, patients are vulnerable to infections. Therefore, healthcare providers follow certain procedures intended to mitigate their likelihood. To establish and maintain a sterile field, operating room members follow specific procedures related to its set up and upkeep. Aseptic technique, the "set of specific practices and procedures performed under carefully controlled conditions with the goal of minimizing contamination by pathogens," (Narins, 2013) is used to mitigate the likelihood of infections induced in healthcare (HAIs). Procedures are mandated for donning gowns and gloves, the use of sterile drapes, sterile field preparation, opening sterile items, transferring medications and solutions, covering the sterile field, moving within or around the sterile field as well as procedures to follow when the sterile field is broken (AORN Recommended Practices Committee, 2006a; AST Education and Professional Standards Committee, 2008b; Fallis, 2013). Aseptic technique helps to prevent contamination of the surgical environment, reducing the potential incidence of HAIs.

2.4.1 The Operating Room

The operating room (OR) is an area where surgical procedures are performed. It is a restricted area because of the requirement to maintain a controlled environment with minimum traffic in order to maintain sterile and aseptic technique (Phillips, 2016). An OR consists of an instrument table, mayo stand, preparation table, trash container, linen hamper, disposal container for sharp objects, anesthesia machine and supplies, an electrosurgical unit (ESU), a

suction apparatus, X-ray view boxes, circulator's work area (see Figure 3) and an operating bed (Phillips, 2016).

Preoperative, intraoperative and postoperative environments comprise the perioperative environment. The preoperative phase initiates when the patient is informed about a surgical procedure and ends when the patient is transferred to the OR. In this phase, nurses work on diagnoses, identify potential outcomes and develop a care plan (Phillips, 2016). The intraoperative phase starts when the patient is placed in the OR and lasts until the patient is admitted to a postoperative/recovery area. During the intraoperative phase, the care plan is implemented (Phillips, 2016). The postoperative phase starts when the patient is admitted to the post-procedure area (i.e. an intensive care unit or a post-anesthesia care unit) and ends when the patient is discharged (Phillips, 2016).

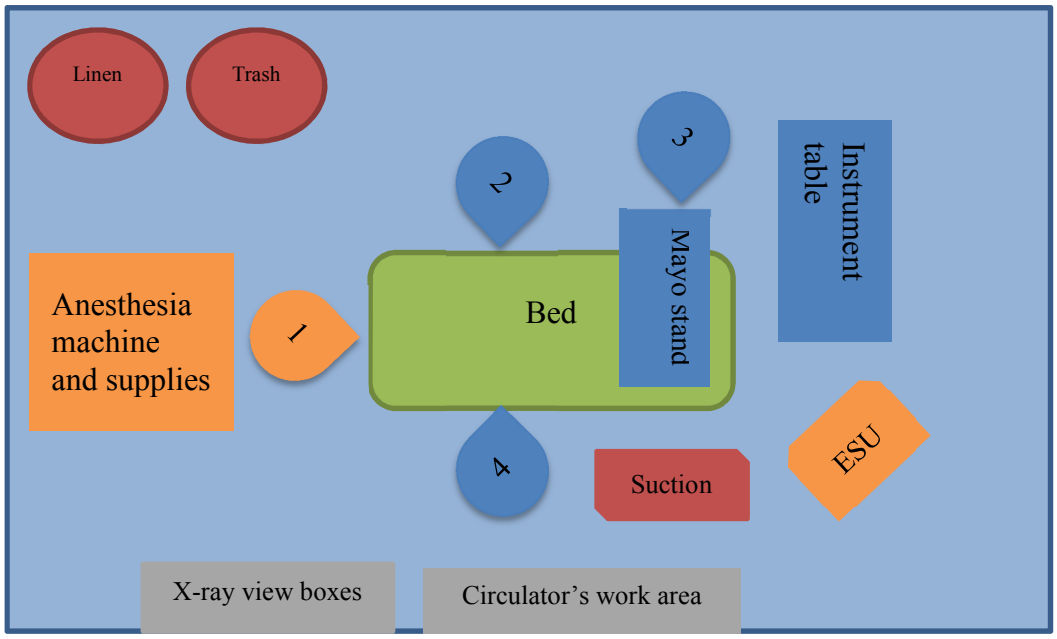


Figure 3. Operating room setting (intraoperative phase) – 1. Anesthesia provider 2. First assistant 3. Scrub person 4. Surgeon. ■ Sterile personnel/areas ■ Non-sterile personnel/equipment adapted from Berry &Kohn's Operating Room Technique book (Phillips, 2016)

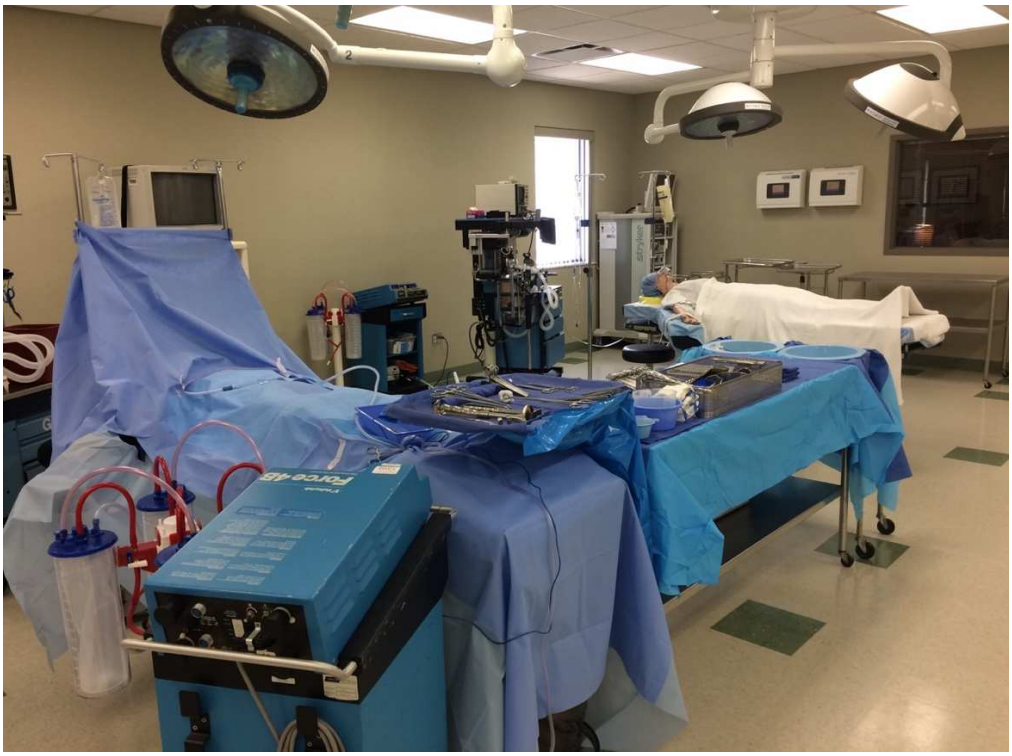


Figure 4. Operating room setting at Baker College (Clinton Twp., MI, USA)

2.4.1.1 Operating Room Personnel

During surgery, the patient is surrounded by an operating team that consists of a surgeon, one or two assistants, a surgical technologist, an anesthesia provider and a circulating nurse. The team is also subdivided by sterility status; some members comprise the sterile team, others represent non-scrubbed, or unsterile, personnel. The sterile team consists of a surgeon, assistants to the surgeon and a scrub person (see Figure 3). The surgeon is in charge of the surgical procedure. The assistants are divided into first assistant in surgery: a qualified surgeon or a resident enrolled in an accredited educational program and qualified to perform the procedure for the primary surgeon and a second assistant to the surgeon is comprised of qualified nurses or surgical technologists that assist the surgeon (Fortunato, 2000). Second assistants are not involved in the surgery but rather work with minimally invasive procedures such as holding equipment. Personnel involved as first assistants include:

- Physician assistants (PA) who are divided into physician's clinical assistants and physician's surgical assistants. Both require additional surgical training in order to serve this role.
- Registered nurses (RN) first assistant, considered as a certified perioperative nurse who has completed the Registered Nurse First Assistant program offered by the Association of PeriOperative Registered Nurses (AORN) (Fortunato, 2000).
- Surgical technologist first assistant, a certified surgical technologist (CST) who was also trained to be a first assistant (Fortunato, 2000).

A scrub person is responsible for maintaining the integrity and efficacy of the sterile field during surgical procedures. This role can be filled by a registered nurse (RN) or a surgical technologist (ST) (Fortunato, 2000).

The unsterile members include an anesthesia provider, a circulator, and others. The aesthesia provider is generally a qualified RN in charge of administering anesthetics to the patient. A CRNA is a certified registered nurse anesthetist accredited from a nurse anesthetist program (Fortunato, 2000). The anesthesia provider serves as a guardian to the patient and observes principles of aseptic technique. Frequently, the circulator role is filled by an RN, however, surgical technologists can perform circulator duties under RN supervision (Fortunato, 2000). Among the roles of the circulator are the creation and maintenance of a safe environment by applying principles of asepsis, recognizing any break in technique, and assuring that all required equipment is in place or is available if needed for the procedure (Fortunato, 2000).

2.4.2 Sterile Field

Within the OR is theoretical space, of great importance to this work, the sterile field. The sterile field is defined as:

> "[The] area around the site of incision into tissue or site of introduction of an instrument into a body orifice that has been prepared for the use of sterile supplies and equipment. This area includes furniture covered with sterile drapes and all personnel who are properly attired in sterile garb." (Phillips, 2016) (see Figure 4)

Creating a sterile field helps to prevent risk of infection for patients. The sterile field consists of tables (mayo stands and instrument tables) covered with sterile drapes where instruments are going to be placed. Drapes serve as a "barrier between a surgical field and possible sources of microbes" (AST Education and Professional Standards Committee, 2008b). AORN recommends that the unscrubbed personnel avoid leaning across or reaching over the sterile field when delivering an item as it might contaminate the sterile field (Spruce, 2017).

It been suggested that, when opening packages, a margin of safety is maintained, although thorough review of current standards, guidelines, and research inconsistently indicates what comprises an appropriate margin of safety. Phillips (2016) indicates that the sterile field is defined by the interior area of a draped surface bounded by a 1-inch border (see Figure 5). Other specifications outlined by standards bodies and authors are not in consistent agreement regarding what dimensions define the sterile border. Others suggest a 2-inch border should be used to bound the area considered as the sterile field (Simmers, 2008).

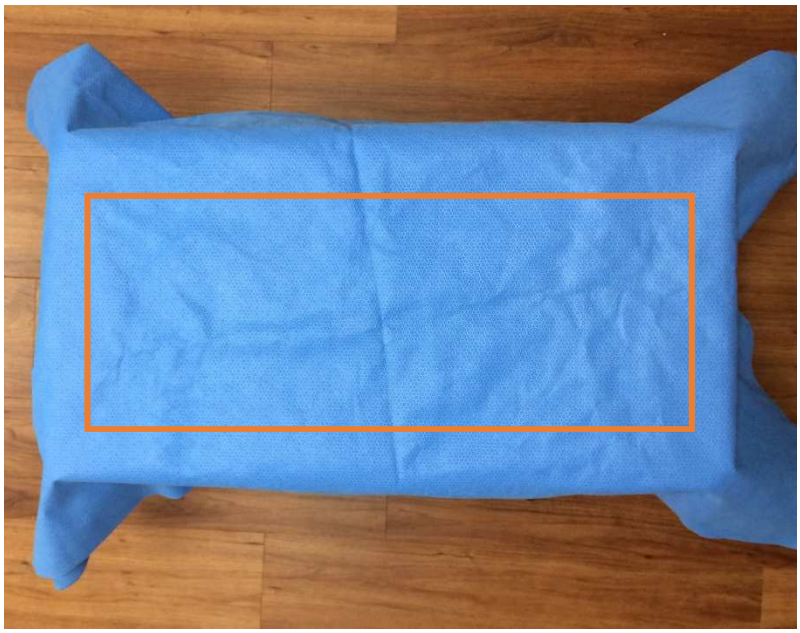


Figure 5. Draped table. Rectangle indicates the sterile area.

2.4.3 Aseptic Transfer

There are two broad mechanical approaches related to opening and transferring sterile supplies to the sterile field:

1. The first method consists of the retrieval of package contents by a scrub person. "Expose the contents so the scrub person can remove the item from the wrapper or package by using forceps or by grasping the item. The scrub person avoids touching the unsterile outside. Remember that the sterile boundary of a peel-open package is the inner aspect, never the edges." (Phillips, 2016)
2. The second method consists of using the "flipping, bombing, or dumping" technique. "Flip only small, rigid items (e.g., suture), and do so with caution. Flipping an item from a package may result in the item missing the intended sterile surface and landing on the floor. Flipping creates air turbulence and thus is the least preferred method of sterile transfer. Larger items, such as staplers or

implants, can become contaminated or damaged and therefore are never flipped." (Phillips, 2016)

Detailed specifics regarding preparation and maintenance of, and transfer of items to, the sterile field are published in a number of standards. Methods published by two organizations (reviewed below), The Association of PeriOperative Registered Nurses (AORN) and The Association of Surgical Technologists (AST) are widely accepted. While practices and techniques described in documents published by both of these Associations are widely accepted, and even taught, as part of the education and training healthcare providers receive, their efficacy has yet to be objectively evaluated.

2.4.3.1 Aseptic Technique Standards

Two of the more recognized sets of standards come from associations comprised of healthcare providers that take significant responsibility for the creation and maintenance of the sterile environment, namely nurses and surgical technologists. *Recommended Practices for the Care and Handling of Specimens in the Perioperative Environment* (AORN Recommended Practices Committee, 2006b) and the *Recommended Practices for Maintaining a Sterile Field* (AORN Recommended Practices Committee, 2006a) are the published standards authored and maintained by AORN most relevant to this work. The kindred standards published by AST are, *Standards of Practice for Handling and Care of Specimens in the Operating Room* (AST Education and Professional Standards Committee, 2008a) and the *Standards of Practice for Creating a Sterile Field* (Fallis, 2013). Table 1 describes the AORN and AST standards for packaging handling in the sterile field.

Table 1. Comparison between AORN and AST standards related to packaging and the handling of sterile devices.

AORN Standard **Recommended Practices for Maintaining a Sterile Field** **Recommended Practice IV**	**AST Standard** **Standards of Practice for Creating a Sterile Field** **Standard of Practice III**
"Unscrubbed individuals should open the wrapper flap farthest away from them first, to prevent contamination from passing an unsterile arm over a sterile item. Next, they should open each of the side flaps. The nearest wrapper flap should be opened last."	
"Sterile items should be presented to the scrubbed person or placed securely on the sterile field. Items tossed onto a sterile field may roll off the edge, create a hole in the sterile drape, or cause other items to be displaced, leading to contamination of the sterile field."	*"Small wrapped items, peel packs and suture packets should be opened and "flipped" onto the sterile field using aseptic technique. The glued area of peel packs and suture packets is considered the boundary between non- sterile and sterile. Items should be opened in such manner that the non- sterile person is not extending over the sterile field."*
"Sharp and heavy objects should be presented to the scrubbed person or opened on a separate surface. These heavy items may penetrate the sterile barrier if dropped onto the sterile field. *Peel pouches should be presented to the scrubbed person to prevent contamination of the contents. The edges of the package may curl and the contents may slide over the unsterile edge, contaminating the contents of the package."*	*"Peel packs that contain a heavy or difficult item(s), e.g. pliers, multiple clamps, should not be opened and flipped onto the sterile field. The item could puncture the sterile cover. The item should be opened into a basin on a ring stand or preferably a non-scrubbed person should open the peel pack and pass the sterile item(s) using aseptic technique to the CST in the first scrub role." [sic]*
"Rigid containers should be opened on a separate surface. Locks should be inspected for security to verify there has not been a breach of the container seal prior use. The lid should be lifted toward the person opening the container and away from the container."	*"Rigid instrument containers should be inspected prior to opening. The tray locking mechanisms should be checked for integrity, and if the chemical indicator on the seal lock changed color to confirm that the container was exposed to a sterilization process. The lid should be lifted upward, take a step back and away from the container to prevent contamination."*

As mentioned previously, there is a lack of uniformity in the published standards related to aseptic transfer, likely because they are an artifact of historical practice, as opposed to being based in, or informed by, objective evidence.

AST standard advocates that small peel packs should be opened and "flipped" onto the sterile field using aseptic technique and considers the seal area as the boundary between sterile and non-sterile areas (Fallis, 2013). In contrast, AORN suggests that items tossed onto the sterile field might lead to contamination as these items might roll off the edge or create a hole. As such, they advocate for a "retrieval of contents" technique, consisting of presentation of the package contents to sterile personnel so they can carefully be removed, avoiding contamination. While AST standards indicate that items can be "flipped" on to the sterile field, there has been some concern regarding this approach. Schultz reports that nurses who do not approve of flipping items onto the sterile field believe that, "the rapid jerking movement of the hands and wrists, necessary to propel the object from the package to the sterile surface, may also propel skin debris and microorganisms onto the field," (Schultz, 1978), and advocate that sterile items should be handed to a scrubbed person (i.e. a "pick"). By contrast, the population that agrees with flipping items urges that required handling involved in the picking action has the potential to lead to contamination of the scrubbed person's gloves and gown because they could contact the hands of the circulating nurse or the outside portion of the package by accident (Schultz, 1978).

No evidence corroborates what either standard postulates, suggesting the need to empirically investigate the impact of varied opening techniques in delivering items to the field and maintenance of the same.

2.4.3.2 Breaks in Sterile Technique

In his book, *Medical Device Packaging Handbook,* Sherman describes the most common reasons for contamination during aseptic presentation as:

1. "the generation of unsterile fibers or particles during opening process, which settle on the contained product";
2. "attached pieces or fragments contiguous to the unsterile exterior of the package, which fall or curl inward and contaminate the contents;"
3. "package design that prevents easy access and removal of the contents in an aseptic manner." (Sherman, 1998)

Although standards have been created to prevent breaks impacting the sterile field, there is no objective evidence for the basis of such standards. Hopper and Moss (2010) suggest that common breaches in appropriate process for field set up and preparation include: failure to check sterility indicators, failure to identify breaches in the SBS during the course of pre-procedure inspections, failure to recognize the presence of moisture or contact between the device and a non-sterile surface, breach of the sterile plane defined perpendicularly to the edge of the draped field (i.e. reaching over the field) during transfer of the device or when an unsterile item is transferred to the field, resulting in contamination of the entire field. (Hopper & Moss, 2010).

The important role that the SBS plays in aseptic technique is recognized in industry standards and an emerging discussion related to usability and aseptic transfer.

2.4.4 Industry Standards

The medical device packaging industry is guided by ISO standards 11607 - Part 1: *Requirements for materials, sterile barrier systems and packaging systems* and Part 2: *Validation*

requirements for forming, sealing and assembly processes (Technical Committee ISO/TC 198, 2006a, 2006b). Part 2 refers to the development and validation of the manufacturing process; manufacturers must provide evidence that systems consistently produce reliable SBSs, to keep the product safe from microorganisms from the manufacturing stage to point of use.

In Part 1, the standard describes a series of design requirements and test methods for packaging materials, including the SBS (Technical Committee ISO/TC 198, 2006a). Despite the fact that the standard specifies that the SBS must enable sterile transfer, there is limited information about opening techniques and design features that might affect the transfer of sterile contents onto the sterile field, or tests that can be employed to objectively verify their performance. Although some organizations have developed standards regarding handling (AORN Recommended Practices Committee, 2006a; Fallis, 2013), none of these standards have been evidence-based.

ISO 11607 is currently under revision and review. Proposed changes to the existing document include the addition of requirements evaluating and documenting usability related to aseptic transfer; essentially, this would require manufacturers to validate a product's performance regarding aseptic presentation. If changes are supported, evaluation would require information such as opening location, opening technique and the aseptic performance of the SBS.

Proposed changes in the ISO 11607 document are intended to better align with European requirements for medical devices. The European Parliament and the Council of the European Union published the regulation EU 2017/645 for medical devices and in vitro devices. The new Medical Device Regulation (MRD) and In Vitro Diagnostic Regulation (IVDR) introduces a more rigorous process to ensure quality, safety, and efficacy of medical devices in order to

protect patients and users. One of the guidelines that describes requirements regarding design and manufacturing indicates:

> "Devices and their manufacturing processes shall be designed in such a way as to eliminate or to reduce as far as possible the risk of infection to patients, users and, where applicable, other persons. The design shall:
>
> a. reduce as far as possible and appropriate the risks from unintended cuts and pricks, such as needle stick injuries,
> b. allow easy and safe handling,
> c. reduce as far as possible any microbial leakage from the device and/or microbial exposure during use, and
> d. prevent microbial contamination of the device or its content such as specimens or fluids." (European Commission, 2017)

Objective characterization of the user interactions with packaging; specifically, how design features and opening techniques enable or hinder asepsis, will allow designers to create medical packages that facilitate opening and transfer of sterile contents from SBSs in an aseptic manner. In turn, this has the potential to reduce infection risk for patients by reducing the probability that devices contact non-sterile surfaces in intraoperative environments.

These emerging requirements are part of a larger movement in the field of packaging, which objectively investigates the impact that design has on usability.

2.4.5 Design for Usability

Human factors engineering, or more simply, human factors, is defined as the "application of knowledge about human behavior, abilities, limitations, and other characteristics to the design of tools, machines, equipment, systems, tasks, jobs, and environments to achieve productive, safe, comfortable, and effective human use" (AAMI Human Factors Engineering Committee, 2009)

Human factors principles are being increasingly applied to assist with the design of efficient medical packages. de la Fuente developed a human-package interaction model (H-PIM)

by adapting and combining models used in the fields of cognitive psychology and human factors. The resultant H-PIM model provides a user-center approach that allows designers to consider users, context of interactions and tasks during package development (de la Fuente, 2013). The author intended the tool to provide a useful frame to organize the myriad of factors having potential to impact a design's usability, serving to inform the design itself, or the evaluations intended to characterize the design's usability.

Human factors principles have been integrated into the medical device design process to garner understanding regarding the interactions between users and the device with the goal of avoiding potential errors. Within the past ten years, the U.S. Food and Drug Administration (FDA) has issued guidance for applying human factors to medical devices. The guidance recommends considering human factors or usability during device development, focusing mainly on user interaction with the "product", including packaging. The goal of the guidance is to ensure product safety by understanding the device user interface (FDA, 2011).This suggests the need to investigate how specific packaging design aspects and opening techniques would facilitate the interaction between the user and the package in order to maintain the sterility of the device to assure the patient's safety.

As mentioned previously, The European Parliament and the Council of the European Union also included new requirements for human-centered design as part of the new Medical Device Regulation (MRD) and In Vitro Diagnostic Regulation (IVDR) including packaging requirements for medical devices. Sections (c) "allow easy and safe handling" and (d) "prevent microbial contamination of the device or its content such as specimens or fluids" were among the recent additions with impact for packaging, indicating that packages must be designed to allow easy and safe handling and prevent any possible microbial contamination of the device. Design

features and opening techniques that allow for aseptic presentation are critical when handling sterile packages as they can increase or decrease the possibility of device contamination during aseptic presentation.

de la Fuente et al. (2014) also developed an affordance-based methodology that adapts Gibson's affordance theory that can be leveraged to the benefit of emerging design requirements by using a series of steps to enhance packaging functionality. Affordance is a term used to describe actionable possibilities that a user may take when presented with an object in the environment; Gibson further theorized that these actionable possibilities exist whether or not the user perceives them (Gibson, 1977, 1979). Norman (1988, 1999), however, changed the model, indicating that an actionable possibility only exists if perceived by the person interacting with the object in the environment, and that perceptions are signaled through design cues (Norman, 1988, 1999).

In the context of packaging design, the ability of a package to communicate intended actions for proper use are critical for proper operation and to avoid unnecessary frustrations. Consider, for instance, a pouch used to deliver medical devices. Design cues such as tabs for opening and seals that signal the presence of two layers of material that will enable separation of seals, signal to the user how to begin a task (e.g., opening); other characteristics related to the user (e.g., their behaviors, habits, beliefs and abilities) and the environment (e.g., emergency, routine) further influence the approach and ability to successfully, sterilely transfer the package contents.

To demonstrate the concept, consider a chevron pouch, commonly used to contain medical devices. The intended affordance for opening is that users will separate the two layers of film at the center point of the package at the top-center of the pouch. After separating the films,

the users will use a single, fluid motion to open and empty the package contents onto the field, without allowing the medical device to touch either their hands or the outside of the pouch, both of which are not considered sterile. A shortcoming of the existing design is that it frequently cues users to employ a "false opening affordance." A false affordance occurs when the object misinform the user, resulting in an inappropriate action (Winder, 2006). Specifically, the large areas of unsealed material (see Figure 6, highlighted in red) enable the user to employ a stronger grip to separate the films at the corners, but increase the fore required to open the package compared to the force required when opening from the top center.

Trier attempted to objectively characterize affordance behaviors related to this observation with perioperative personnel and investigated the potential ramifications of this false affordance on opening and transfer of devices. Using an Instron Universal Testing Machine in the tensile mode, he studied the relationship between peel path and whole package peel forces as well as the affordance behaviors of perioperative personnel to understand potential influences of the same on opening behavior and contamination of the contents when pouches are opened from the top center versus the corners. Trier conducted interviews with a subset of participants and characterized the starting opening position and subsequent usage (at the center or corners) during sterile opening to look at the association between signifiers and affordances. He then questioned participants about the reasoning behind their approach. Some participants chose to open the pouch from the top center because the package itself communicated where the action was to take place (signifier) (Norman, 2013). Some of the perceived signifiers associated with the package were: the chevron peak, a thumb notch, the experience of a smoother peel, or the perception that this would help control material curling. The actions associated with those signifiers (affordances) were the ability of the package to be opened ("peel-ability"), the ability to access

the contents (“access-ability”), the ability to flip the contents (flip-ability) and the ability to control material curling (“control-ability”). Similarly, other participants chose to begin their openings at the corners because they perceived a large material space to grip. This led to different actions such as the ability to cover participant’s arm (“cover-ability”), the ability to identify opening area (“access-ability”), the ability to control the package when it is large (“control-ability”) and the ability to afford the stronger grip provided by the extra material (“grip-ability”). To further understand the impact of opening location, the author conducted a laboratory-based test to investigate the impact of opening location on contamination of the interior of the packages. A series of chevron pouches were opened using an Instron Universal Test Machine. These pilot tests included peeling pouches from the two different locations (center and corner) using different jaw separations and speeds. As a contamination simulant, the author used a fine powder that fluoresces under UV blacklight. Trier found that 3 out of 20 pouches were contaminated when opened from the center and 16 out of 19 were contaminated when opened from the corner (T. Trier, 2016).

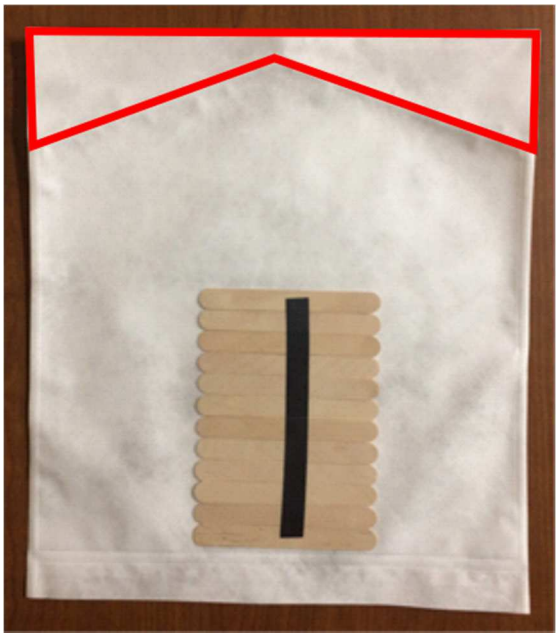


Figure 6. Chevron pouch – unseal material

2.4.6 Research on Packaging as a Potential Source of Contamination

A limited number of studies have investigated the possibility of device contamination during aseptic opening. Crick et al. (2008) developed a methodology to address potential contamination of orthopedic implants comprised of individually wrapped screws. The authors hypothesized that opening individually wrapped items introduces a possible source of contamination of the surgical set-up and suggest that repeated opening compounds this potential. The packaging systems consisted of an outer (non-sterile) "packet" containing an inner (sterile) package. Authors utilized 100 screws, individually placed in heat-sealed pouches. Packages were divided into 5 groups of 20 and labeled. Five nurses were selected to take part in the study. Each participant coated his or her hands with Glitterbug, a contamination simulant cream that fluoresces when placed under black light. Packages were opened in a dark room and scanned using UV light to evaluate transfer of Glitterbug onto the inner barrier. During the second phase of the experiment, the same five nurses opened a packaged screw bank after applying Glitterbug

on their hands. It was found that one sample out of 100 was contaminated with the lotion while no contaminations were observed on the screw bank (Crick et al., 2008).

AORN subscribes to an "event-related sterility system" when creating and maintaining a sterile field (AORN Recommended Practices Committee, 2006a). The concept dictates that the sterility of the package is not altered by time itself, but might likely be affected by environmental conditions, such as the amount of handling that occurs over time. Several studies lend credibility to the idea that increased handling during aseptic transfer has the potential to lead to increased rates of contaminated medical devices.

Smith et al. (2006) studied the possibility that increased handling of "packets" resulted in increased rates of contamination using individually double packed screws. The outer package was considered non-sterile and while the inner package was considered sterile. In an attempt to recreate standard practices of packet opening, a "scout nurse", a circulating nurse without gloves, handled the outer packet, placing the exterior of the package on a sheep's blood agar petri dish. This package was then opened over a draped instrument table above a second sheep's blood agar petri dish. A scrub nurse with cultured hands remove the inner package from the outer package. Ten sheep's blood petri dishes were left opened to the air as the control group. Results show that 24 out of 50 of the exterior of the packets had colony forming units while 7 out of 50 petri dishes from the opening area showed colony forming units. No colony growth was observed on the control group. (Smith et al., 2009).

Trier et al. (2014) studied the role of packaging size on a simulated device's contact with non-sterile surfaces (the outside of the pouch and/or the hands of the provider) during aseptic presentation. Ninety-seven healthcare providers were recruited to open three sizes of pouches (small, medium, large); each pouch size was opened twice for a total of 582 openings (six

openings per participant). Trier (2012) utilized the methods published by Crick et al., applying Glitterbug to nonsterile surfaces and then inspecting transferred items for its presence, to identify the contact that occurred between the medical device and non-sterile surfaces in a binary fashion. Both the pouches and the gloves of participants were coated with simulant; however, the working digits of the hand were not coated as this could potentially cause changes in the friction at the interface due to the fact that the analyte is a lotion. Results suggested that large pouches (LSME±SEM: 14.7±2.9%) induced a greater rate of contact between transferred devices and non-sterile surfaces (provider hands and/or the outside of the package) when compared to smaller pouches (LSME±SEM: 6.0±1.7%) (P=0.0130) (Trier et al., 2014).

In a follow up study, Trier (2016) also investigated the source of contact (pouch or hands). Participants opened a series of pouches of two different sizes using two different contamination simulants (acrylic paint and Glitterbug) to capture the source of contamination. Even though results suggested that there was insufficient evidence to establish a difference between sources of contamination, the author confirmed that larger packages resulted on higher contamination rates (T. Trier, 2016).

Minckley (1969) studied the sterility of sutures contained within "packets" that were exposed to different sources of contamination. The author tested the sterility of packets that were exposed to two possible sources of contamination including: personnel hands and the OR floor. In this study, 80 suture packets were tested. Four methods of handling were used for the sutures prior to opening in the manner dictated by the manufacturer. In the first handling condition, unopened sutures were selected from a very used box from within the health system, the assumption being that when packets are being handled more often and had been expose to contaminants they are more likely to have their inner contents become contaminated. Packets

were dropped on the floor where contamination was demonstrated to be present by preliminary culture. The second handling treatment consisted of selecting a suture from the same very used box and evaluating it to determine if it was safe to use. Third, suture packets from brand new boxes were opened and then cultured. Fourth, a packet was opened in an aseptic manner after the opener's hands were washed for two minutes. Bacterial growth was present on the operating room floors where the number of colonies was up to 41. The opener's fingers also showed bacterial growth resulting in more than 100 colonies and even after hand washing fingertips resulted in 41 to 58 colonies. The results showed that the manufacturer guarantee that the outer package protects the inner package from contamination; no bacterial contamination was found even though bacteria were shown to be present on the opener's hands (Minckley, 1969).

2.4.6.1 Material curling during handling: a potential source of contamination

Several authors have recognized the importance of packaging as a potential source of contamination during aseptic presentation (Crick et al., 2008; G. Smith et al., 2009; T. Trier, 2016; T. Trier et al., 2014). Packaging features have the possibility of increasing the probability of contamination resulting from the contact of sterile items with non-sterile surfaces. Curling has been suggested as a packaging feature with the potential to increase the probability of sterile device contamination (AORN Recommended Practices Committee, 2006a; Cai, 2012; Trier, 2016) but the relationship of material curl and rate of contamination has not been objectively measured to date.

The topic is also addressed in one of the recommended practices by AORN that suggests that "peel pouches should be presented to the scrubbed person to prevent contamination of the contents (i.e. the medical device) as the edges of the package may curl and the contents of the package may touch unsterile edges" (AORN Recommended Practices Committee, 2006a).

The idea that curling is a problem related to medical device packaging, with the potential to impact the ability of providers to sterilely transfer items to the field is a consistent theme of conjecture within the literature of recommended practice make this an important topic for study. Hopper et al. (2010) describe potential breaks in sterile technique, suggesting that, when handling an item, both the circulating nurse and scrub nurse pay special attention to their actions in order to identify potential breaks in sterile techniques. The authors also indicate that there is a possibility of touching the inside portions of the package during opening as well as the outside portion (non-sterile) of the package contacting the inside, which is considered to be sterile (Hopper & Moss, 2010). Cai explored perceptions of medical device packaging with perioperative personnel in a series of focus groups intended to assess healthcare providers' perceptions of different packaging styles and the difficulties they experienced. The study suggested that contamination of corner peel pouches could be caused during the opening of large packages because "flaps might curl back" and "touch the product." (Cai, 2012)

Trier (2016) conducted guided interviews with perioperative personnel to explore how they were educated with regard to aseptic transfer and challenges to successful transfers. Material curling was indicated to be a negative design feature of packaging by 60% of Trier's interview participants (T. Trier, 2016) discussing aseptic transfer. Specifically, participants expressed that watching the corners of the packages was part of "good technique", suggesting that when packages are opened, the film side of the package might curl in, touching sterile contents. When asked about opening technique, participants consistently mentioned staffing levels as a deciding factor related to technique (i.e. a "pick" where the item is presented to a scrubbed team member vs a "dump," where the item is dumped onto the sterile field). Explicitly, when staffing is limited, dumping or bombing was reported as the transfer technique. Other

factors that emerged as critical to the decision of what technique to use included package size, with providers preferring to use the picking technique with large packages (T. Trier, 2016).

Although it is reasonable to assume that curling edges of the pouch could contaminate sterile contents, and several authors have suggested it as problematic (Cai, 2012; Hopper & Moss, 2010; T. Trier, 2016), the impact of curling on product sterility during aseptic presentation has not been studied empirically until now.

As described above, work to date has focused on device contamination when sterile devices come in contact with non-sterile surfaces such as the gloves or the exterior of the package during aseptic transfer. However, the role of design factors (such as the effects of material curling, peel path, and peel forces) and opening technique on the probability of a sterile device coming in contact with non-sterile surfaces during aseptic transfer is still unknown. Work presented herein fills this critical gap.

CHAPTER III

REDUCING LEVELS OF MEDICAL DEVICE CONTAMINATION THROUGH PACKAGE REDESIGN AND OPENING TECHNIQUE

Paula Perez[1], Tamara Reid Bush[2], Wu Pan[2], Larissa Miller, [3]Laura Bix*[1]

School of Packaging, Michigan State University, East Lansing, MI, USA[1]

Mechanical Engineering Dept., Michigan State University, East Lansing, MI, USA[2]

Advanced Chronic Nursing Care, Nursing Program, Lansing Community College, Lansing, MI, USA[3]

Submitted to PloS One Journal

*Corresponding Author

Laura Bix, PhD

448 Wilson, 114 Packaging

East Lansing, MI 48824

517 355 4556

517 353 8999 (fax)

bixlaura@msu.edu

Abstract

Objectives

The goal of this research was to objectively evaluate how a biomechanical approach to sterile transfer of a medical device and packaging design factors, namely, material curl and package structure influences rates of contact between non-sterile surfaces and sterile devices.

Methods

One hundred and thirty-six individuals with practical experience in aseptic technique were recruited. Participants were asked to present the contents of four different pouch designs using two transfer techniques. During the first block of trials "standard technique" was used; participants presented using their typical methods to the sterile field. Trials in the second block employed "modified technique"; participants were instructed to grab the package at the top center and present package contents using a single, fluid motion. The outside of the pouch and the backs of the participants' hands were coated using a simulated contaminant before each trial. The simulant was undetectable in the visible spectrum, but fluoresced under a black light. The dependent variable was recorded in a binary fashion and analyzed using a generalized linear mixed model.

Results

Recruited subjects ranged from 20-57 years old and averaged 5.06 years of experience in aseptic technique. Results indicated significant main effects of pouch design ($p<0.001$; inward, outward, standard and tab) and aseptic technique ($P = 0.0189$; standard vs. modified). Specifically, pouches that were designed so that the material curled outward resulted in less contamination than all other styles; this was true regardless of the technique participants used to open, standard ($p<0.0140$, $p<0.0418$, $p<0.0047$) or modified ($p<0.0001$).

Conclusion

Results presented here contribute to a growing body of knowledge that investigates packaging as a potential route of contamination for sterile devices during aseptic presentation. Specifically, we provide insights regarding how both package design and opening technique can be informed in ways that build safety into the healthcare system.

Key words

Aseptic technique, aseptic presentation, packaging, package design, health-acquired infections, contamination, sterile transfer.

3.1 Introduction

Healthcare acquired infections (HAIs), infections patients get while receiving medical treatment, were categorized among the ten leading causes of morbidity and mortality in the United States (Johnson et al., 2014). In 2011, 722,000 cases of HAIs were reported (Magill et al., 2014). It has been indicated that one in every 25 patients in acute care hospitals have acquired a HAI (Magill et al., 2014). These infections not only result in illness and suffering, they also impose an economic burden due to prolonged lengths of stay (LOS) and costs associated with patients' medical treatments. Although it is difficult to predict the exact costs associated with HAIs, it was estimated that, for patients with ventilator-associated pneumonia (VAP), on average they were on a mechanical ventilation 9.6 days, had an additional 6.1 days in an intensive care unit (ICU) and 11.5 additional days in the hospital, resulting in an average increase of US$40,000 compared to patients without VAP (Rello et al., 2002). Among HAIs, pneumonia is considered to be the leading cause of death (Fagon et al., 1993). Similarly, studies suggest a significant increase in LOS for patients with hospital-acquired clostridium, which is associated with an increase in medical costs. Kyne et al. suggested that the adjusted estimated hospital cost for a patient with *Clostridium difficile* was US$10,489, a 54% increase (US$3,669) compared to typical patients (Kyne, Hamel, Polavaram, & Kelly, 2002). Ghantoji et al. reported in a systematic review that the incremental costs in U.S.-based studies ranged from $US2,871 to US$4,846 for patients with primary clostridium difficile infections (Ghantoji, Sail, Lairson, & Dupont, 2010). Song et al. suggested that the direct costs associated with *Clostridium difficile–*

associated disease (CDAD) after 2004 increased to $US6,326 per case (Ghantoji et al., 2010; Kyne et al., 2002; Song et al., 2008; Wilcox, Cunniffe, Trundle, & Redpath, 1996). This type of infection not only prolonged the duration of a patient's stay in the hospital but it also increased the risk of death. For every 10 patients acquiring the infection, one person died (Oake et al., 2010). Other HAIs, such as staphylococcus aureus are also associated with increased LOS and increased costs. In New York City hospitals, the average LOS attributed to staphylococcus aureus was 20 days, which was three times the average for any other type of hospitalization, with a cost per case of US$32,100 (Rubin et al., 1999).

HAIs can be transmitted directly, from a single person to the patient, or indirectly, through an intermediate object or person (Siegel et al., 2007). HAI data suggest invasive devices are potential vehicles for indirect transmission. When medical devices serve as a vehicle for indirect transmission, the initial contamination tends to occur from a small number of micro-organisms that are transferred to the device, either from healthcare provider's hands or any other environmental sources (von Eiff, Jansen, Kohnen, & Becker, 2005). In an analysis of 1,022 outbreaks related to HAIs, 12% were associated with a medical device (Gastmeier et al., 2005). Similarly, Richards et al. suggested that bloodstream, urinary track and respiratory infections occurring in medical-surgical intensive care units were positively associated with the use of invasive devices (Richards et al., 2000).

One potential pathway for an infectious agent to be indirectly transferred to a patient is via a sterile medical device touching a non-sterile surface. Despite the fact that sterile medical devices experience a sterilization process, only the inside portion of the package is sterile. This is because during transportation, handling and storage, packages are exposed to non-sterile environments prior to the use of the device. As a result, if the sterile device contacts the outside

of the package, or the hands of the person transferring it, the potential for an indirect transfer of microbes exists. Some microorganisms, such as Methicillin-resistant *Staphylococcus aureus* (MRSA), can survive on packaged goods for more than 38 months (Dietze, Rath, Wendt, & Martiny, 2001). As a result, proper aseptic opening and package handling play an important role in avoiding contamination of sterile items.

Nurses and clinicians are trained in how to open sterile packages and transfer the package contents to the sterile field using procedures intended to avoid device contamination (Technical Committee ISO/TC 198, 2006a) through an approach termed "aseptic technique." The goal of learning this technique is to reduce the incidence of device contamination during aseptic transfer of the device to a sterile field. Understanding the importance of aseptic technique, the Association of peri-Operative Registered Nurses (AORN) and the Association of Surgical Technologists (AST) have each created standards concerning appropriate package handling and the transfer of the device to the sterile field (AORN Recommended Practices Committee, 2006a; Fallis, 2013). However, the organizations differ on some aspects of their guidelines for aseptic technique, and opening techniques are not widely standardized across all hospitals (T. Trier, 2016).

AST standards suggest that small peel packs should be opened and flipped on to the sterile field using aseptic technique with the "glue area" of the package considered as the boundary between sterile and non-sterile areas (Fallis, 2013). In contrast to AST recommendations, AORN indicates that two people should use a technique commonly referred to as a "pick." In this technique a circulator, someone preparing the room that is not considered sterile, handling only the outside of the package, would present the contents to someone who was "scrubbed" (considered sterile) so that they could carefully remove the contents without touching

anything that was not sterile. AORN's reasoning for this approach is, "peel pouches should be presented to the scrubbed person to prevent contamination of the contents (i.e. the medical device) as the edges of the package may curl and the contents of the package may touch unsterile edges" (AORN Recommended Practices Committee, 2006a).

Although it is reasonable to assume that curling edges of the pouch could contaminate sterile contents, evidence is needed to validate that assumption, and a search of the literature yields little work regarding the relationship between packaging design, transfer technique and contamination. The available, published literature focuses on operating room traffic (Dalstrom, 2008) and package integrity (Kassarjian, 2011). Within our scope (packaging as a vehicle of microbe transfer), a dearth of information is available. Crick et al. suggested that removal of a sterile inner package from a double barrier resulted in increased rates of contamination. They suggest that contact with the outer/non-sterile portion of the package and increased rates of handling induced by double barrier systems led to higher contamination rates as compared with products packaged in a single barrier system (Crick et al., 2008). Similarly, Smith et al. studied the probability of contamination of the sterile field when airborne contaminants settled after high opening forces and handling scattered them (G. Smith et al., 2009). Trier et al. studied how package size impacted contamination rates during aseptic technique. Researchers concluded that large packages induced higher rates of contact with non-sterile surfaces compared to transfers that utilized smaller packages (P=0.0130). Authors also suggested that the number of hand repositionings increased with increasing pouch size (T. Trier et al., 2014). Hopper et al. indicated that corners of flexible pouches "might curl into package," contaminating the product, which would be considered a break in sterile technique (Hopper & Moss, 2010).

In summary, the literature suggests that packaging and aseptic technique both have the potential to play a role in contamination; yet little work has been done to objectively characterize factors that facilitate (or hinder) successful transfers to the sterile field. The goal of this study was to objectively characterize the impact of opening technique, material curling and tab design on rates of contact between non-sterile surfaces and sterile medical devices during aseptic transfer.

3.2 Materials and Methods

3.2.1 Participants

To participate in the study, individuals were required to: be at least 18 years old, have no known history of a skin condition (e.g., eczema, latex allergy, etc.), have a history of employment as a healthcare professional with experience in aseptic technique to sterile fields or be a healthcare student with practical experience with aseptic transfer, and be willing to be videotaped presenting devices to a simulated sterile field. All methods were conducted in accordance with procedures approved under Social /Behavioral Educational Institutional Review Board (15-1199) (see Appendix A).

A total of a hundred and thirty-seven participants were recruited via emails and list serves intended to reach professionals and students with practical experience in aseptic technique. Three healthcare programs which taught aseptic technique (e.g., nursing, surgical technology, etc.). distributed emails and provided testing facilities. These were: Lansing Community College (Lansing, MI), Baker College (Clinton Twp., MI) and Grand Valley State University (Grand Rapids, MI). Additionally, flyers were distributed through Sparrow Hospital (Lansing, MI), and Michigan State University's College of Nursing (East Lansing, MI); both of these locations served as test sites as well.

Written informed consent was obtained from all participants (see Appendix A). Following the consent process, participants were asked to provide basic demographic information, such as age, gender, and information regarding their professional experience as a healthcare provider.

3.2.2 Simulating Contamination

To detect contamination, methods first proposed by Crick et al. (Crick et al., 2008) and adapted by Trier et al. (T. Trier et al., 2014) were employed to identify contact between package contents and non-sterile surfaces, specifically the provider's hands or the outside of the pouch. Glitterbug, a lotion commonly used in infection control programs as a model for germ transfer and classes on hand hygiene (Brevis Corporation, Salt Lake City, UT), was applied to the outer portion of the pouch and the gloves of the healthcare provider. The lotion is not visible unless black light (368 nm, 8 W) is shined on it. After the device was transferred to the sterile field, it was scanned with the UV light (Brevis Corporation) inside a black tent H1900 (ePhotoInc Hayward, CA) to detect transfer of Glitterbug. Presence of the analyte was indicative of contact with the outside of the pouch or hands of the provider making the transfer (i.e. nonsterile surfaces). In the analysis, this contact is termed "contamination". Configuration of the lights and samples within the tent are presented in Figure 7; contamination was recorded for each trial in binary fashion (present/absent) and each sample was photographed (once on each side) to enable post-hoc review of sample contamination.

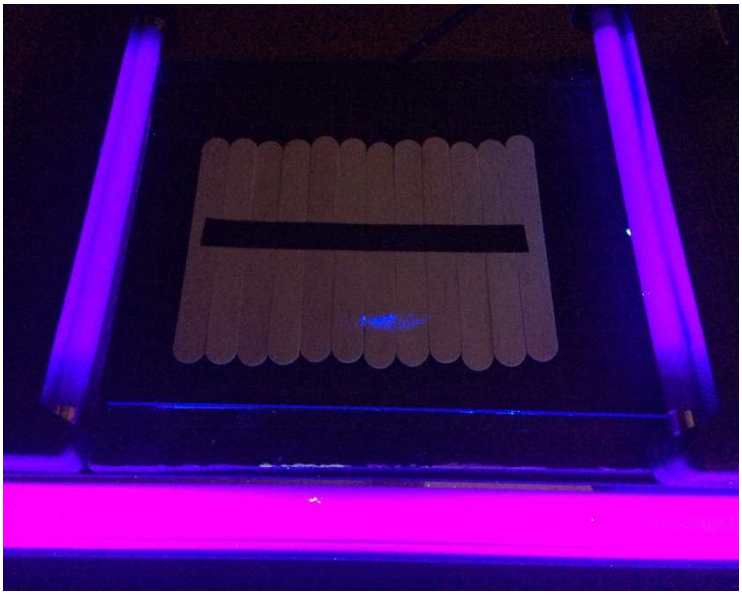


Figure 7. UV light configuration

3.2.3 Device

Tongue depressors were used to model the device transferred to the field. They were chosen because they represented a low cost, easily accessible medical device with a porous structure that allowed for the ready transfer of the simulated contaminant. A series of 12 tongue depressors per package was used based on an aspect ratio (area of pouch/area of tongue depressors) of 6.4 established in previous studies (T. Trier, 2016; T. M. Trier, 2012). Tongue depressors were taped together horizontally on both sides of the mock device using black electric tape (see Figure 7); taping of the depressors into a single object prevented them from flowing or tumbling as individual components during their transfer to the simulated field.

3.2.4 Pouch Designs

3.2.4.1 Standard Pouch

A standard chevron pouch (see Figure 8) sized, 40.64 cm x 45.72 manufactured from Allegro® T, 48 ga PET/28.8# material by Rollprint, Packaging Products (Addison, IL, USA) comprised one of the four treatments used in the study. Further, it was used as a design base to

create three more design treatments: (1) a variation with an inward curl, (2) a variation with an outward curl, and (3) an altered physical structure comprised of a single tab in the top center (no curl induced) (see Figure 8).

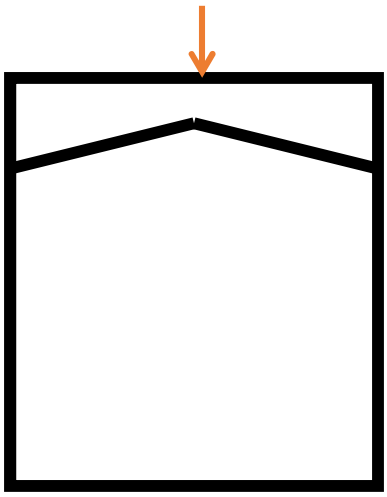


Figure 8. Chevron pouch intended opening location. Intended opening involves a single motion along the pouch length with grip directly centered above the chevron.

3.2.4.2 Creation of Inward Curl

To induce inward curling, we utilized a Sencorp dual shuttle tray sealer Model MD2420, Serial No.: 015 outfitted with a customized flat plate (Sencorp White, Hyannis, MA). The pressure component was eliminated, allowing the team to use the equipment as a consistent heat source. The heat sealer was set to a temperature of 250°C with five second dwell. The pouch was placed on the flat plate horizontally (opening area facing the left side with the film portion facing the heated platen). After the five-second exposure time, the pouch was removed and stored (see Figure 9).

Figure 9. Inward curl

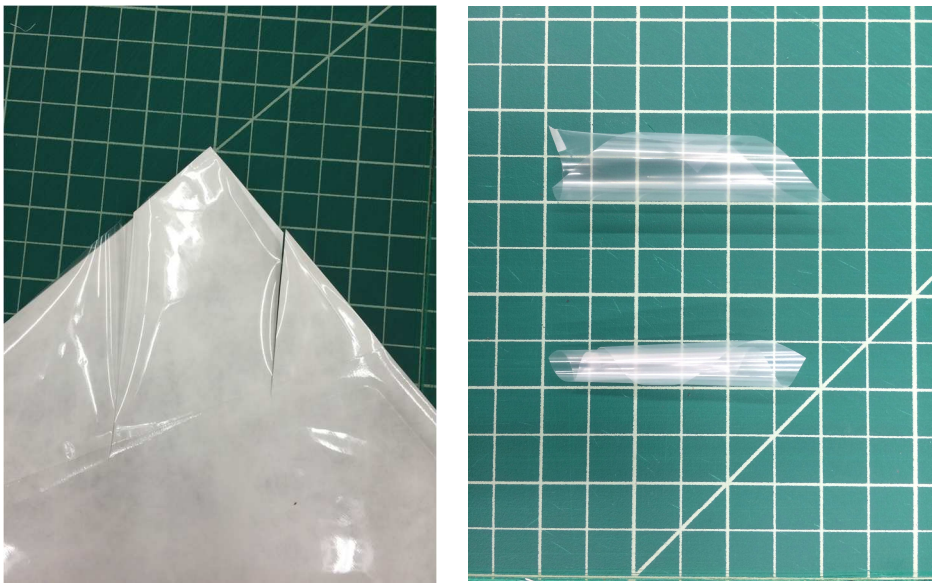
To characterize inward curl, a series of samples were obtained from the top corners of each of 10 randomly selected pouches (five standard and five after inducing the inward curl) to characterize the diameter of the curl before and after heat exposure (see Table 2). Samples were cut perpendicular to the seal area using the corner as the center point. Samples were place on a flat surface allowing the material to curl without restraint and dimensions were taken from the center of the sample using calipers (see Figure 10).

Table 2. Diameter of corners curl on standard pouch before and after heat exposure

Samples	**Standard Pouch (No Heat)**		**Standard Pouch (5 sec/ 250°C)**	
	Diameter Side 1 (in)	**Diameter Side 2 (in)**	**Diameter Side 1 (in)**	**Diameter Side 2 (in)**
1	0.668	0.662	0.462	0.471
2	0.677	0.627	0.474	0.426
3	0.664	0.667	0.465	0.453
4	0.683	0.663	0.472	0.448

Table 2 (cont'd)

5	0.688	0.660	0.470	0.450
Average	0.676	0.656	0.469	0.450
Standard Deviation	0.010	0.016	0.005	0.016



(a) Location of the samples (b) Samples before and after heat exposure

Figure 10. Measure of curl

3.2.4.3 Creation of Outward Curl

To induce the outward curling treatment using the standard pouches, an extra layer of film CLEARFOIL®M3 (Rollprint Packaging Products) was adhered to the top half of the outer layer of the film side of the pouch; namely, the half that included the chevron feature. The extra layer was adhered using a Super 77 multipurpose adhesive spray (3M Company, Maplewood,

MN) so that the added film curled away from the opening area. The material was cut in the same shape and half size of the original package (see Figure 11).

(a) Spray application (b) Film adherence (c) Final product

Figure 11. Process for inducing outward curling

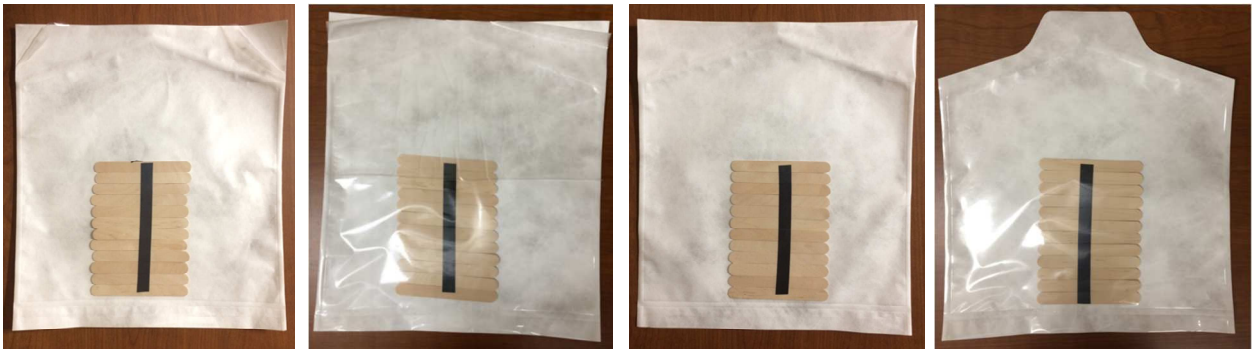
3.2.4.4 Creation of Pouches with a Pull Tab Feature

To create the pouches with a single pull tab, the pouch manufacturer (Rollprint Packaging Products) provided a gripping area that was larger than what is typically employed; specifically, an additional 3.81 cm of extra material was added to the chevron area of each pouch. A metal cutting template was machined from steel so that the extra material could be cut in the form of a tab (see Figure 12). To produce consistent pouches, researchers laid the template over each pouch and cut around the template with an Exacto-style blade (see Appendix C).

(a) Template placement (b) Cutting material (d) Final product

Figure 12. Single tab procedure

All pouches were filled with a set of tongue depressors and the bottom seal of the pouch was formed using a Sencorp Pouch Sealer Model 24AS/1 Serial No. 06-04236, (Sencorp White). The parameters used were: 250°F, three seconds, and 50 pounds per square inch (PSI) (see Figure 13).



(a) Inward (b) Outward (c) Standard (d) Tab

Figure 13. Pouch Treatments

3.2.5 Data Collection

For each opening trial, participants were provided a new set of gloves (Fingertip Textured Flexal Nitrile Powder-Free Exam Gloves manufactured for Cardinal Health, Waukegan, IL) of the participant's choice of size (small, medium, or large). Height adjustable tables (38.1 cm x 76.2 cm) were used to simulate the sterile field. Tables were either provided by the test locations (Lansing Community College, Baker College, Grand Valley State University, Center for Innovation in Research at Sparrow, Michigan State University) or brought to the location by the research team. Participants were asked to adjust the table to their desired height prior to starting the experiment. The exterior portion of the package and the dorsum side of the hand for each participant were coated with Glitterbug (Brevis Corporation) to serve as a simulant for contamination. Application of the lotion excluded the provider's finger pads to reduce the likelihood of changing the frictional relationship between the providers' hands and the pouch.

Order of presentation of test treatments (inward, outward, tab and standard; each appearing twice within a block) was randomized within two blocks, each comprised of eight openings, for a total of 16 openings per participant. For the first block of eight openings, participants were instructed to "transfer the content onto the sterile field using aseptic technique." For the second block of openings, participants were instructed to "grasp each pouch at the center top, pull the package apart in one large movement, and transfer the contents onto the sterile field using aseptic technique." This approach was termed "modified aseptic technique."

To avoid cross-contamination during the preparation and testing of the samples, two teams of researchers were used; "dirty" personnel were responsible for coating pouches as well as applying the simulated contaminant to the gloved hands of the participants. In contrast, the "clean" team was in charge of recording trial results: reading opening instructions; replacing

drapes between trials; transferring scanning and documenting samples in the black tent (see Figure 14 and Figure 15). Each tent was equipped with a Canon Power Shot camera set to high speed burst and flash deactivated; the rest of the settings were kept as default.

Figure 14. Two stations (left and right) were run simultaneously during testing

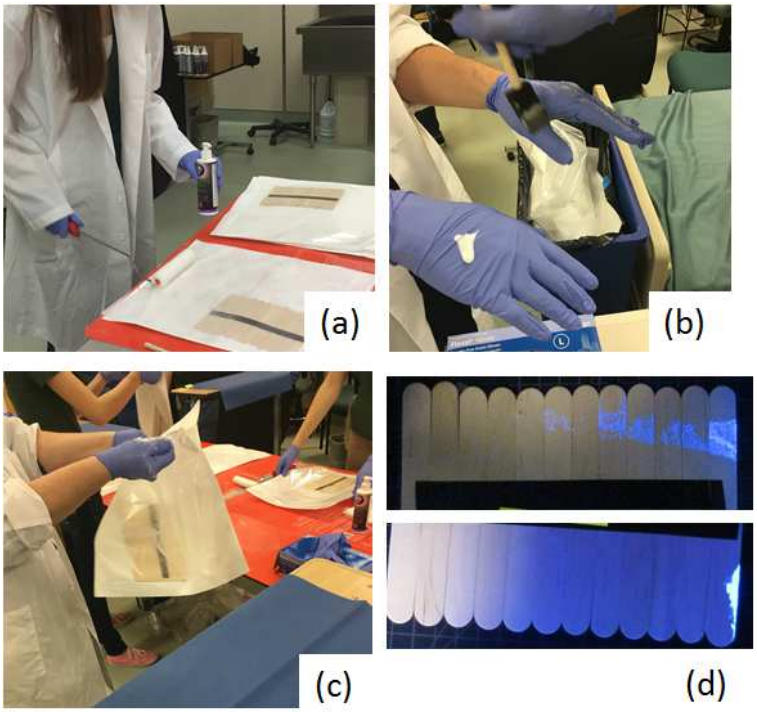


Figure 15. Contamination testing: a) coating the outside of the package, b) coating the dorsum side of participant's hand, c) participant opening package using aseptic technique, d) contamination fluoresced under UV light

An exit survey was administered upon completion of the trials. The intention of the survey was to evaluate participant's preferences regarding the varied designs. Three questions were asked to understand the perception of participants in relation to easiness or difficultness of the designs. The questions were: "1) Of the packages you opened today, were any more challenging to open than others? If so, could you point them out and indicate what about them made opening more challenging? 2) Of the packages you opened today, were any easier to open than others? If so, could you point them out and indicate what about them made them easier to open? 3) Do you have any other comments you would like to share about the packages, or about the study?

3.2.6 Statistical Methods

Data were recorded as a binary response (contamination: yes/no) and analyzed using generalized linear mixed model fitted with a logit link function assuming a Bernoulli distribution. The model excluded demographic factors (e.g., sex, age, handedness, etc.) since they did not suggest significance. Factors included in the linear predictor model were: treatment (inward, outward, standard, tab), and instruction for opening termed "modified technique"; years of experience with aseptic technique was included as a covariate. Subject was considered a random effect. Data analysis was performed using PROC GLIMMIX of SAS (Version 9.4 TS Level 1M1, SAS Institute Inc., Cary, NC) implemented using Newton-Raphson with ridging as the optimization technique. Pairwise comparisons were conducted using Bonferroni adjustments, as it is considered conservative method that protect against Type I error inflation since multiple comparisons between different treatments were made. Results were presented as least square estimates (LSMEAN) and standard error mean (SE). The α level was set at 0.05.

3.3 Results

3.3.1 Participant Demographics

A total of 137 participants registered for the study. One of the participants participated twice; as a result, a set of the data collected from this participant was removed. Another participant wrote 0 as years of experience in aseptic technique after agreeing with the requirements that addressed experience in aseptic technique as a condition of the study (clearly stated on the consent form-see Appendix A). Data collected from this subject was also removed. During the statistical analysis, some data points were missing due to incomplete datasets. As such, the final analysis comprised a total of 128 completed datasets contributed by 19 male participants and 109 female participants. Females ranged in age from 20-57 years old (Standard

Deviation (SD) = 8.44) and males from 25-51 (SD=8.15). Participant's occupations were: Certified Nursing Assistants (CAN or CENA), Certified Surgical Technologists (CST), Surgical Technologists (ST), Emergency Medical Technicians (EMT), Licensed Practical Nurse (LPN), Registered Nurse (RN), Physical Therapists (PT), Paramedics, Phlebotomists, RN students, and Nursing students. Participants averaged 5.06 years of experience in aseptic technique with ranges from 5 months – 36 years (SD=7.38) performing this activity.

3.3.2 Effect of Pouch Design

Results indicated significant main effects of pouch design ((P = <0.001; inward, outward, standard, tab (see Figure 16)) and aseptic technique (P = 0.0189; uninstructed, modified (see Figure 17)) on the probability of contact between the device and non-sterile surfaces; years of experience in aseptic technique did not provide evidence of having a significant effect (P = 0.3591). None of the two-way and three-way interactions were suggested as significant (years of experience in aseptic technique * pouch design: P = 0.2418, years of experience in aseptic technique*aseptic technique: P = 0.1672, pouch design * aseptic technique: P = 0.443 and experience in aseptic technique*pouch design*aseptic technique: P = 0.7463). Pouches designed to curl outward resulted in less contact than all other designs (LSMEANS ± SE: outward curl 10%±2.9%, LSMEANS ± SE: inward curl 25±2.8%, commercial 24±1.7%, tab LSMEANS □± SE: 24±2.8%) (see Figure 16).

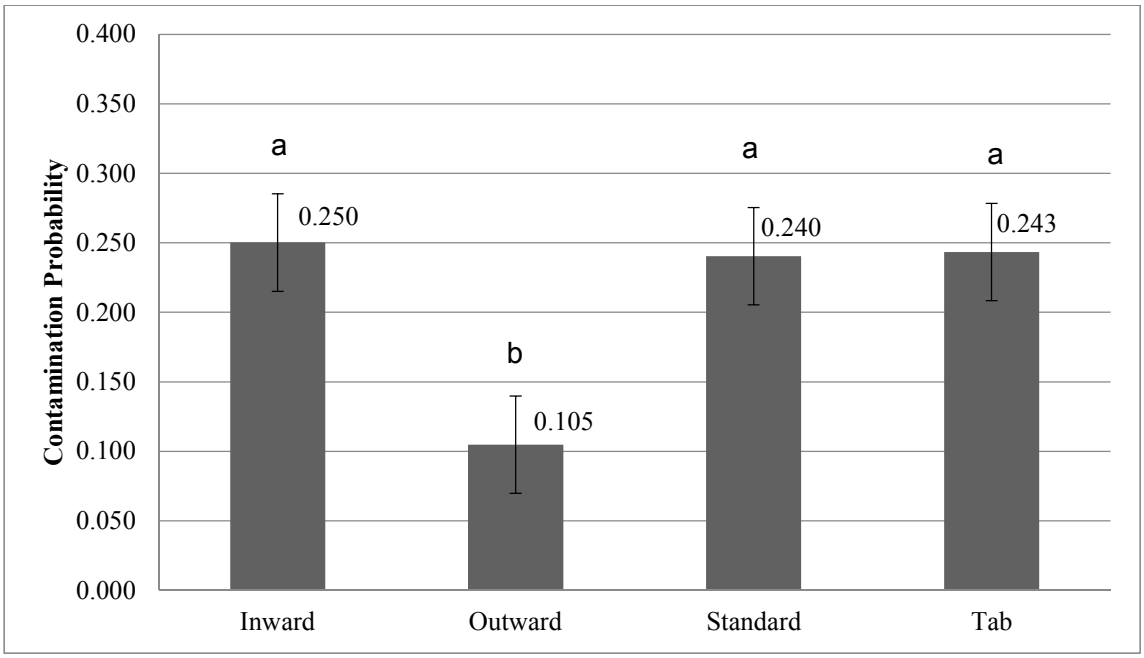


Figure 16. Estimated probability of contamination per treatment. Whiskers indicate error bars with standard errors. Letters indicate evidence of a significant difference between pouch treatments.

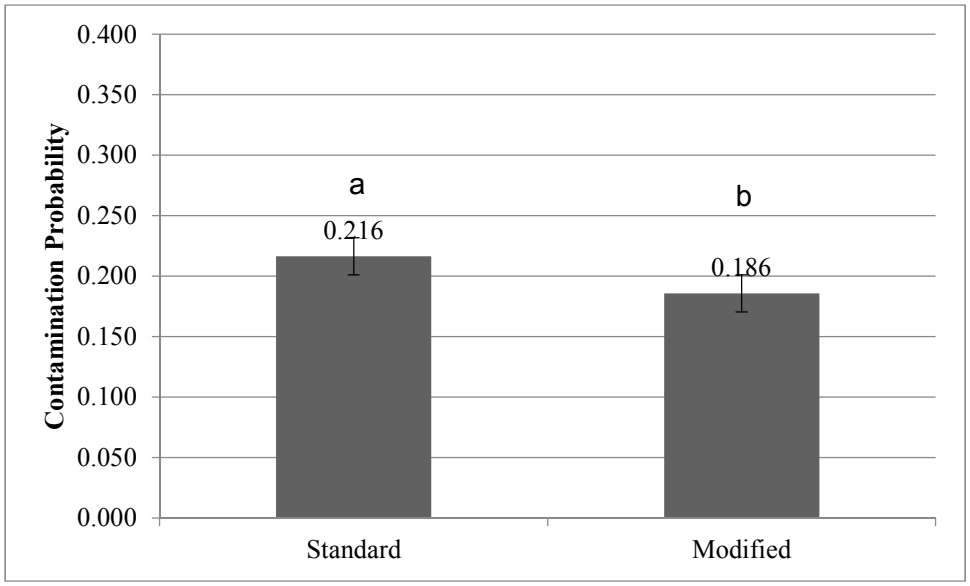


Figure 17. Estimated probability of contamination per aseptic technique. Whiskers indicate error bars with standard errors. Letters indicate evidence of a significant difference between pouch treatments.

We also examined this more closely by investigating design performance (standard, outward, inward and tab) by training block (standard technique and modified technique). Specifically, when using the standard aseptic technique, outward pouch design induced lower rates of contact between devices and non-sterile surfaces compared to all other designs (standard, inward and tab pouch) (LSMEANS ± SE: 14±2.5% vs. LSMEANS ± SE: 26±3.5% ($P < 0.0047$), LSMEANS ± SE: 25±3.4% ($P < 0.0140$) and LSMEANS ± SE: 23±3.3% ($P < 0.0418$) respectively; see Figure 18). Similarly, when using modified aseptic technique (the second block in our design), data indicated that the outward curl design induced lower contamination rates compared to all other designs (standard, inward and tab pouch) (LSMEANS ± SE: 8±1.8% vs. LSMEANS ± SE: 22±3.2%, LSMEANS ± SE: 25±3.5% and LSMEANS ± SEM: 25±3.5% respectively; all comparisons $P < 0.0001$). In terms of contamination rates based on aseptic opening, mean differences were apparent on the outward treatment ($P = 0.0135$). Although the tab design did not result in lower contamination rates regardless of the opening technique employed (standard or modified- See Figure 18), 70% of participants chose it as the preferred design due to ease of opening.

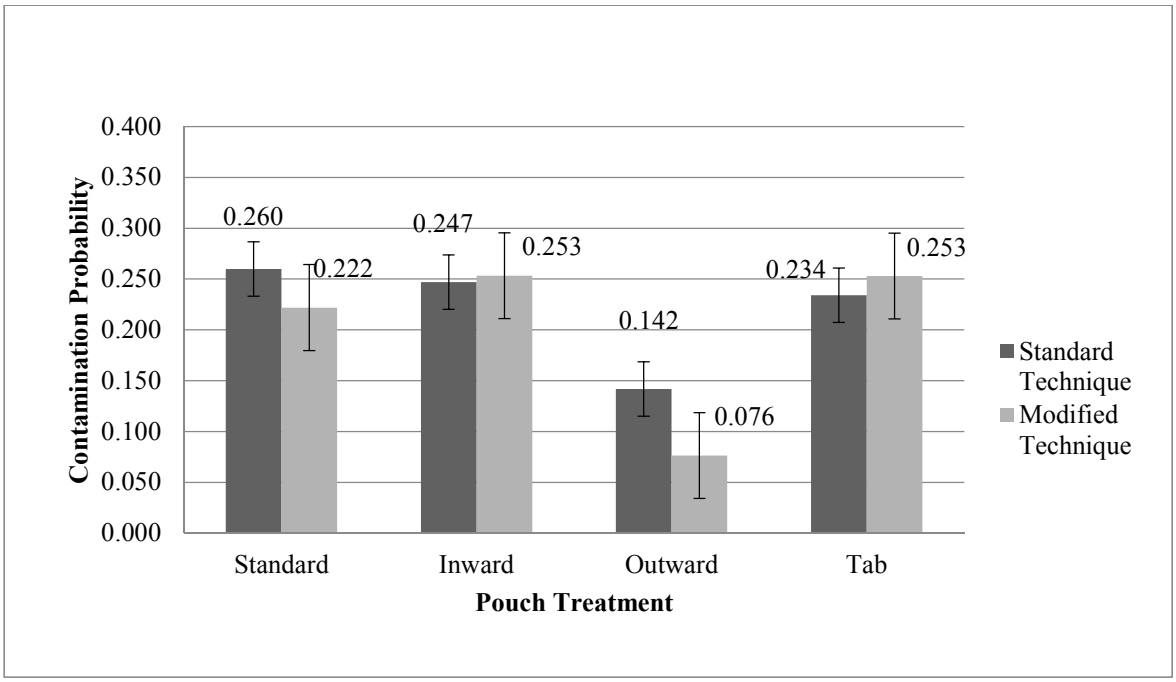


Figure 18. Contamination comparison between treatments and opening technique (block one vs. block two).

3.4 Conclusions

The literature suggests that large pouches and increased rates of handling during opening are associated with higher contamination rates (Trier et al., 2014). We empirically investigated how specific aspects of design and opening approach affected the likelihood of a device contacting the hands of the provider or outside of the package (each of which are not considered sterile) during aseptic transfer. During aseptic transfer, pouches that had outward curling of material resulted in significantly lower contamination rates. Intuitively, this is likely because in these treatments the edges of the package curled away from the opening area, reducing the likelihood of contact between package contents and the unsterile portion of the package, the outside. This design resulted in even lower contamination rates when participants were instructed to grip the package in the center and use a single, fluid motion to open and dump the contents

(modified technique). Standard designs and those where inward curling was induced resulted in significantly high contamination rates.

While the research team hypothesized that the use of a large tab would encourage a center grip with a single pull, and that less excess material would combine to result in lower rates of contact between devices and non-sterile surfaces; results suggested the opposite to be true. Post-hoc review of collected video suggests that the walls of the film side of the package curl in, a likely cause of the significant increase in contact with non-sterile surfaces. Despite the fact that the proportion of contaminated trials was similar to those obtained in trials with the standard pouch, (LSMEANS ± SEM: 26±3.5% and LSMEANS ± SEM: 22±3.2%) 70% of the participants indicated the tab design as the best design for aseptic presentation when asked in the exit survey, and 40 % of the participants stated that the standard design was hard to open because it did not provide enough material to grab and open from the center.

Although, the "Tab" design was preferred by a large number of participants because of ease of opening, it resulted in higher contamination rates. Future study should be conducted to investigate how the addition of a curling outward layer might reduce the contamination rates with a tab design.

3.5 Limitations

The study was executed in contexts that do not represent the stresses of an operating room, which might affect opening behavior. Future study should be conducted to understand how the stresses of different environments affect opening behavior and the likelihood of contamination of sterile devices.

The authors acknowledge that the size of the pouch is large for the presented contents; however, this was chosen as a worst-case representation. In an effort to maintain consistency of

the coating process, consistent amounts of Glitterbug were applied to the pouch and provider hands; however, the relationship between this rate of coating and microbial loads presented on the outside of packages has not been characterized. As a result, a positive transfer only represents contact with a non-sterile surface; it does not necessarily indicate an infection.

Additional factors that likely contribute to the likelihood of contact with sterile surfaces require further study. Our intention was to characterize how opening technique and two package design factors (material curl and physical structure) impact contact with non-sterile surfaces during aseptic transfer to the sterile field. To do this, we used a simple structure that was porous in nature to model the medical device. Further investigation is needed to understand how device properties (e.g., center of gravity, weight, flexibility, etc.) affect transfers.

Although, the "Tab" design was preferred by a large number of participants because of ease of opening, it resulted in higher contamination rates. Future study should be conducted to investigate how the addition of a curling outward layer might reduce the contamination rates with a tab design.

CHAPTER IV

A NOVEL METHOD FOR CREATIVE PROTOTYPING IN POUCHES

Paula Perez[1], Maria Rubino, PhD[1], Tamara Reid Bush, PhD[2], Laura Bix, PhD*[1]

School of Packaging, Michigan State University, East Lansing, MI, USA[1]

Mechanical Engineering Dept., Michigan State University, East Lansing, MI, USA[2]

*Corresponding Author

Laura Bix, PhD

448 Wilson, 114 Packaging

East Lansing, MI 48824

517 355 4556

517 353 8999 (fax)

bixlaura@msu.edu

Abstract

Purpose

To develop a reliable, relatively easy and cost-effective method to creatively prototype and produce new pouch designs, driven by the need for more user-focused packages for medical devices.

Methods

We developed a novel method to create pouches with virtually any seal geometry. Utilizing 3D printing, molds are produced. These molds are filled with a chemical-resistant silicone and cured using a series of steps, ultimately producing diversely shaped rubber gaskets. Gaskets are mounted onto a customized flat plate affixed to our MD 2420 dual-shuttle tray sealer. Two layers

of substrate are combined to form the pouch using the tray sealer's typical mechanism, while a glass jacket prevents scorching, and. excess material is trimmed.

To characterize the variability in the system and the ability of our novel method to create seals that withstand sterilization, a series of experiments were conducted. Two heights of seals (0.5 cm and 0.7 cm) were created in three widths (0.7 cm, 1.0 cm and 1.3 cm), for a total of six molds per set. To add potential run order effects, a set of six was produced on each of three days, for a total of 18 molds. Seals were sterilized using gamma radiation and compared with pristine seals to examine potential effects of sterilization on seal strength.

Results

No evidence of main effects of mold set (day of production of mold) ($P = 0.2383$) or gasket height ($P = 0.3431$) was present when seal strengths were compared. As expected, seal width yielded a significant effect (0.7 cm: 0.653 lbf, 1.0 cm: 0.845 lbf, 1.3 cm: 1.045 lbf, $P < 0.001$). There was no evidence that gamma sterilization impacted seal strength on pouches created by using this method ($P=0.6027$) and commercial pouches ($P=0.1966$).

Conclusions

Our novel methodology has the potential to enable packaging designers to create innovative, flexible pouches. Because of the breadth of seal characteristics and seal geometries that can be created, this does not only have ramifications for industry, but also for research. Unique pouch and seal designs can be created quickly to develop a better understanding of peel forces and peel behavior. This is particularly relevant to designers in the medical device industry, who are increasingly being asked to validate the performance of their packaging in the hands of healthcare providers, who, in many cases, must remove and transfer the contents of the package without having them contact non-sterile surfaces.

Key words

Packaging, peel force, seal geometry, design, mold, cavity, gasket, seal, rapid-prototyping.

4.1 Introduction

Flexible pouches have been widely adopted by the medical device industry due to the flexibility they enable with regard to volume at a relatively low cost (Sherman, 1998). The typical medical device pouch is comprised of two webs sealed along the perimeter and is generally available in a very limited number of styles (e.g., chevron, corner peel, header bag, and tear pouch). Within the medical device industry it is very common that one of the two webs consists of a porous component (e.g., Tyvek® or paper), permitting terminal sterilization, or sterilization that occurs after the device has been loaded into the package and seals have been formed (Bix & de la Fuente, 2010). Pouches can be structurally manipulated to leverage many benefits. Specifically, they are easily manufactured in varied sizes, accommodating the needs of different device manufacturers, and transparent layers can be incorporated to provide product visibility, while features and seals can be designed for easy opening. That said, pouches are not ideally suited for all devices. They are inefficient for bulky items and devices that are susceptible to damage during distribution (Sherman, 1998). Further, items with sharp profiles have the potential to puncture the barrier system, and while this is problematic for most products, it can be dire for many medical devices, given the importance of sterility in this product category.

Unlike many flexible packages created for foods and consumer goods, those created for medical devices are limited in terms of the range of designs. This is likely reflective of the historical approach to package design in this sector, which has focused heavily on producing packages that enable and maintain sterility in order to protect medical devices from microbial contamination. Although such considerations are crucial to safe and effective medical devices,

solely focusing efforts in this way omits the importance of user interaction with the package as part of the process of transferring sterile products safely.

The industry primarily produces four styles of pouches for use with medical devices: chevron-style pouches, header bags, tear bags, and corner peel pouches (Cai, 2012; Sherman, 1998; Yambrach, 2010). These designs all must allow for aseptic presentation, defined as the "introduction and transfer of a sterile product using conditions and procedures that exclude microbial contamination" (Technical Committee ISO/TC 198, 2006a). However, reports suggest design features of many of these pouch designs are not positively perceived by healthcare professionals (Cai, 2012; T. Trier, 2016).

Cai (2012) reported that both tear pouches and header pouches were indicated by focus groups comprised of healthcare professionals to be difficult to transfer aseptically, specifically noting that tear pouches required high opening forces and contained opening areas that were difficult to identify (Cai, 2012). Participants also described corner peel pouches as difficult to handle since tabs were frequently not large enough to allow for gripping, and that these same designs granted limited control of package contents compared to chevron pouches, because "flaps might curl back" and touch the product, leading to contamination (Cai, 2012).

While the available corners of chevron pouches may appeal to participants because of the ability to use a more powerful grip, chevron pouches are not designed for this approach to opening. They are designed to be pulled in a long, continuous motion with a beginning grip at the top center of the pouch. That said, it is not only Cai's focus groups suggest that participants frequently begin at the corners. (Sherman, 1998; T. Trier, 2016) A post-hoc review of an opening study of aseptic transfers using three sizes of chevron pouch revealed that 91.2% of trial subjects began with their hands centered (as intended) for small pouches, 52% for medium pouches, and

only 42.3% for the large (T. Trier, 2013). Although healthcare professionals prefer chevron designs (Cai, 2012), a recent survey conducted by the researcher suggested that 40% of the participants who opened these pouches found them difficult to open because of the lack of gripping space at the top center.

Considering the user interface created by pouch designs is becoming more important as the population of nurses ages. According to the 2008 National Sample Survey of Registered Nurses (NSSRN), RNs over age 50 increased from 33% of the total RN population in 2000 to 44.7% in 2008. Designers will need to adjust designs to compensate for a decline in physical and perceptual ability of this aging population.

Canty et al. (2012) investigated opening forces and finger friction required to open rigid plastic containers with peelable lids. The authors reported that the older population experienced difficulty manipulating the package and the tab, which resulted in using a grip choice that facilitates opening. The authors suggested that improving accessibility of this type of package requires a focus on tab shape and design so that people with less dexterous fingers can successfully manipulate the package.

Designs can be driven from a product-centered design (PCD) platform, where the properties of the product determine the level of functional capability required for the user to effectively interact with the product, or by a user centered design (UCD) platform, where the needs of the user are the primary drivers during decision making (Keates & Clarkson, 2004).

Packaging has generally been designed from a PCD platform, where the design decisions are driven by the demands of the product (sterility, filling efficiency, shelf-life, etc.). For medical devices, decisions which enable or maintain the integrity of the sterile barrier system tend to be central in decision making (Berns, 1981). The medical packaging standard, ISO 11607,

references a number of standards which can be used to both design and evaluate packaging, all of which have to do with protection or evaluation of the relationship between the product and the package (see). These standards challenge the materials used and the packaging design itself, by emulating physical stresses induced by many environments that the packaged product will face, including processing, distribution, sterilization, and storage.

Table 3. Standards referenced by ISO 11607 Part 1

Purpose	Standard Reference
Microbial Barrier	ASTM F1608 – Standard Test Method for Microbial Ranking of Porous packaging Materials (Exposure Chamber Method) ASTM F2638 – Standard Test Method for Using Aerosol Filtration for Measuring the Performance of Porous Packaging Materials as a Surrogate Microbial Barrier DIN 58953–6 – Sterilization — Sterile supply — Part 6: Microbial barrier testing of packaging materials for medical devices which are to be sterilized; subclause 3: Testing for germ proofness in moisture and subclause 4: Testing for germ proofness with passage of air BS 6256 – Specification for paper for steam sterilization paper bags, pouches and reels for medical use Appendix C: Methods for determination of methylene blue particulate penetration ASTM F2101 – Test method for evaluating the bacterial filtration efficiency (BFE) of medical face masks materials, using a biological aerosol of staphylococcus aureus SS 876 0019 – Health care textiles — Bacterial penetration — Wet

Table 3 (cont'd)

Peel-open characteristic	EN 868-5 – Packaging for terminally sterilized medical devices - Part 5: Sealable pouches and reels of porous materials and plastic film construction - Requirements and test methods (Annex E: Determination of peel characteristics of paper/plastic laminate products)
Puncture	ASTM D1709 – Standard test method for impact resistance of plastic film by free-falling dart method ASTM F1306 – Standard test method for slow rate penetration resistance of flexible barrier films and laminates ASTM D3420 – Standard test method for pendulum impact resistance of plastic film
Seal Strength	ASTM F88/ F88M – Standard test method for seal strength of flexible Barrier materials EN 868–5 – Packaging for terminally sterilized medical devices — Part 5: Sealable pouches and reels of porous materials and plastic film construction — Requirements and test methods

Table 3 (cont'd)

Sterile Barrier System Integrity	ASTM F2228 – Standard test method for non-destructive detection of leaks in medical packaging which incorporates porous barrier material by CO2 tracer gas method ASTM F3039 – Standard Test Method for Detecting Leaks in Nonporous Packaging or Flexible Barrier Materials by Dye Penetration ASTM F1929 – Standard test method for detecting seal leaks in porous medical packaging by dye penetration ASTM F2227 – Standard test method for non-destructive detection of leaks in non-sealed and empty medical packaging trays by CO2 tracer gas method ASTM F2391 – Standard Test Method for Measuring Package and Seal Integrity Using Helium as the Tracer Gas ASTM F209 – Standard test method for detecting gross leaks in packaging by internal pressurization (Bubble test) ASTM F1886/ F1886M – Standard test method for determining integrity of seals for medical packaging by visual inspection ASTM F2338 – Standard test method for non-destructive detection of leaks in packages by vacuum decay ASTM D3078 – Standard test method for de-termination of leaks in flexible packaging by bubble emission ASTM F2095 – Standard test methods for pressure decay leak test for flexible packages with and without restraining plates ASTM F3004 – Standard test method for evaluation of seal quality and integrity using airborne ultrasound

Table 3 (cont'd)

Performance Testing	ASTM D4169 – Practice for performance testing of shipping containers and systems ISTA 3A&3B – International Safe Transit Association Preshipment Test Procedures ISTA 4A&4B – Packaged – product for shipment in known distribution channels ISTA 7D – Thermal controlled transport packaging for parcel delivery system shipment ISO 4180 – Packaging — Complete, filled transport packages — General rules for the compilation of performance test schedules EN 868–8 – Packaging for terminally sterilized medical devices – Part 8: Re-usable sterilization containers for steam sterilizers con- forming to EN 285 — Requirements and test methods ASTM F2825 – Standard Practice for Climatic Stressing of Packaging Systems for Single Parcel Delivery ASTM D7386 – Standard Practice for Performance Testing of Packages for Single Parcel Delivery Systems

Clearly, careful thought goes into ensuring that the package performs as intended in terms of its function related to the device (i.e. enabling and maintaining the sterile barrier). However, objective methods for evaluating and designing from a user-centered perspective (UCD) are much more limited. Packaging design features that allow for the user activity of aseptic presentation are mandated by the ISO 11607 document, but there is no specific guidance, nor test standards in support of accomplishing this (from either a design or evaluation perspective). That said, emerging regulatory documents and standards suggest that packaging designers will soon

have to incorporate a more user-centered, data-driven approach into their decisions about the design and validation processes for medical packaging.

Human factors have been increasingly incorporated into the medical device design process to gain understanding regarding the potential interactions between users and the product with the goal of avoiding or reducing potential errors. Although the increased emphasis on UCD began with devices themselves (Applying Human Factors and Usability Engineering to Optimize Medical Device Design, Regulation of the European Parliament and of the Council on Medical Devices, (European Commission, 2017; FDA, 2011)), our review of the current regulations and standards suggests that this concept is being extended into the design and evaluation of medical packaging (see Table 4).

Table 4. User-centered approach to medical packaging design literature

Title	Author	Date	Description
Human Factors Engineering--- Design of Medical Devices	ANSI/AAMI HE75, 2009(R)2013	2013	The objective of the standard is to safely and effectively apply new technologies to patients as well as encourage new technologies. Provides guidance on packaging design and principles of a good medical packaging design.
Guide for addressing accessibility in standards	SO/IEC Guide 71:2014	2014	Provides guidance in addressing accessibility requirements and recommendations on systems used by people. Assist developers in considering the needs of older person and people with disabilities. Include packaging aspects such as opening, closing, use and disposal.
Packaging-Accessible design-Ease of opening	ISO 17480:2015	2015	Provides requirements and recommendations for packaging accessibility focusing on ease of opening.

Table 4 (cont'd)

Packaging-Accessible design-General requirements	ISO 11156:2011	2011	Provides a context for packaging design and evaluation considering people from different backgrounds including cultural and language differences as well as people with disabilities.
Packaging-Accessible design-Information and marking	ISO 19809-2017(en)	2017	Provides requirements and recommendations for packaging designs concentrating on accessibility and focusing information and marking.
Packaging-Accessible design handling and manipulation	ISO/CD 22015	(Under development)	
Packaging for terminally sterilized medical devices—Part 1: Requirements for materials, sterile barrier systems, and packaging systems	ISO 11607	(Under review)	Provides guidance on medical packaging design including material selection, sterile barrier systems and aseptic presentation.
Applying Human Factors and Usability Engineering to Optimize Medical Device Design	Food and Drug Administration (FDA)	2011	The goal of the guidance is to ensure product safety by understanding device user interface and recommends considering human factors or usability during device development, focusing mainly on user interaction with the product, including packaging.
Regulation of The European Parliament And Of The Council on medical devices	Council of the European Union	2017	The documents contains new requirements as part of the new Medical Device Regulation (MRD) and In Vitro Diagnostic Regulation (IVDR) including packaging requirements for medical devices.

ISO 11607 (currently under review) proposes changes which would require manufacturers to conduct a usability evaluation regarding the package's ability to facilitate aseptic presentation. The proposed language suggests a documented usability evaluation where requirements for aseptic presentation can be met. This evaluation includes evidence of the opening location, opening technique and aseptic presentation. The ISO revisions are intended to be aligned with new requirements released by the European Parliament and the Council of the European Union as part of the new Medical Device Regulation (MDR) and the In Vitro Diagnostic Regulation (IVDR) that includes packaging requirements for medical devices. Among the added requirements are: sections that (c) "allow easy and safe handling" and (d) "prevent microbial contamination of the device or its content such as specimens or fluids" (European Commission, 2017). Although the EU requirements are specifically focused on medical devices, the wording within directly impacts packaging design, indicating that packages must be designed to allow easy and safe handling and prevent any potential microbial contamination of the device.

The emerging requirements regarding assessing the user's ability to transfer items to the sterile field and the call from healthcare providers expressing the need for designs that enable sterile transfer mandates the creation of new designs and the ability to objectively evaluate the relationship between packaging design and human performance as part of the design process. However, to date we have been restricted in our ability to easily produce pouches with varied design characteristics.

4.2 Research Objectives

The overarching objective of this research was to develop a reliable, rapid, relatively easy and cost-effective method that could be used to creatively prototype and produce new flexible pouches.

In order to validate and characterize the variability inherent in the proposed methodology, we conducted a series of experiments. The objectives of the validation experiments were as follows:

Study One - Method Validation

1. To test the consistency of peel strength of seals produced by the novel method
2. To test the variability inherent in the molds produced by the rapid-prototype process
3. To test the capability of the process to create different seal with differing widths.

Study Two – Implementation of the method

1. To test the ability of the novel method to create pouches with the desired geometry
2. To test the ability of novel seals, designed using the method, to withstand sterilization

4.3 Materials and Methods

The method that we developed to rapidly and creatively prototype pouches with any seal geometry employs 3D modeling software (Solidworks Education Edition, Academic Year 2015-2016/2015 SP4.0, Dassault Systèmes Solidworks Corporation, Waltham, MA) to create mold cavities that are used to produce silicone gaskets (Chemical-Resistant Silicone; Medium Hard 65A) (Silpak Inc., Pomona, CA). Gaskets are produced from a compound consisting of liquid

silicone and a silicone catalyst cast within the mold. Silicone gaskets, which can be produced in virtually any shape, are subsequently mounted to a uniform plate installed on an MD 2420 dual shuttle tray sealer (Sencorp-White, Hyannis, MA). Two substrates which ultimately constitute the completed pouch are laid over the gasket beneath a "glass jacket" comprised of a Teflon material (Sencorp-White). Pouches created for this project were comprised of 48 ga PET/28.8# (Rollprint Packaging Products, Addison, IL) and an uncoated 1073B Tyvek (DuPont; Richmond, VA) (Rollprint Packaging Products provided both substrates).

This study was conducted in two parts. In the first part, customized molds were created to make sealing gaskets with different dimensions and evaluated to validate the method. The second part was intended to demonstrate the method's ability to create prototypes that are similar to commercially available chevron pouches, using seal strength as the point of comparison. Seals were evaluated both before and after sterilization.

4.3.1 Study One -Method validation

The objectives of this study were to test consistency of peel strength, variability inherent in the mold sets produced by the rapid prototype process, and the ability of the method to create different seal widths.

To thoroughly characterize the contribution of different aspects of the new sealing process (rapid prototype process, seal width, gasket height) in providing consistent seals, a series of standalone seals were created using the novel, rapid prototyping method (see Table 5). Created seals varied in height and width. We crossed height (2 levels- 0.5 cm and 0.7 cm) with gasket width (3 levels- 0.7 cm, 1.0 cm, and 1.3 cm) for a total of six molds with unique dimensions. Each possible combination was replicated on three different days, each day considered a "set", for a total of 18 molds. Color-coding was done to easily identify the mold set,

corresponding to the day the mold was produced. For instance, the first set of molds labeled as "Green" consisted of six uniquely sized molds created in the same day (three different widths (0.7 cm, 1.0 cm, 1.3 cm) by two different heights (0.5 cm, 0.7 cm)). Likewise, the blue set and the red set were each comprised of six uniquely sized molds; with the blue being produced on a separate day then the red (see Figure 19 and Figure 20).

Table 5. Parameters to be tested

Factor	Number of levels	Level values
Set (produced on different days)	3	Green, Blue, Red
Mold Width (cm)	3	0.7, 1.0, 1.3
Mold Height (cm)	2	0.5, 0.7

4.3.1.1 3D Modeling

To create the molds, the 3D modeling software Solidworks (Solidworks Education Edition, Academic Year 2015-2016/2015 SP4.0) was used. The following graph shows an example of the dimensional specifications of the molds.

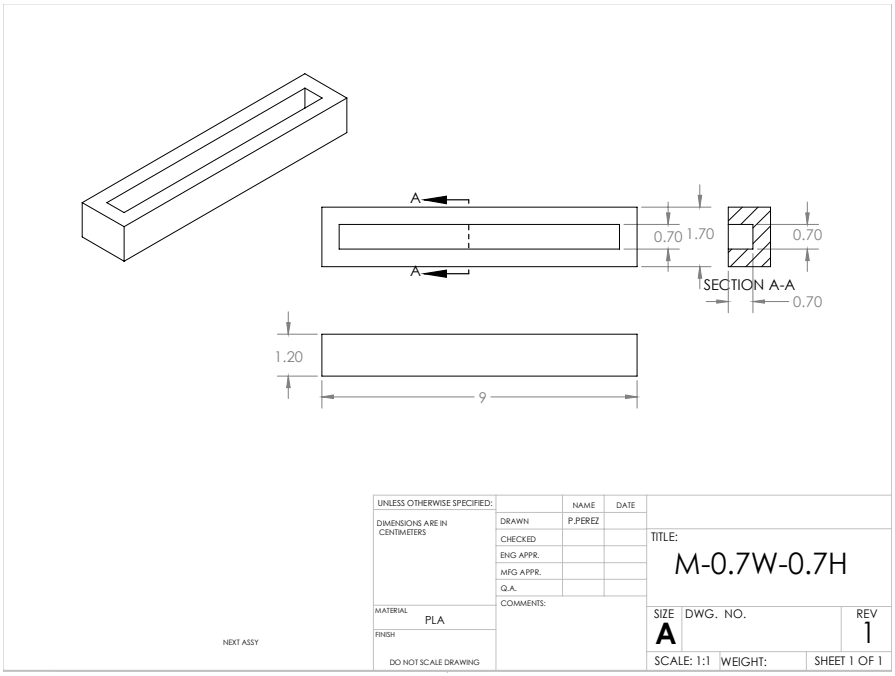


Figure 19. 0.7 cm width/ 0.7 cm height mold

4.3.1.2 Rapid Prototyping

Each set of molds was rapid-prototyped using a MakerBot Replicator 5th Generation machine (MakerBot Industries, LLC Brooklyn, NY) and a Fortus 250mc printer (Stratasys Ltd., Eden Prairie, MN). The material used to manufacture the molds was comprised of PLA 3D Printer Filament/ MakerBot PLA and ABS-M30 / P430 ABS / P430XL ABS / ABSplus Model Material (Stratasys Ltd.). 3D filaments were provided by the manufacturer on different colors (see Figure 20).

Figure 20. Rapid prototyped molds

4.3.1.3 Compound preparation

To prepare the gaskets which would ultimately create the seals (Silpak Inc. Pomona, CA 91767) components were mixed according to manufacturer instructions, at a ratio of 100 parts base to 10 parts curing agent. The compound was mixed and placed in a vacuum chamber (VWR

Sheldon Manufacturing Inc., Cornelius OR) to remove trapped air. The vacuum chamber was set to a vacuum gauge of 25 in. Hg. for 5 minutes. The compound was then removed from the vacuum and carefully transferred into the mold using a modified 30ml syringe (BD, Franklin Lakes, NJ). The end of the syringe was removed and a 0.4 cm hole was machined in its tip using a drill (see Figure 21). Mold cavities were filled and extra compound was removed using a plastic scraper so that the surface of the finished gasket was even with the top of the mold. The mold was cured at room temperature for 24 hours. After curing at room temperature, gaskets were de-molded and placed into a Thelco Laboratory Oven Model 130 Serial No. 9511-104 (Precision Scientific Inc., Chicago, IL) for 1 hour at 400°F.

Figure 21. Compound used to create sealing gaskets

4.3.1.4 Sealing process

Seals were created by mounting the gaskets created with the molds onto a customized flat plate made for our tray sealer (Model MD2420, Sencorp-White). Gaskets were placed at the center of the flat plate with approximately 1-inch separation between seals. No adhesive was

required to mount the gaskets used to make seal bars (see Figure 22). Seals were created by bonding PET film to Tyvek®. The Tyvek® material was placed directly on the gaskets with the film positioned over it, facing the heat-sealing platen of the sealer. Film and Tyvek® were placed so that both were centered over the gasket. Materials were covered using a glass jacket to protect the material from direct heat. Materials were sealed at 150°C temperature, with a pressure of 60 PSI for 3 seconds. Finished sealed samples were conditioned at 23°C and 50% relative humidity for a minimum of 48 hours prior to peel testing. Five finished seal bars were created using each unique mold for each gasket for a total of 90 samples.

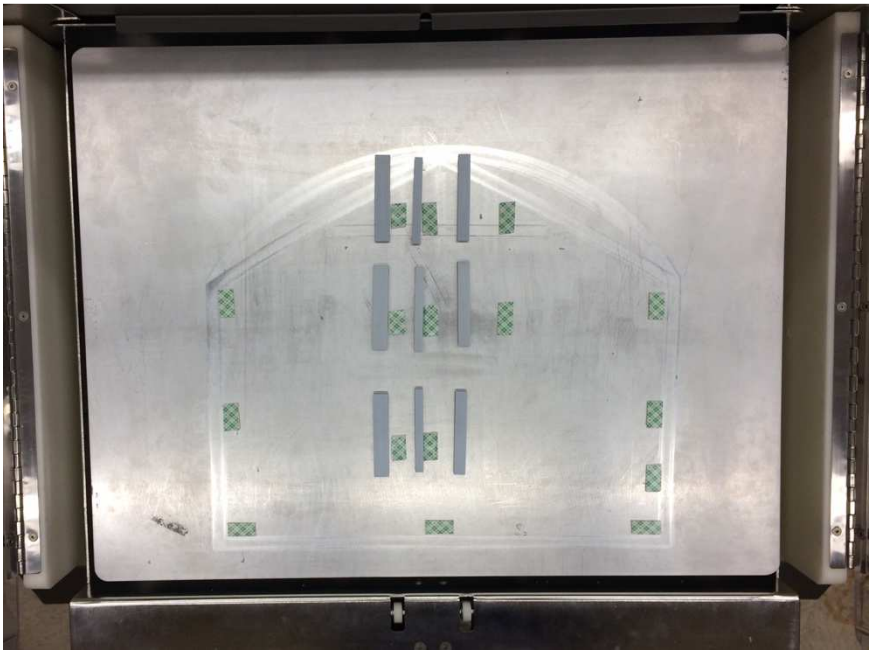


Figure 22. Gasket set up

4.3.1.5 Test Fixture

To evaluate the peel forces generated by the seals, a customized test fixture first proposed by de la Fuente (2012) (see Figure 23) was used (de la Fuente, 2013). The fixture was mounted to an Instron Universal Testing Machine model 5565 (Instron, Norwood, MA) outfitted with a 10kN load cell. The fixture enables a consistent peel angle and rate throughout the entire test.

Each piece of seal was trimmed such that 0.5 in was left on both sides of the seal and one "end" with the other "end" trimmed to 1 inch long so that it could be placed in the jaw for peeling.

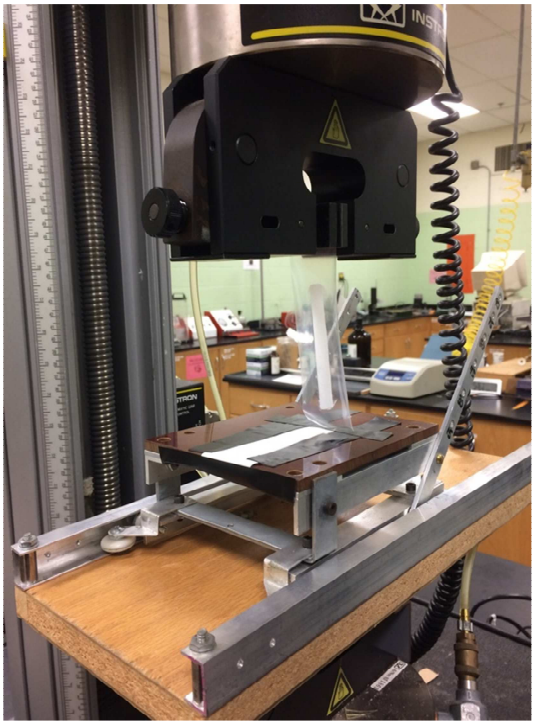


Figure 23. Peel test fixture

4.3.1.6 Peel test

Peel tests were conducted by adapting the standard ASTM F88 (Standard Test Method for Seal Strength of Flexible Barrier Materials) to test the ability of the prototyping method to provide consistent seals given the factors associated with the described method (rapid-prototype process, seal width, and gasket height). The fixture was set to be pulled at 90°. The samples were placed at the center of the fixture and the Tyvek® side was affixed to the flat platen of the fixture. Each seal sample was tested at a rate of 12 in/min. Average load was calculated by averaging all measured data points.

4.3.1.7 Statistical analysis

Data were analyzed with SAS software version 9.4 (TS Level 1M1, SAS Institute Inc., Cary, NC) and Excel 2016 (Microsoft Corporation, Redmond, WA). A 3-way ANOVA was used to test for significance effects ($\alpha = 0.05$) of main factors: consistency of the rapid prototyped process (molds created on different days- sets), ability of the method to create varied seal widths (width), and the effect of the gasket height on peel strength (height), were used in an attempt to evaluate the ability of the method to create consistent seals.

4.3.2 Study Two - Application of the methodology

The objectives of this portion of the study were to test the ability of the method to create pouches with desired geometries and the ability of the novel seals to withstand sterilization.

After investigating the consistency of parts produced from different molds and generally validating the process, in the interest of testing the practicality of the method and its ability to produce desired geometries and pouches that withstand sterilization, we created molds that formed whole packages, specifically, a chevron pouch (see Figure 24). The mold was created in two pieces and glued together using Super Glue (The Gorilla Glue Company, Cincinnati, OH) (see Figure 25). Materials used were the same as those described when creating the peel samples and production parameters used for seal in-house pouches were: 145°C, for 2.5 seconds at 55 PSI (see Figure 26). Excess material was trimmed from the both sides of the pouch flush with the edges of the seals. Consistent with commercial practice, the distance between the chevron and the top edge was 0.5 in..

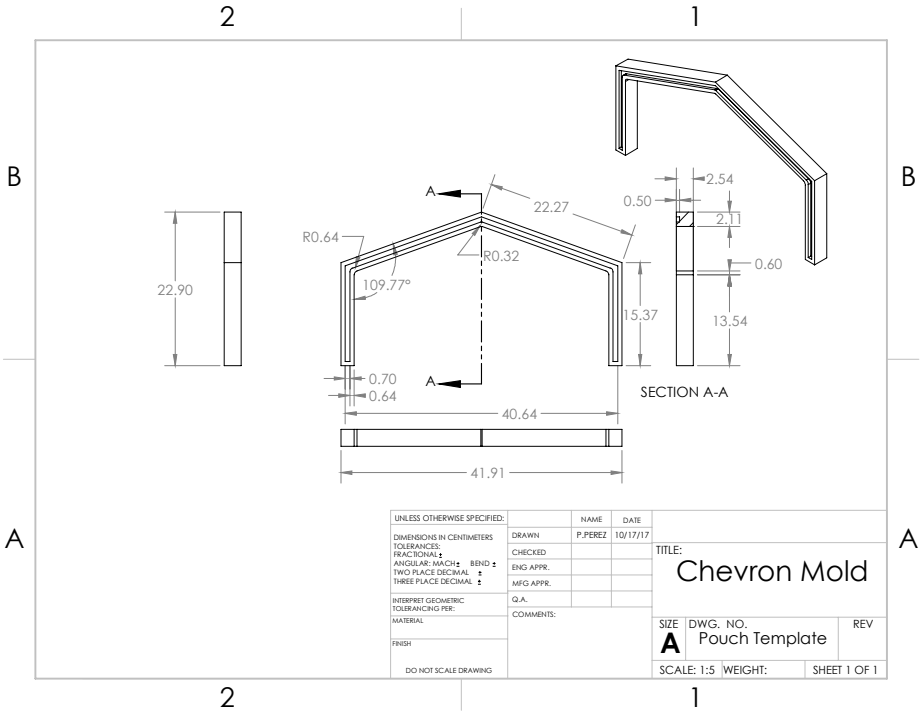


Figure 24. Chevron mold

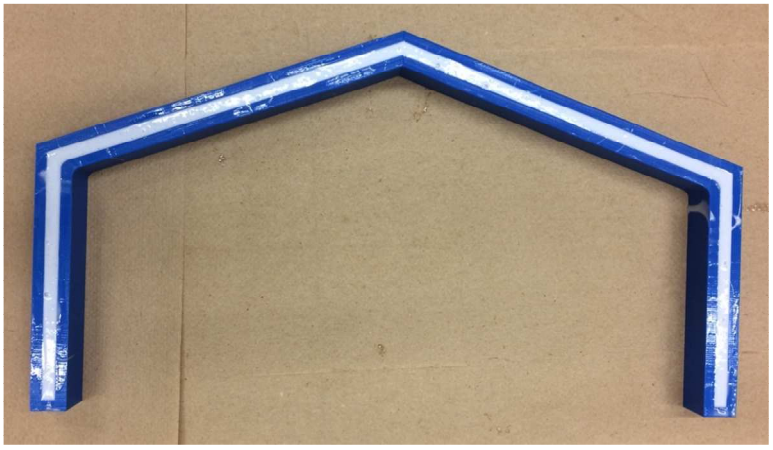


Figure 25. Filled mold

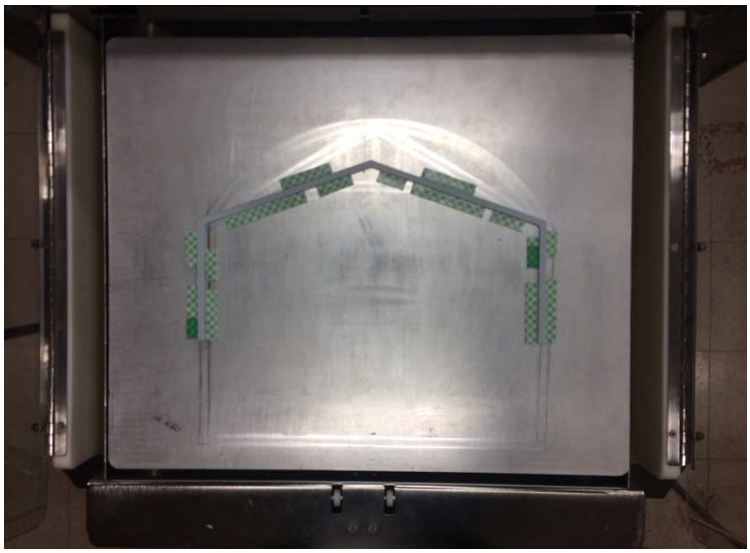


Figure 26. Chevron gasket placed on the plate

Figure 27 shows the final product, a chevron pouch created using our novel technique with the same dimensions as the commercial chevron pouch. The final dimensions were 40.64 x 22.86 cm (16 in x 9 in).

(a) In-house chevron pouch

(b) Commercial chevron pouch

Figure 27. Chevron design using the described method vs. standard commercial chevron

4.3.2.1 Sterilization

To fully test the ability of the method to make seals that withstand sterilization, a series of pouches, including in-house pouches created with the novel prototyping technique and commercial pouches, were sterilized using gamma sterilization. Twenty samples of pouches of each treatment (novel and commercial) were packed in a 16.25” x 9.25” x 4.75” c-flute regular slotted container (RSC). Packages were sterilized under gamma sterilization (SteriPack Contract

Manufacturing, Lakeland, FL). The samples were exposed to maximum conditions in order to stress the material to its fullest potential. Gamma samples were irradiated at 42.2-48.5 kGy.

4.3.2.2 Peel Test

To characterize the seal strength of both pouches created with our novel method and commercial pouches prior to sterilization, seven novel pouches and commercial pouches that had not been exposed to sterilization were tested for peel strength. Peel strength in unsterilized treatments were compared against sterilized treatments (for both novel and commercial pouches). Four samples were obtained from four locations in order to measure peel forces associated with different seals (see Figure 28). Each section consisted of a 4 in seal with 0.5 in extra material on one side for consistency of peel samples across all locations. Samples were obtained from the left and right side of the pouch and from the chevron area. Samples from the chevron area were cut 1 in away from the peak and the extra material above the seal was removed leaving only enough material below the seal to adhere the Tyvek® side to a customized fixture. Peel tests were conducted with samples drawn from: the left side, the right side, the top left and the top right.

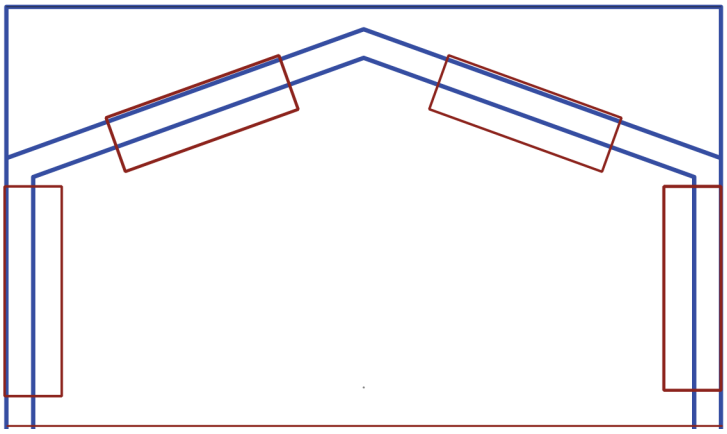


Figure 28. Diagram of the location of peel test samples

4.3.2.3 Statistical Method

Data were analyzed with SAS software version 9.4 (SAS Institute Inc.). T-testing was used to test equivalence between peel forces of commercial pouch and in-house manufactured pouch before and after gamma sterilization.

4.4 Results

4.4.1 Results of Study 1 – Method validation

Table 6. Statistical results of the main effects on peel forces

Source	DF	Type III SS	Mean Square	F Value	Pr > F
Set	2	0.0041	0.0021	1.46	0.2383
Width	**2**	**2.3131**	**1.1566**	**820.26**	**<.0001**
Height	1	0.0013	0.0013	0.91	0.3431
Set*Width	4	0.0018	0.0004	0.32	0.8659
Set*Height	2	0.0034	0.0017	1.22	0.3011
Width*Height	2	0.0001	0.0001	0.05	0.9486
Set*Width*Height	4	0.0022	0.0006	0.39	0.8145

Based on the results presented in Table 6, analysis of seal strength yielded no evidence of significant differences when results from the three sets of molds (green, blue, red) were compared. This suggests that the rapid-prototype process was consistent day to day, with molds producing seals that resulted in similar seal strengths ($P = 0.2383$). Further, seals produced from the gaskets with differing heights suggested no evidence of a significant different between seals produced ($P = 0.3431$). There was no evidence of any significant two- or three-way interactions. As expected, a main effect of seal width was noted on seal strength ($P < 0.001$), whereby seals with larger widths resulted in significantly higher peel forces (see Table 7).

Table 7. LSMEAN, standard error and confidence intervals attributed to force and seal width

Width (cm)	Force LSMEAN (lbf)	Standard Error	95% Confidence Limits	
0.7	0.653	0.0069	0.639	0.667
1	0.845	0.0069	0.832	0.859
1.3	1.045	0.0069	1.032	1.059

4.4.2 Results of Study 2- Application of the methodology

For medical device applications, there is an important need for seals to not be significantly impacted by sterilization process. As such, we investigated the seal strength of commercial and novel pouches pre and post gamma sterilization. There was no evidence that gamma sterilization impacted seal strength for either package type (in-house pouches: P=0.6027 and commercial pouches: P=0.1966). (see Table 8 and Table 9).

Table 8. Peel force comparison between in-house samples before and after sterilization

Sample Location	Mean Values (lbf) (Before)	Mean Values (lbf) (After)	t-Value (before-after)	P value
Left Side	0.544	0.540	0.16	0.8740
Right Side	0.507	0.495	0.84	0.4156
Top Left	0.531	0.534	-0.19	0.8560
Top Right	0.484	0.474	0.71	0.4916

Table 9. Peel force comparison between commercial samples before and after sterilization

Sample Location	Mean Values (lbf) (Before)	Mean Values (lbf) (After)	t-Value (before-after)	P value
Left Side	0.741	0.757	-0.57	0.5798
Right Side	0.770	0.778	-0.72	0.4829
Top Left	0.736	0.747	-0.75	0.4672
Top Right	0.695	0.720	-1.23	0.2422

4.5 Discussion

The methodology is intended to enable the design and development of creative designs for flexible pouches. The creative prototyping that it enables will allow research related to how seal geometries impact peel forces, and ultimately how package design impacts user experience and performance. The described methodology was applied to investigate the effect of pouch designs, specifically seal geometry and peel forces on contamination rates during aseptic presentation. The authors created two different geometries (a chevron and a round style (see Figure 29) and suggested that seal geometries were found to have a significant effect on contamination rates where chevron style resulted on higher contamination rates compared to round style ($P = 0.0108$). Given the importance of seal geometry on contamination rates, the increasing tendency to move towards a user-centered approach to design and proposed changes to ISO 11607 which would require medical device manufacturers to validate the ability of the design of a SBS to transfer devices sterilely, this method is an important new development.

Figure 29. Pouch geometries created using the described method.

4.6 Conclusion

Work herein represents the creation and validation of a method that enables the rapid prototyping of pouches and holds the potential to enable the production of diverse seal configurations. It provides the flexibility to create and evaluate designs adequate to the end user

and the environment, in this case referring to the safe handling and aseptic transfer of sterile products in a sterile environment.

4.7 Limitations

Normal machine variation is likely to impact peel forces. It is recommended to evaluate machine temperature and pressure for consistency. Additionally, a limited number of gasket factors were tested. Additional shapes and sizes of gaskets should be evaluated.

CHAPTER V

OBJECTIVE INVESTIGATION OF THE ROLE OF PEEL GEOMETRY ON A MEDICAL DEVICE'S CONTACT WITH NON-STERILE SURFACES DURING ASEPTIC TRANSFER

Paula Perez[1], Tamara Reid Bush, PhD[2], Wu Pan, PhD[2], Jack Michalski[2], Laura Bix, PhD*[1]

School of Packaging, Michigan State University, East Lansing, MI, USA[1]

Mechanical Engineering Dept., Michigan State University, East Lansing, MI, USA[2]

Submitted to Packaging Technology and Science

*Corresponding Author

Laura Bix, PhD

448 Wilson, 114 Packaging

East Lansing, MI 48824

517 355 4556

517 353 8999 (fax)

bixlaura@msu.edu

Abstract

Purpose

Investigate the relationship of peel geometries used for pouch seals and the likelihood of contact between a medical device and non-sterile surfaces during aseptic transfer.

Methods

One hundred and thirty-six health-care providers with practical experience in aseptic technique were recruited. Two seal geometries were created: a chevron style, and a pouch with a rounded seal. Each geometry was modified with the addition of an extra seal that was intended to result in

abrupt differentials in force during opening. Geometry (chevron vs. rounded) and force differentials (even distribution vs. abrupt changes) were crossed for a total of four treatments. The backs of the participants' hands and the outside of the pouches were coated with an analyte, invisible in the visible spectrum, but detectable under black light. This analyte transfers to surfaces upon contact, serving as a simulated contaminant. Participants were asked to transfer package contents using sterile technique and transferred items were examined under black light for the presence of analyte. Each of the four configurations were transferred in two replicates, for a total of 8 trials. Devices were inspected under black light and results were recorded as binary data, analyte present (yes/no).

Results

A hundred and twenty-nine completed data sets were used for the statistical analysis. Subjects ranged from 20-57 years old, averaging 5 years of experience in aseptic technique. Data analysis yielded evidence of a significant effect of geometry (chevron vs. rounded) ($P = 0.0108$). Specifically, items transferred from chevron geometries resulted in a significantly higher rate of contact with non-sterile surfaces (LSMEANS ± SE: 42%±3%) than those in the round geometry (35%±2%). Data did not support the idea that the addition of the bar intended to induce abrupt transitions in force had an effect on contamination rates ($P = 0.1002$). Contamination probability for abrupt change was: LSMEANS ± SEM: 41%±3% vs. 36%±2% for those with smooth distributions.

Conclusion

This work adds to a small but growing body of knowledge regarding how package design influences sterile transfer. Specifically, it fills a critical gap in understanding; how peel force and

seal geometry impact the probability of a sterile device coming in contact with non-sterile surfaces during aseptic presentation.

Key words

Aseptic transfer, aseptic technique, packaging, peel force, seal geometry, health-acquired infections (HAIs), indirect contamination

5.1 Introduction

Healthcare Acquired Infections (HAIs), also referred to as nosocomial infections, cause substantial pain and emotional distress. In addition to added pain, suffering and loss of productivity, HAI patients frequently require longer hospital stays (Ducel et al., 2002). This is costly; patients with HAIs require additional treatment and are more likely to be readmitted to the hospital (Emerson et al., 2012). Although precise evaluation is challenging, estimates for US data collected in 2007 suggested that HAIs cost between $35.7 billion and $45 billion (Scott, 2009). HAIs can be transmitted to patients directly, from a contaminated person to the patient, or indirectly, when contamination is transferred through an object or an intermediate person to the patient (Siegel et al., 2007).

Work focused on indirect contamination transfers is limited, primarily focusing on operating room traffic (Dalstrom, 2008), hospital surfaces (Bhalla et al., 2004; Kramer et al., 2006) and sterile barrier integrity (Kassarjian, 2011; Moghimi et al., 2016), which refers to the ability of a package to maintain the sterility of the product throughout distribution and storage. Integrity maintenance depends on the efficacy of the sterile barrier system (SBS), defined by The International Organization for Standardization (ISO) as, the "minimum package that prevents ingress of microorganisms and allows aseptic presentation of the product at the point of use" in ISO 11607, its standard on packaging (Technical Committee ISO/TC 198, 2006a).

Although, by definition, the SBS protects devices from microbial contamination throughout distribution and handling, it also has the potential to serve as a vehicle for indirect contamination during aseptic presentation as part of the definition of the SBS mandates that it facilitate "the introduction and transfer of a sterile product using conditions and procedures that exclude microbial contamination" (Technical Committee ISO/TC 198, 2006a). Because only the inside and contents of the SBS are sterile, proper aseptic technique dictates that devices be transferred without contacting non-sterile surfaces (i.e. the outside of the package or hands of the provider). Clearly, SBS design must facilitate aseptic presentation (Sherman, 1998).

Despite the important relationship between package design and aseptic presentation, the published literature objectively investigating this topic is quite limited (Crick et al., 2008; G. Smith et al., 2009; T. Trier et al., 2014), and few articles focus on how opening features (e.g. seal strength (de la Fuente, 2013; T. Trier, 2016), tear features (Liebmann, Schreib, Schlözer, & Majschak, 2012)) and approaches (path or angle of peel employed by users (de la Fuente, 2013; T. Trier, 2016)) impact things like opening force and, potentially, the ability to effectively transfer items to the sterile field.

Smith et al. suggest that seals which require large forces during opening can cause airborne contamination of the sterile field. In their study, packages were pressed into a powder and opened from a 10 cm height over a dark surface. Results of the study suggested that forces required to open the package impacted the scattering of the powder over a 36 cm x 36 cm area representing the sterile field (G. Smith et al., 2009). Trier (2016) investigated how peel paths, seal strength, and peel speed impacted the likelihood of contamination. To do so, Trier performed a novel whole-package peel test using an Instron Universal tester to open chevron pouches. In one treatment, the path of the peel was an "intended peel path," beginning at the top

center, traveling parallel to the length of the pouch. In another treatment, the jaws of the Instron began in the corner, perpendicular to the angled portion of the chevron seal. The author also hypothesized a relationship between rate of opening and the prevalence of contamination. To investigate this, the author conducted pilot tests where pouches were modified to create two different treatments for opening location; these pouches were then opened at different peel rates (6 in/min, 12 in/min, 18 in/min). To investigate the effect of these factors on rates of contamination, a small amount of Glo Germ® (Glo Germ Company, Moab, UT), a powdery substance that fluoresces under black light, was added to the fixture that separated the layers of the test specimens. Findings, which were indicated as preliminary, suggested that chevron pouches opened at the corner resulted in higher contamination rates compared to the intended openings, those which began at the center top of the pouch (84.2% vs. 15%), when opened at a rate of 12 in/min. Results from the pilot test suggested that pouches that were opened from the center had no contamination when opened at 6 and 18 in/min whereas pouches that were opened at the corner resulted in three out of five pouches contaminated when opened at 6 in/min and five pouches contaminated when opened at 18 in/min (T. Trier, 2016). When the resultant forces for pouches pulled at the same rate of speed, 12 in/min, from the center and the corner were compared, those beginning with the intended starting position (the center) measured less (mean: 2.42 lbf, SD: 0.33) than those beginning at the corner position (5.39 lbf, SD: 0.99). This suggests that pouches opened from the corner may require a higher opening force as compared to those opened as intended (beginning at a center position and opening parallel to the length dimension of the pouch). Additionally, higher contamination rates were observed in pouches opened from the corner. These preliminary findings led the author to suggest the need for further work in this area.

de la Fuente also examined the relationship of peel path on forces, but did so with trays. Specifically, de la Fuente explored how the peel path users employ to remove the lid from a tray, and how the angle formed between the lid and the tray influenced the force required to remove the lidstock. Differing peel paths result in varied seal widths being peeled in order to separate the substrates (i.e. remove the lid); findings suggested that peel forces are directly affected by the width of the peel, with wider seals requiring larger forces to remove the lid from a rigid tray (de la Fuente, 2013). The author suggested that as a result of this relationship, people opening trays tend to find the "optimum peel" path (that which results in a minimum width of seal being peeled at any given point in the peeling process) by adjusting the path of the peel. Similar to finding an optimal peel path, users also tended to employ an angle (forged between the top of the lidstock being removed and the plane of the tray) that minimized resultant forces during opening. Specifically, opening forces were minimized when the lid was peeled in a range of angles that centered at approximately $\alpha=45°$ (de la Fuente, 2013).

Canty et al. researched the relationship of peel forces and grip type, pull direction, peel angle and force exerted when removing lids from yogurt cups. The authors suggested that during the initial stages of peeling when removing the lidstock from a cup of yogurt, "force builds up to a peak which occurs when the seal is broken"; remaining fluctuations of the opening forces were associated with the difference during opening of both sides of the lid (Canty, Lewis, & Yoxall, 2012). Considering both de la Fuente's (2013) findings which suggest force is directly related to peel width and Canty's (2012), that the initiation force is the highest point, it would be reasonable to conclude that chevron pouches that are opened by beginning a peel path from the corner (see Figure 30-left) will require a larger force than when peel propagation begins as intended (from the top center--- see Figure 30-right).

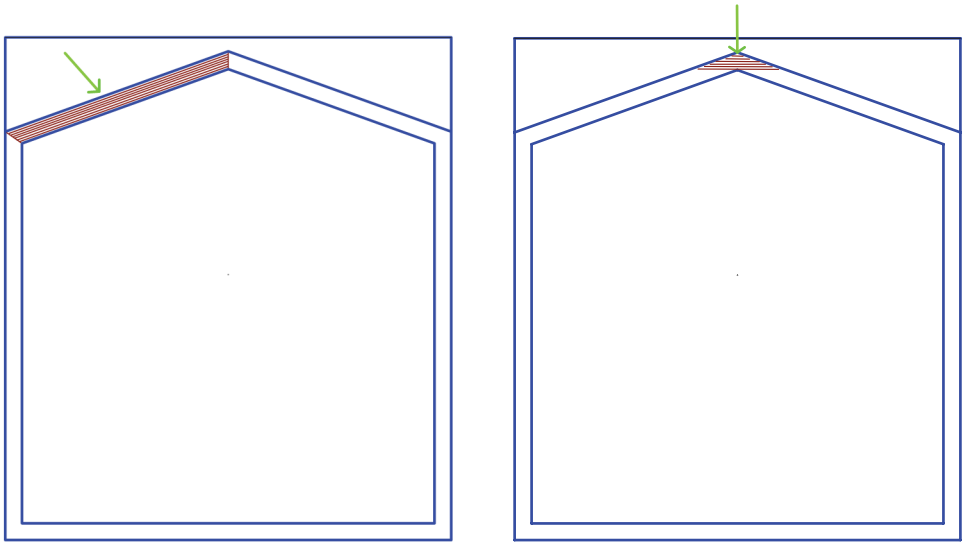


Figure 30. Chevron Pouch: The Relationship of Peel Path to Peel Width (Indicated by Red Lines): Corner opening (left), top center opening (right)

Liebmann et al. (2012) studied the effect of peel angles and opening speed as part of the development of a test standard to measure opening forces. The standard is intended to be used on peelable packages, such as cups and trays. The authors suggested that when opening a peelable closure a "tear angle" greater than 90° (as measured by the plane of the container and the sealed side of lidding being removed; the compliment angle of de la Fuente's reference angle) is chosen since it is easier to open. Removal forces, or "tear" forces in the author's terminology, were obtained with angles of 90°, 135° and 165°, and opened at speeds of 100, 800 and 3,000 mm/min. Consistent with Canty et al., the author identified "tear initiation force" as critical since it is considered as the maximum opening force required to breach the package. While Liebmann proposed that angles are optimized by users in order to minimize forces based on observation, de la Fuente utilized quantitative methods. Specifically, de la Fuente investigated peel angle and peel direction of opening for lidded trays under realistic conditions and evaluated the effect of experimental setup on peel direction (restrained vs. unrestrained). Using a Qualisys Motion

System, the author measured participants as using an average peel angle of 44° (as measured between the lidding face and plane of sealing, the corollary to Liebmann's definition of angle), which falls in the "optimal range" of 45° ±15° where peel forces are minimized (de la Fuente, 2013).

Given that the direction of the peel impacts the width of the peel (see Figure 30) and, in turn, the force required to open packages (de la Fuente, 2013), which Smith (G. Smith et al., 2009) suggest has the potential to impact sterile transfer, understanding how healthcare providers position their hands during the initial grip and subsequent opening process when opening a chevron pouch is important. Trier (2013) attempted to do just that in a post-hoc review of digital recordings comprised of 582 openings of chevron pouches in three sizes (small, medium and large) that were typical for the medical device industry. In 91.2% of trials of the small pouches (7.62 cm x 20.32 cm), the providers began with their hands centered directly above the chevron (as they were intended to be opened) (see Figure 30 right). For medium pouches, only 52% of providers began with their hands positioned in the top center, and less than half, 42.3%, of the trials comprised of large pouches had providers beginning from the intended, center position (T. Trier, 2013).

Given de la Fuente's (2013) work, which suggests that peel width is related to peel force, starting opening at the corners, as a majority of Trier's candidates opening large pouches did (2012), has the potential to be problematic; when packages are opened from the corner and the peel path traveled is at 45° relative to the intended path (see Figure 30 left), the user must separate a seal of a much larger width (compare red lines) than they would if they travel the intended path (parallel to the length of the pouch- see Figure 30 right), and, a correspondingly higher opening force. Continuing down this (unintended) path, the participant eventually will

have peeled through the portion of the seal with this large width, reaching the apex of the chevron and the seal that closes the side of the pouch, which, together represent a much smaller peel, and lower force (see Figure 30 left). These sudden and abrupt changes in the width of seal being peeled through have the potential to result in large differentials in the forces required to separate the materials in opening the package. We hypothesize that these large differentials result in a "jerking motion" during the opening process with a greater probability of contact between the device being transferred with non-sterile surfaces than if the user employed the intended path (see Figure 30 right) which would result in a much more even peel width and correspondingly smooth distribution of forces.

5.2 Objectives

In support of these hypotheses we conducted two broad studies comprised of the following objectives:

Study One- Develop, Produce and Characterize Pouches

1. Develop a method capable of rapidly creating pouches with a myriad of peel geometries and produce pouches
2. Model the relationship between peel path and seal width of developed pouches.
3. Measure resultant peel forces for developed designs along two peel paths (center and from corner).

Study Two- Objectively Test Pouches Developed in Study One for an Influence on Rates of Contamination.

1. Investigate how peel geometry impacts rates of contact between the device and non-sterile surfaces during aseptic transfer

2. Investigate how large force differentials that result in a "jerking motion" during the opening process impact rates of contact between the device and non-sterile surfaces.

5.3 Study One-Develop and Objectively Characterize Pouches

5.3.1 Objective 1- Develop a method capable of rapidly creating pouches with a myriad of peel geometries

Four treatments were created by crossing seal geometry at two levels (chevron style vs. rounded) with two designs expected to induce two levels of force profile ((1) a consistent force to open and (2) a large force differential). The four resultant treatments were: a chevron with an even force distribution; a chevron with abrupt force differential; a rounded seal with an even force distribution and a rounded seal with an abrupt force differential. Peel profiles that were expected to result in abrupt force differentials, the "doppelganger" partner, were created by taking the seal geometry (chevron or rounded) and adding a straight-line seal (7.5 in x 0.3937 in) (see Figure 31 -A Styles). The additional bar was positioned at a distance of 11-3/8 in from the bottom seal (see Figure 31-A styles). Treatments created with the intention of inducing smooth peels are hereafter referred to as "B styles", while their "doppelgangers," intended to result in abrupt differentials, are referred to as "A styles" (see Figure 31).

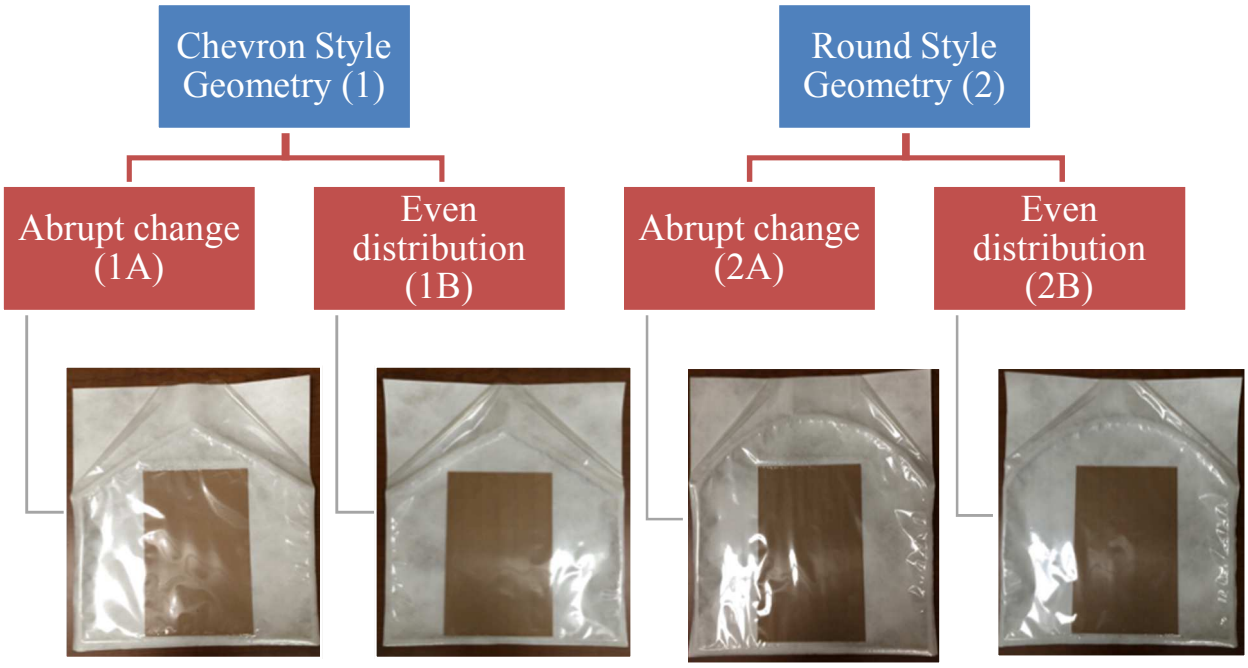


Figure 31 Pouch treatment: Designs 1A and 2A contain an extra seal bar.

The purpose of the addition of the straight-line seal was to create a larger seal width that required a higher opening force, creating the hypothesized "jerking motion," or sudden movement, during opening when the user traveled the intended peel path..

To create different seal geometries, 3D modeling software (Solidworks Education Edition, Academic Year 2015-2016/2015 SP4.0, Dassault Systèmes Solidworks Corporation, Waltham, MA) was used to design molds which produced the gaskets used to create the pouch seals (see Figure 32). Molds were rapid-prototyped using a MakerBot Replicator 5th Generation machine (MakerBot Industries, LLC, Brooklyn, NY) and a Fortus 250mc printer (Stratasys Ltd., Eden Prairie, MN). The material used to manufacture the molds was PLA 3D Printer Filament/ MakerBot PLA and ABS-M30 / P430 ABS / P430XL ABS / ABSplus Model Material (Stratasys Ltd.). Due to machine constraints, the molds were fabricated in four separate

pieces and glued together. Figure 32 depicts the dimensional specifications of the molds used to create each of the two geometries.

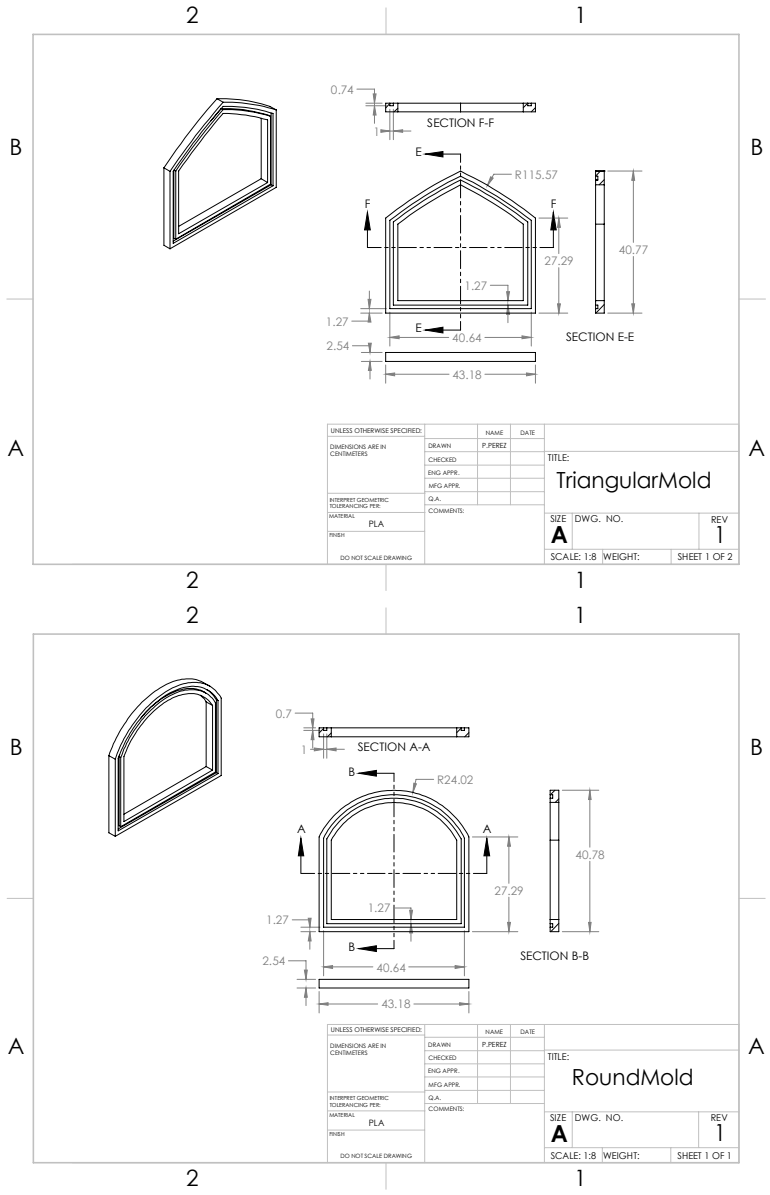
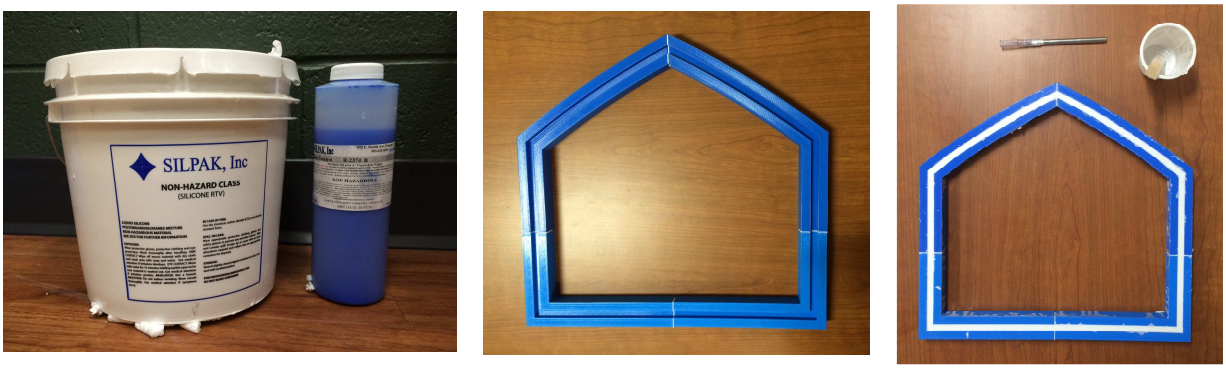


Figure 32. Mold for chevron-style geometry (top), mold for round-style geometry (bottom)

The material used to create the gaskets which ultimately were used to create the pouch seals, was Chemical-Resistant Silicone, Medium Hard (65A) (Silpak Inc. Pomona, CA). The compound consisted of two-part silicone rubber: a base and a curing agent (see Figure 33 on left). Per manufacturer instructions, components were mixed at a ratio of 100 parts base to 10 parts curing agent. The compound was mixed and placed in a vacuum chamber (VWR Sheldon Manufacturing Inc. Cornelius OR) to remove trapped air. The vacuum chamber was set to a Vacuum gauge 25 in. Hg. for 5 minutes or until the material stopped growing. The compound was then removed from the vacuum and carefully poured in the mold. Cavities were evenly filled and extra compound was removed using a plastic leveling tool. The mold was cured at room temperature for 24 hours on a level surface. Visual inspection was used to verify even filling of the molds as different gasket heights have the potential to lead to peel force variation. After room-temperature curing, gaskets were de-molded and placed into a Thelco Laboratory Oven Model 130 Serial No. 9511-104 (Precision Scientific Inc. Chicago, IL) for 1 hour at 400°F (see Figure 33).



Chemical compound (left) Mold (center) Filled mold (right)

Figure 33. Filling process

Once the "post-cure" process ended, and gaskets were cooled, pouch creation commenced. To manufacture pouches, a Sencorp dual shuttle tray sealer Model MD2420, Serial No. 015 tray sealer which was outfitted with a customized, flat plate (Sencorp-White, Hyannis, MA) was employed. Gaskets were placed at the center of the flat plate on the heat sealer. To avoid displacement of the gaskets, double-sided tape manufactured by Scotch (3M, Maplewood, MN) was used to secure gaskets to the flat plate (see Figure 34).

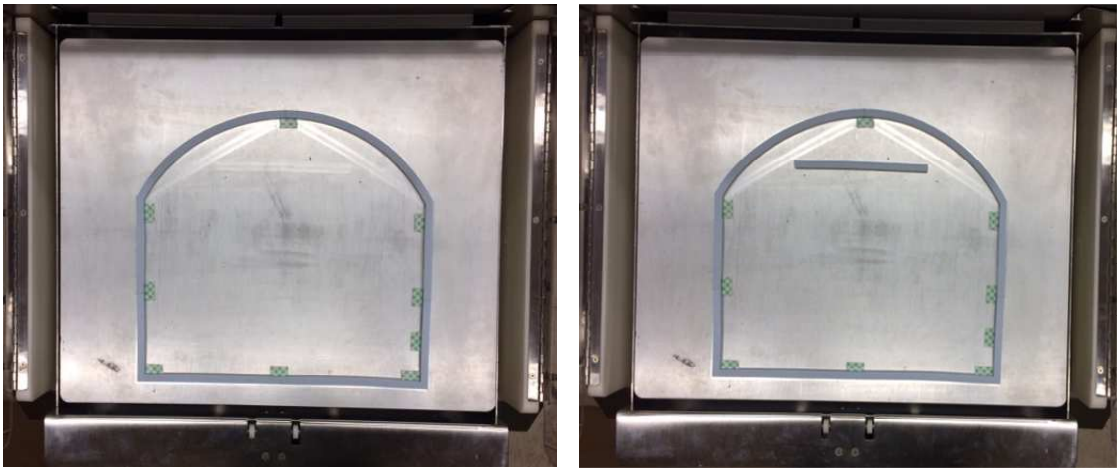


Figure 34 Round style geometry even distribution (left) and abrupt change (right)

Forty-eight ga PET/28.8# (Rollprint Packaging Products, Addison, IL) and an uncoated 1073B Tyvek® (DuPont, Richmond, VA) were cut into 45.72 cm x 40.64 cm segments to create pouches. The PET film was centered over the gaskets and the Tyvek® was aligned with the PET, positioned so that it was nearest the heat sealing platen.

To simulate a device, a die cut corrugated E-Flute sample (27.95 cm x 18.415 cm) was placed between the two materials used to create the pouch. The corrugated pieces were designed using ArtiosCad (Version 16.0 Build 1462) and cut using a Kongsberg table machine Premium Line 1930 (Irvine, CA). The machine was operated by gcw2000 software (Artios Corporation).

This was placed between the Tyvek and PET prior to sealing, oriented such that the length dimension of the gasket materials which would form the pouch and the length dimension of the simulated device were parallel to one another.

A glass jacket was positioned over the materials used to form the pouches so that they would not come in direct contact with the heat sealing platen, preventing burning and scorching. Pouches were sealed at 150°C, for 3 seconds with a pressure of 60 pounds per square inch (psi). Once sealed, pouches were placed on a cutting mat and extraneous material from the left, right and bottom was removed using a rotary cutter and straight edge in order to leave only the seal area on the bottom and sides of each sample. Once excess material was removed from the bottom and sides of the pouches, they were measured to verify the final dimensions. Extra material from the top area was also removed if needed. Pouches were verified as appropriately constructed through dimensioning of finished prototypes, which were verified to be 40.6 cm x 44.7 cm.

5.3.1.1 Center opening vs. corner opening of a commercial standard chevron pouch

In addition to the four designs described above, a standard commercial chevron pouch Allegro® T, made from 48 ga PET/28.8# (Rollprint Packaging Products, Addison, IL) (see Figure 35) was also evaluated in some sections of the study. Compared with the similar looking treatment 1B (see Figures 31), the commercial standard chevron pouch has a different chevron angle and a smaller grip area above the peak of the chevron.

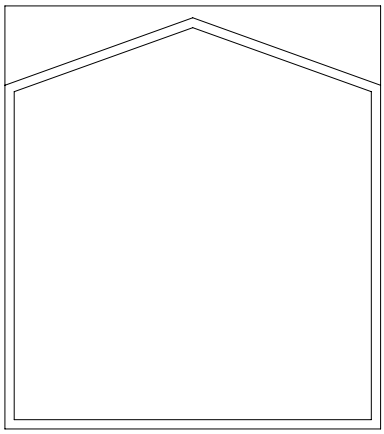
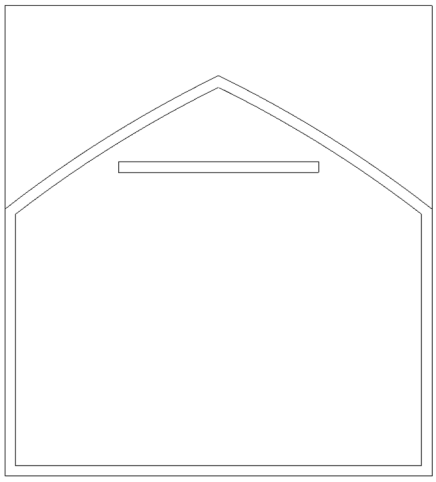


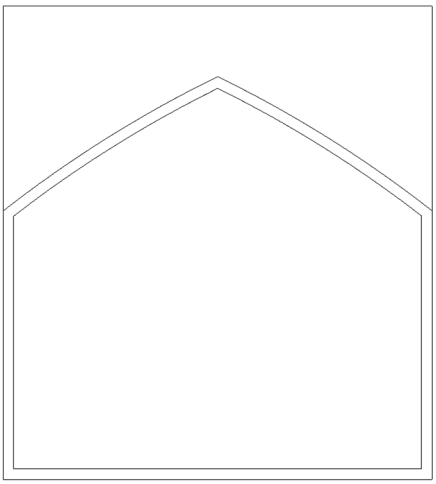
Figure 35. Commercial standard chevron pouch

5.3.2 Objective 2- Peel path modeling

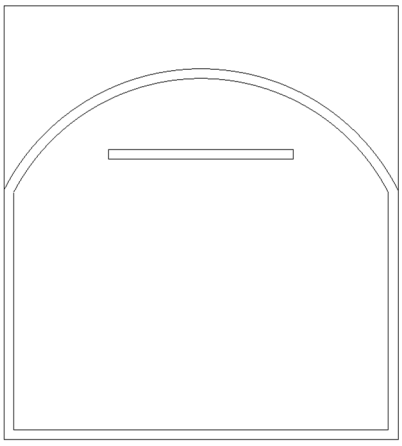
Given the work of others which suggests that the width of the peel path relates to the resultant peel forces (Canty et al., 2012; de la Fuente, 2013), we modeled the widths of the peel of four novel pouch designs assuming that participants took the intended peel path (i.e. straight through the design parallel to the pouch length) using AutoCad for Mac (O.48.M.294, Autodesk, San Rafael, CA) and Matlab (R2015b 8.6.0.267246 academic license, Mathworks, Natick, MA) (see Figure 36).



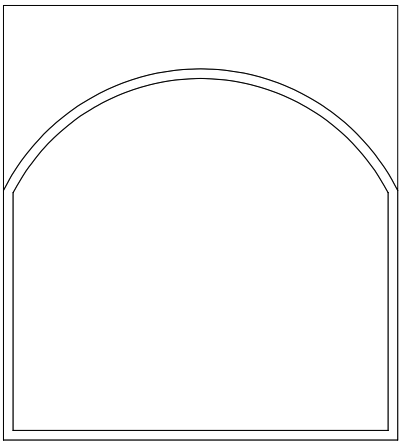
Chevron Style (Abrupt Change)



Chevron Style (Smooth Distribution)



Round Style (Abrupt Change)



Round Style (Smooth Distribution)

Figure 36. Proposed designs

Dimensioned drawings created in Autocad were analyzed, using a code authored in Matlab, to calculate the width of the seal area being separated when traveling the expected peel path. Calculations were made with a frequency of 0.025 cm and plotted assuming a path parallel to the pouch's length for all four treatments (see Figure 36). The total peel width was plotted and juxtaposed against the pouch at scale in Figure 37 and Figure 38. The bottom seal was not included, as pouches are not usually peeled completely during aseptic transfer.

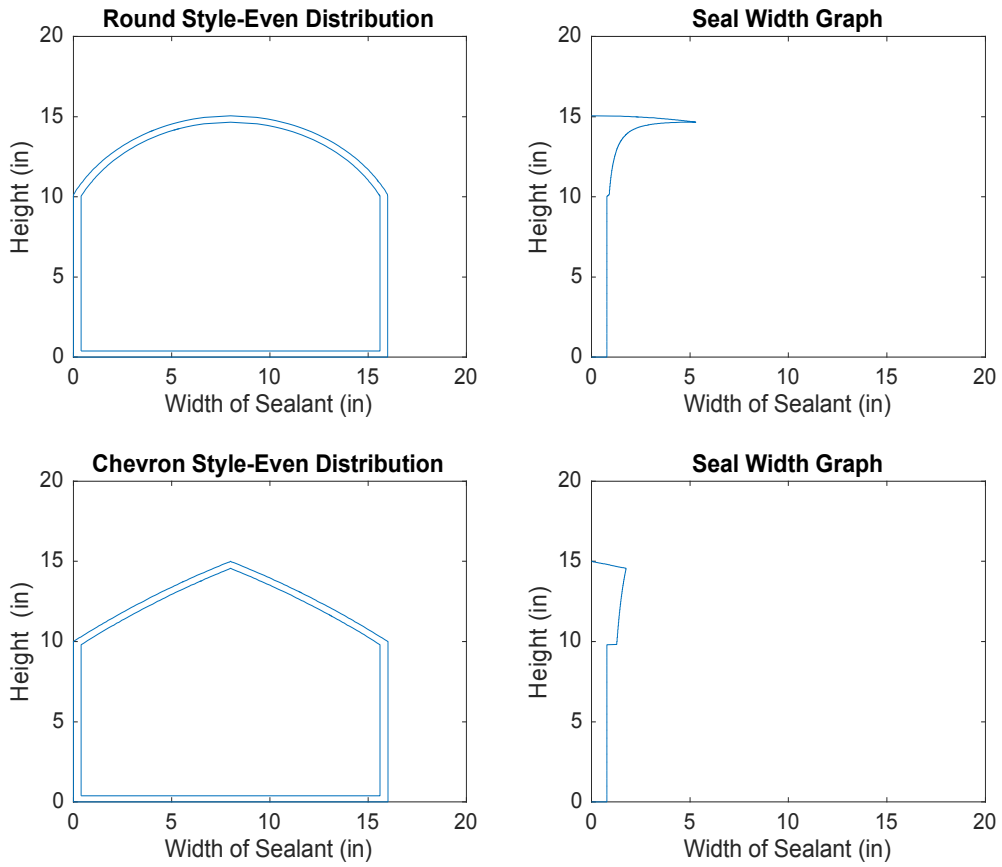


Figure 37. Even force distribution geometries and peel paths

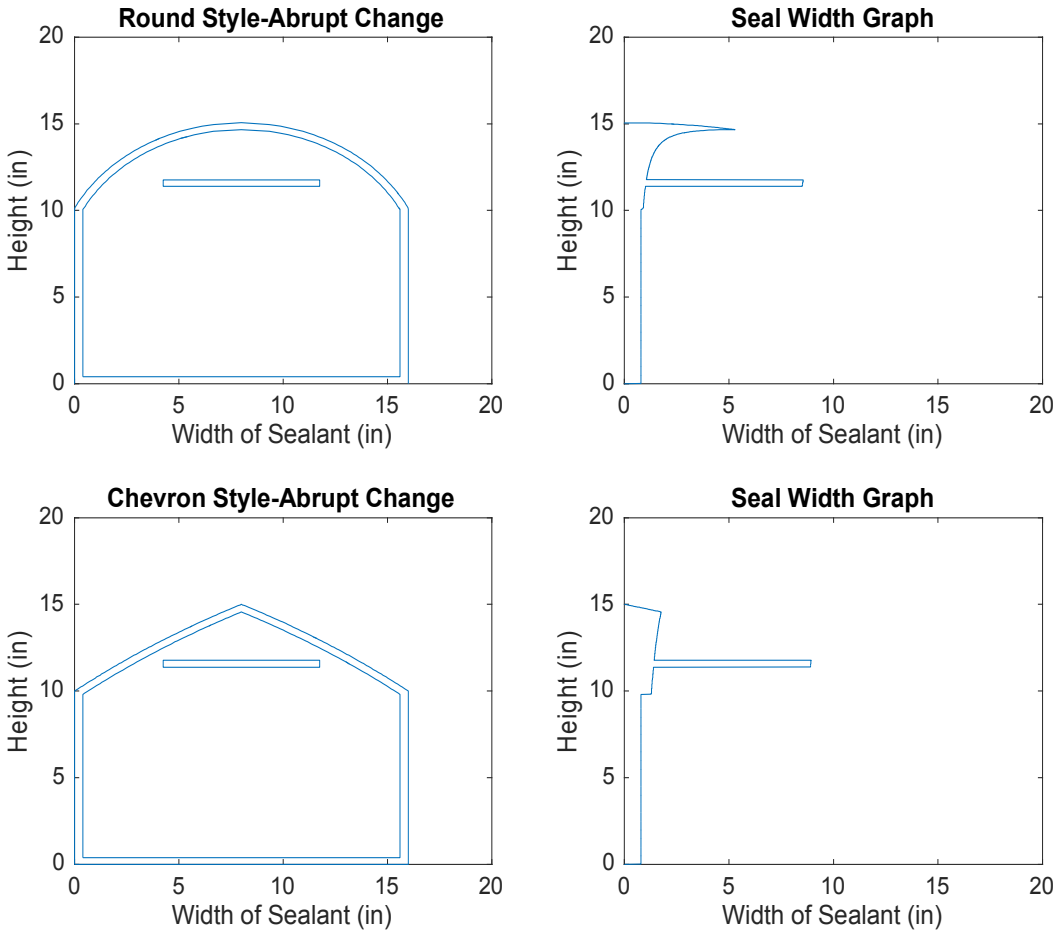


Figure 38. Abrupt change geometries and peel paths

5.3.3 Objective 3: Measure resultant peel forces developed designs along two peel paths (center and from corner)

5.3.3.1 Participants

To measure the forces generated by the pouches used in the study, six healthy volunteers were recruited from the biomechanics lab at Michigan State University. To qualify, these participants were at least 18 years old with no history of loss of hand function. Participants were asked to open packages while force data were collected throughout the opening process using a

multi-axis load cell. Testing took place in the Biomedical Design Research Laboratory on Michigan State University's campus. All methods were conducted in accordance with procedures approved by the Social Science/Behavioral Educational Institutional Review Board (09-179).

To characterize the forces that were generated by various peel profiles during whole package opening, a custom device was developed. The device was secured onto a multi-axis load cell (AMTI, MA) where packages could be mounted so that they did not slip during the opening sequence (see Figure 39). Load cells utilized a sampling frequency of 60 Hz. and were equipped to monitor the time as well as the force, which was recorded in metric units. One side of the pouch was secured to the load cell, while the other was free for the participant to grab. Using Newton's third law of motion, which states that forces occur in equal and opposite sets, we estimated the opening force.

Silicone gel was placed on the inside of the gripping faces of the clamping mechanism, which was cut to roughly the same size as a human thumb and index finger to hold the package in place. Two bolts secured the gripping face of the load cell device to the fixed face and were tightened to hold the fixed side of the package in place (see Figure 39).

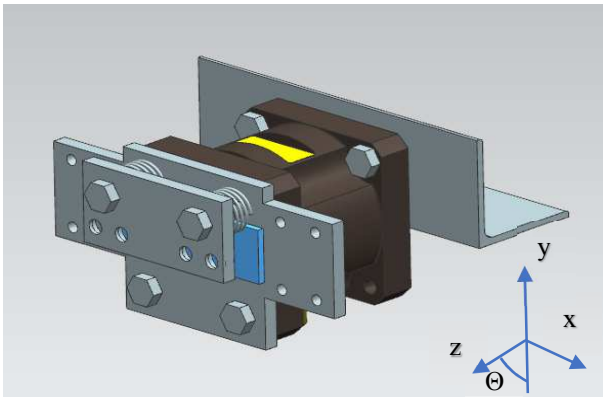


Figure 39. The device created to hold packages. Drawn in NX 11 2.

5.3.3.2 Data Collection

The device was clamped onto an adjustable table which was adjusted to a height where the participant's elbow formed a 90-degree angle when gripping the package when it was loaded. The load cell used was an Advanced Mechanical Technology, Inc. (AMTI). The cell was zeroed out after the package was attached to it and before the participant touched the package. The participants were told to grip the open side of the package and pull until the package was at least halfway open. Each participant opened each pouch design twice for a total of 12 openings. For each trial comprising the novel pouch design created by our team, a sample was inserted into the load cell with the pouches' vertical center aligned with the vertical center of the device. The fifth design, the commercially available chevron pouch, was inserted in two different orientations, one with the intended peel path, beginning at the center and traveling parallel to the length (see Figure 30 on right) and the other beginning at the corner (see Figure 30 on left) and pulling perpendicular to the angled seal.

The maximum magnitude of the opening process and the direction of force application were computed. The resultant force was calculated using the following equation:

1) $$F_r = \sqrt{F_x^2 + F_y^2 + F_z^2}$$

Where F_x, F_y and F_z represent the components of forces in these directions relative to the center of the load cell and F_r is the resultant. The resultant force was then graphed versus time for each trial. Force direction was also calculated. To do this, the angle of the force relative to the vertical face of the load cell was found using the following equations:

2) $$F_R = \sqrt{F_z^2 + F_y^2}$$

3) $$\theta = \sin^{-1}\frac{F_z}{F_R}$$

The predominant force components were the vertical and outward components. The force in the x direction (directed from side to side of the package) was small; as such, it was not used in the angle computation.

5.3.3.3 Statistical Methods

To compare differences in peel forces, pairwise comparisons were conducted using Tukey adjustments. The analysis was conducted with proc GLM of SAS (Version 9.4 TS Level 1M1 SAS Institute Inc., Cary, NC). The generalized linear model was used with a significance level of $\alpha = 0.05$.

5.3.3.4 Characterization of four pouch designs with varying peel forces

Consistent with the idea that larger peel widths are directly related to higher opening forces, higher peel forces were observed in trials of the A style packages (where geometries induced an abrupt change- see Figure 40). This notion was also supported by data obtained from the commercial standard in trials where it was opened from the corner.

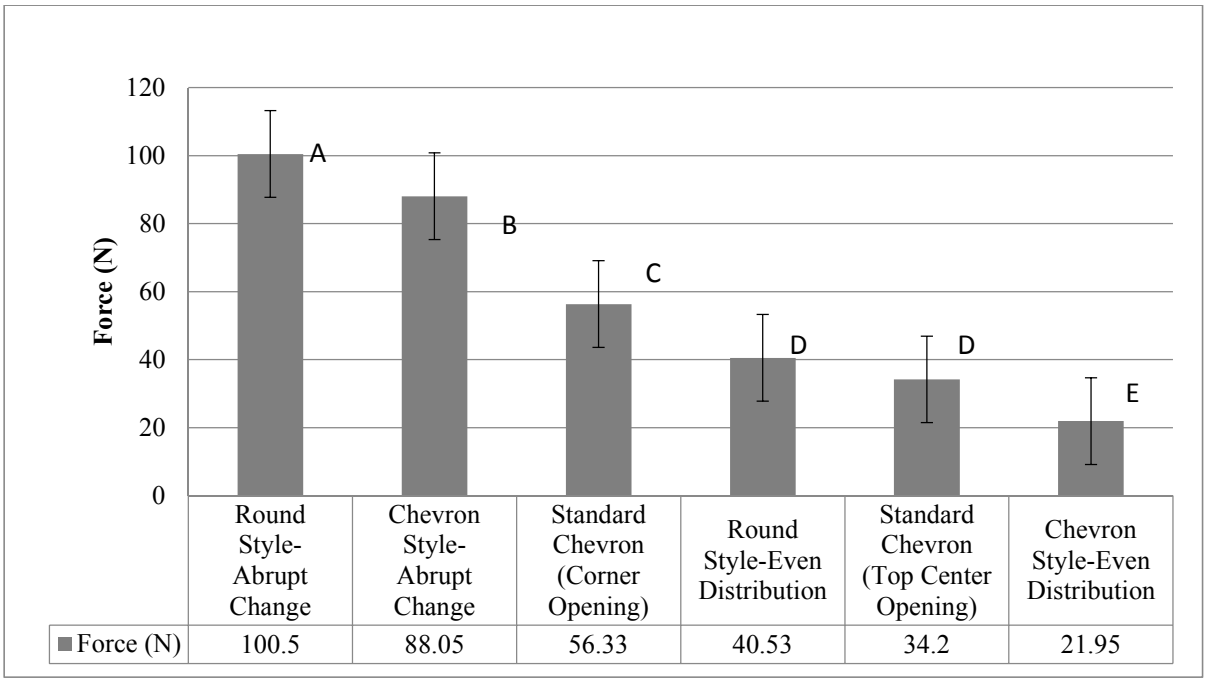


Figure 40. Peel Force (N) vs. Pouch Geometry. Whiskers indicate error bars with standard error. Letters indicate evidence of a significant difference between pouch treatments.

5.4 Study Two- Examining the Effect of Peel Geometry and Peel Profile on Contact with Non-sterile Surfaces During Aseptic Presentation

5.4.1 Method Employed for Study 2

In support of both of the objectives framed under study 2, we used a method adapted from Crick et al. (2008) to evaluate contact between transferred devices and non-sterile surfaces. Participants were recruited and tested in accordance with procedures reviewed and approved by the Social / Behavioral /Education Institutional Review Board (SIRB) at Michigan State University (approval number # 15-1199) (Appendix A). One hundred and thirty-seven healthcare providers and students with practical experience in aseptic transfer were recruited from locations throughout the state of Michigan. Testing locations, which also served as a locus for recruitment emails and flyers were: Lansing Community College (Lansing, MI), Sparrow Hospital (Lansing,

MI), Michigan State University Nursing College (East Lansing, MI), Baker College (Clinton Twp., MI) and Grand Valley State University (Grand Rapids, MI). Additionally, Association of Surgical Technologist (AST) members were recruited via an email blast that was distributed within a 60-mile radius of East Lansing, MI; these participants were tested at the School of Packaging on MSU's campus.

Participants were required to be at least 18 years old, have no known history of a skin condition (e.g. eczema, latex allergy, etc.), have a history of employment as a healthcare professional or be a healthcare student with practical experience in aseptic technique, and be willing to be videotaped presenting devices to a simulated sterile field.

Basic demographic information, including: age, sex, and professional experience was collected to characterize the pool of participants.

To detect contact between non-sterile surfaces and the test devices (corrugated), a contamination simulant was used. Glitterbug (Brevis Corporation, Salt Lake City, UT) is a commercially-available product designed to be invisible to the naked eye but visible under black light. This method was first employed by Crick et al. (Crick et al., 2008), and adapted by Trier et al. (T. Trier et al., 2014) as a method to detect contact between a device and a nonsterile surface during aseptic presentation.

Prior to testing, participants were asked to adjust the mayo table to their desired height and instructed to "grab the pouch at the top center and transfer the contents onto the sterile field using appropriate aseptic technique." The sterile field consisted of a blue 60.96 x 60.96 cm drape (Cardinal Health Sterilization Wrap Dual Layer, CH500, Cardinal Health, Waukegan, IL) that covered the adjustable table horizontal surface of 38.1 cm x 76.2 cm.

Non-sterile surfaces (provider's hands and the outside of the four pouch treatments) were coated with a thin layer of Glitterbug. Participants were outfitted with a new pair of gloves (Fingertip Textured Flexal Nitrile Powder-Free Exam Gloves manufactured for Cardinal Health, Waukegan, IL) for every opening trial. Only the backs of the gloves were coated; pads of the digits were not in order to minimize changes in friction that might impact the way providers moved. Subjects opened a total of eight trials, consisting of the four treatments (See Figure 31), each with a single replicate, in random order.

Once the device was transferred to the sterile field, the drape was transferred (by a team member designated to not prepare samples or interact with the analyte) to a black tent H1900 (ePhotoInc Hayward, CA) and inspected under a set of black lights (368 nm, 8 W) (Brevis Corporation). Three lights, two on each side of the sample table, and a third located at the bottom were used to consistently inspect and photograph (once on each side) all of the transferred devices for the presence of Glitterbug. The presence of the analyte on the device (indicative of contact with a non-sterile surface) was recorded in a binary fashion (yes/no), and each sample was photographed (once on each side) using a Canon Power Shot camera set to high speed burst with flash deactivated, enabling post-hoc review if necessary (see Figure 41).

Figure 41. UV light configuration

To analyze the data, a generalized linear mixed model fitted with a logit link function was used with subject level as a random effect. Data analysis was executed with proc GLIMMIX of SAS (Version 9.4 TS Level 1M1 SAS Institute Inc., Cary, NC) using Newton-Raphson with ridging as the optimization technique. An initial model suggested that demographic factors (e.g., sex, age, handedness, etc.) yielded no evidence of significance. As a result, they were not included in the final model, which included geometry (chevron style and round style) and force differential (even distribution Style "A" and abrupt change Style "B"). Pairwise comparisons were conducted using Tukey adjustments. Results are presented as least square means (LSMEAN) and standard error mean (SE) with a significance level of $\alpha = 0.05$.

5.4.2 Results of Study 2

5.4.2.1 Participant Demographics

One hundred and thirty-seven participants were recruited for the study. A single data set was removed after a subject indicated that it was her second time participating. Another was removed after listing no experience with aseptic presentation, despite the fact that screening criteria clearly indicated it to be a requirement for participation. Six data sets were automatically removed by the statistics software due to missing demographic information in the initial model. As such, statistical analysis of the data included a total of 129 completed data sets. Males (n=19) ranged in age from 25-51 (SD=8.12) and females (n=110) from 21-57 years old (Standard Deviation (SD)=8.44). Reported occupations of the test population included: Certified Nursing Assistants (CAN or CENA), Certified Surgical Technologists (CST), Surgical Technologists (ST), Emergency Medical Technicians (EMT), Licensed Practical Nurse (LPN), Registered Nurse (RN), Physical Therapists (PT), Paramedics, Phlebotomists, RN students, and Nursing

students. Participants averaged 5.1 years of experience in aseptic technique, ranging from 5 months to 36 years (SD=7.41). They had an average of 6.8 years of experience as healthcare professionals, ranging from 6 months - 35 years (SD=7.17).

5.4.2.2 Results-Study 2- Objective 1- Effect of Seal Geometry on Contact with Non-sterile Surfaces

Data analysis indicates a significant main effect of geometry (round vs. chevron) (P =0.0108); whereby the probability of contact with non-sterile surfaces during transfer for the rounded geometry was LSMEANS ± SE: 35%±2% compared to that of the chevron, which was 42%±3% (see Figure 42).

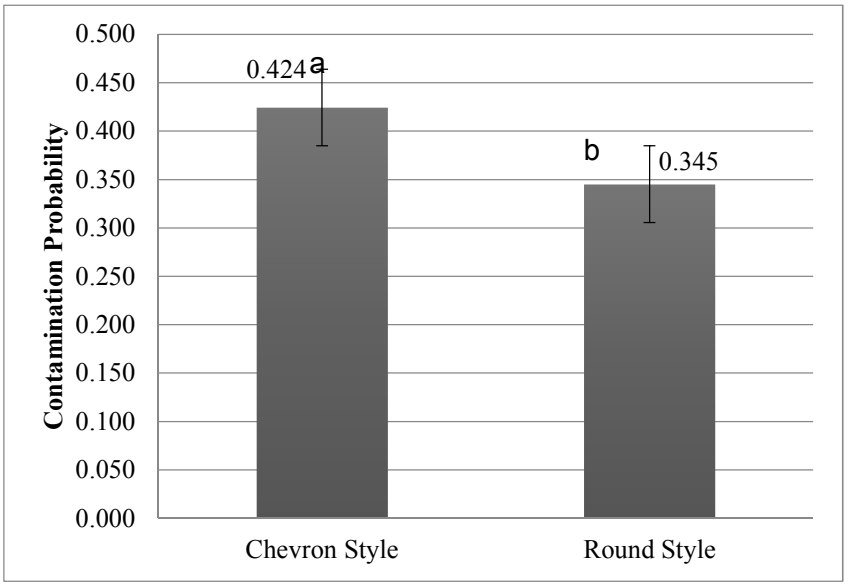


Figure 42. Estimated probability of contamination based on geometry. Whiskers indicate error bars with standard errors. Letters indicate evidence of a significant difference between pouch treatments.

5.4.2.3 Results- Study 2- Objective 2- Effect of Peel Profile on Contact with Non-sterile Surfaces

Analysis of the data yielded no evidence of a significant effect of force differentials (P=0.1002) on the probability of contact with non-sterile surfaces during transfer; the probability of contamination for packages with an abrupt change (the "A Styles") was: LSMEANS ± SE: 41%±3% and for pouches with a smooth distribution (the "B Styles") 36%±2%. Similarly, there was no evidence of a significant interaction term when geometry*peel profile was investigated (P=0.6815) (see Figure 43).

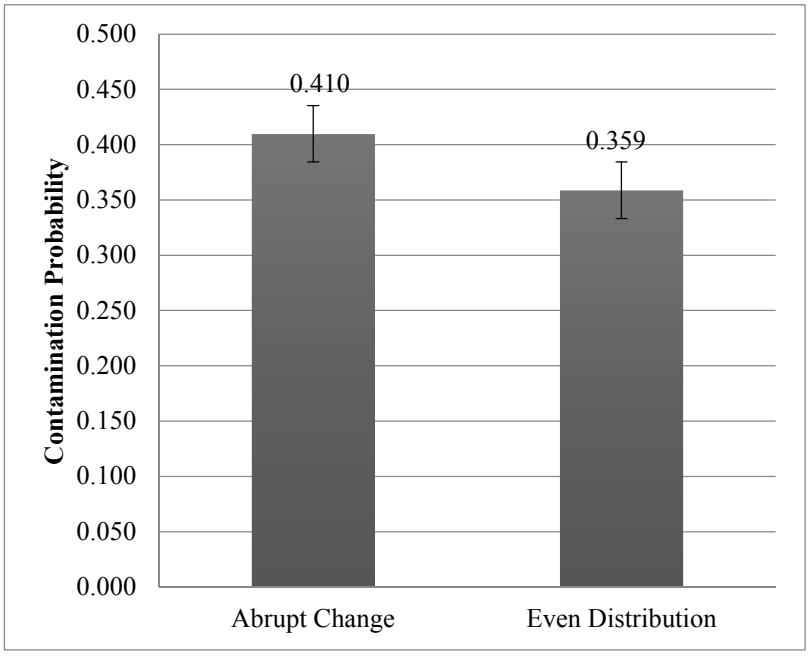


Figure 43. Estimates probability of contamination based on force differential. Whiskers indicate error bars with standard errors.

Despite the fact that statistical analysis yielded no evidence of a significant effect of peel profiles (trials comprised of A Styles compared with trials comprised of B Styles) on rates of contact with non-sterile surfaces, trends in data were consistent across both geometries (round and chevron). Specifically, the profiles with the addition of the seal bar, the abrupt transitions, or

"A Styles," tended to have higher rates of contact than those with smooth transitions, or the "B Styles." The rounded pouches with abrupt transitions yielded a higher average rate of contact of LSMEANS ± SE: 36%±3% compared to treatments with the same geometry (rounded) that had smooth transitions (LSMEANS ± SE: 33%±3%). This same pattern held for the chevron geometry; transfers from chevrons with an abrupt transition yielded LSMEANS ± SE: 46%±3% compared to the chevron with smooth transitions which resulted in a rate of contact of LSMEANS ± SE: 39%±3%. That said, though the general trend (abrupt treatments yielding higher rates of contact within each geometry than its smooth counter-part) was consistent, analysis did not yield evidence of significance (P=0.1002). The trend is visible when conducting pairwise comparisons between all four treatments (see Figure 44).

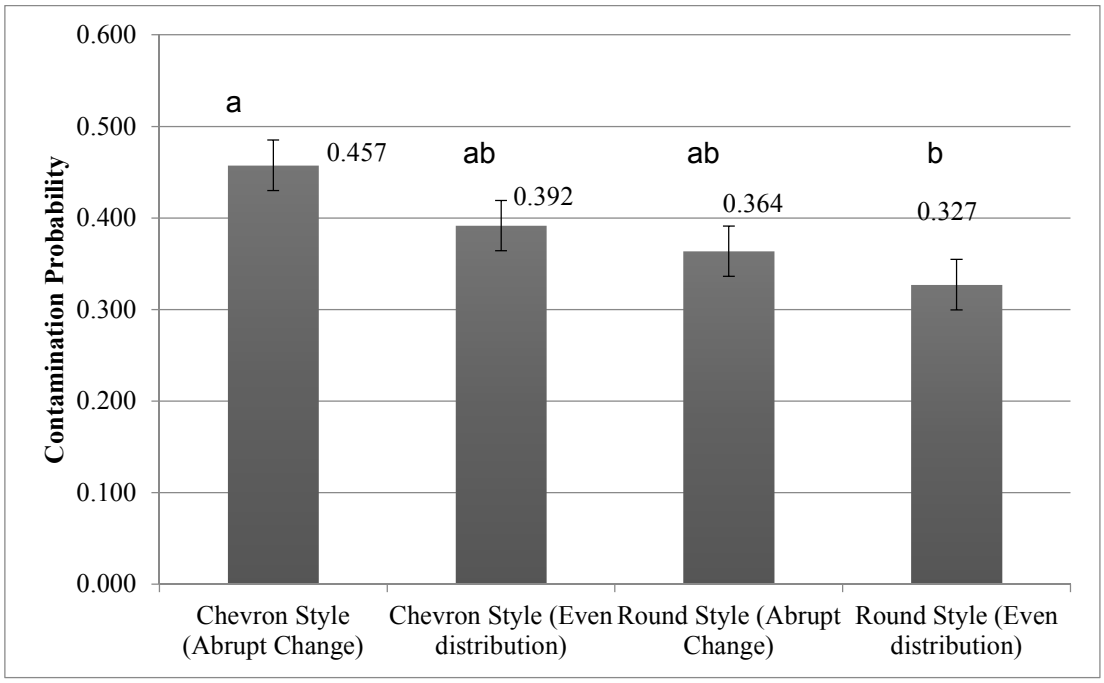


Figure 44. Estimated probability of contamination for all treatments. Whiskers indicate error bars with standard errors. Letters indicate evidence of a significant difference between pouch treatments.

5.4.3 Discussion

Our study is among the first to objectively investigate the relationship between peel geometries, the forces that result from those geometries, and, subsequently contact between a medical device and non-sterile surfaces during aseptic presentation. The limited literature available suggests that increasing peel width corresponds with increasing levels of force required to separate the two substrates. This was supported by our first study, which found that A Styles resulted in significantly higher forces than B Styles (see Figure 40), which were designed to have fewer differentials in the peel width (see Figure 36 and Figure 37) that was being separated as users opened packages. The available literature, combined with these findings, led us to hypothesize that peel profiles crafted to create abrupt transitions in force (and verified to induce higher forces as measured with our load cell unit, the "A Style," would result in a "jerking motion" during opening, enhancing the likelihood of contact with non-sterile surfaces during sterile transfer.

Study two employed a low-fidelity simulation to objectively evaluate this hypothesis. Although no statistically significant difference was evident when peel profiles (Styles A vs B) were compared, both style A treatments (abrupt transitions) resulted in larger rates of contact than their style B counter parts (smooth transitions). There are several reasons why these findings might not present a clear signal.

In contrast to the rigid trays studied by de la Fuente (2013) and Canty et al. (2012) where the dominant hand actively pulls the lid from the tray, in flexible pouches both hands are active which creates variations in the angle of opening (Liebmann et al., 2012). Differences between peel patterns (abrupt change vs. even distribution) might not be readily apparent for several reasons. Larger opening forces, lack of familiarity with this odd design, and the large size of the

pouch all gave participants difficulty. Additionally, it is quite possible that participants adjusted their peel path in an attempt to ease the work required for successful opening. This would be consistent with the de la Fuente (2013) work, which suggested that participants follow an optimal peel path where the seal width is minimum to enable a smooth and relatively easy opening. He hypothesized that, during opening, the user interacts with the package in an iterative feedback loop, allowing for adjustment of peel angles and path to in order to find the opening behaviors that require the least amount of effort.

One result that was somewhat curious to us was the finding related to seal geometry. Specifically, items presented from packages with rounded geometries were significantly less likely to make contact with non-sterile surfaces than those presented from chevrons ($P = 0.0108$; LSMEANS ± SE: 35%±2% vs. LSMEANS ± SE: 42%±3%, respectively).

To explore this further, we looked back to the Matlab plots (See Figure 37 and Figure 38) where the developed code calculated the width of the peel being separated as participants moved through the peel path. The fact that the rounded geometries resulted in significantly lower rates of contact with non-sterile surfaces than their chevron counterparts was counter to our hypothesis of abrupt transitions based on the established relationship between the width being peeled and the force required suggests that other factors are in play.

Other work that we have conducted using this methodology suggests that the curling of the materials used to construct the pouches significantly impacts rates of contact. Therefore, we calculated the surface area of the material above the seal for both treatments, postulating that increased area outside of the seal might present an opportunity for material curling. To investigate the differences in surface area above the seal, we superimposed the CAD drawings and used Matlab to calculate the "free area" above the seal for both the chevron geometry and

the rounded geometry. The free surface area above the chevron seal was calculated to be 192.4 cm (75.7592 in) while the round style was smaller, at 161.3 cm (63.5168 in) (see Figure 45).

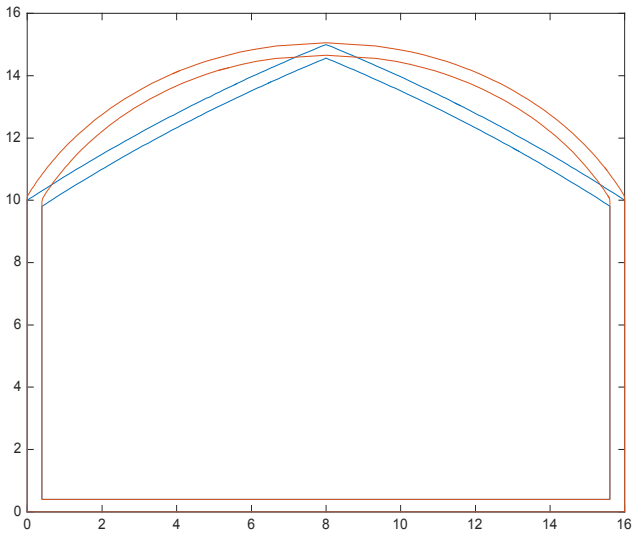


Figure 45. Chevron style vs. round style geometries

Understanding the importance of design factors such as peel forces and seal geometry and given the increasing application of human factors and usability in the medical packaging industry, mathematically modeling the optimal "peel path" by finding the path which has the smallest peel width at any given point in opening is a useful tool.

5.5 Limitations

The author acknowledges that the size of pouch chosen, although commercially available, is very large. Similarly, because the study was focused on how package design facilitates or hinders transfer to the sterile field, a mock device with a simple and consistent profile that was affordable and would readily provide evidence of contact was utilized. As such, factors specific to the devices, such as weight, flexibility of device and complexity of profile, which undoubtedly have the potential to impact transfer success, need to be studied. Since the instructions were to

grab the pouch at the top center in order to induce the abrupt change in force relevant in some trials, participants sometimes repositioned their hands in order to find the right angle to open the package using less force. Recruiting more participants would increase statistical power required to understand this behavior.

Future studies should investigate the impact of different seal geometries and their role in contamination rates during aseptic presentation and the effect of those designs in user's opening behavior. Also, it would be worthwhile to investigate opening angles and chevron angles and their role in package handling and contamination rates.

CHAPTER VI

CONCLUSIONS AND FUTURE WORK

6.1 Conclusions

Four broad objectives, driven by needs identified that were germane to the pouches used for medical devices, drove the work presented herein.

1. To evaluate how package design features (inward curl, outward curl, tab design compared to a traditional, commercial pouch design) affect the likelihood of a device contacting non-sterile surfaces (the package or the hands of the provider).

2. To characterize how aseptic technique (traditional vs. a modified approach) contributes to the likelihood of contact between medical devices and non-sterile surfaces during aseptic transfer.

3. To develop a prototyping methodology capable of rapidly prototyping pouch designs with varying peel geometries using existing equipment.

4. To evaluate how peel geometry (using pouches created with the new prototyping method) impact rates of contact between transferred devices and non-sterile surfaces.

Results of these studies add to a limited body of work suggesting that packaging design features and the opening approach of the providers that handle packaging to present medical devices represents an important factor for study.

To enable empirically framed studies which investigate this imperative objectively into the future, we proposed and validated an innovative methodology that can be utilized to create a myriad of seal shapes. These shapes can either be employed to carefully investigate the seal performance, or incorporated into pouch designs to investigate whole package performance. Additionally, the new method will enable manufacturers more latitude with regard to creative pouch designs.

With the increasing application of human factors and focus on user centered designs in the medical packaging industry, it is important to recognize the contribution of design factors and opening techniques in user experience by facilitating aseptic transfer, potentially minimizing the likelihood of a contaminated medical device being used in a sterile procedure.

6.2 Future Work

Given the industrial and regulatory trends of moving towards a more user-centered approach to the design process, future work should more deeply investigate the impact of seal geometries on the likelihood of contact between sterile and non-sterile surfaces. This study found round vs. chevron seal geometries yielded significantly different levels of contact between sterile surfaces with non-sterile surfaces, which was unexpected. Hence, it would be important to understand what types of creative designs could reduce contact between sterile devices with non-sterile surfaces.

Studies on package seal geometry and opening forces conducted in this report raised the question of whether the angle used by the healthcare professional during the opening process would impact the likelihood of contact between sterile devices with non-sterile surfaces and whether small gripping areas could have an effect on opening forces. As a result, investigating the effect of opening angles on the contact between sterile and non-sterile surfaces as well as the effect of gripping areas on opening forces would add more information to the process of designing medical packages that facilitate the opening and transfer of sterile contents onto the sterile field.

Although the results of the study of high force differentials leading to a jerking motion yielded no significant evidence on the likelihood of contact between sterile devices and non-sterile surfaces, a pattern was evident that evenly distributed forces resulted in lower probability

of contact. As a result, objectively investigating contamination rates based on opening area (center vs. corner) would fill a gap of knowledge that suggests opening location would impact rates of contact. This work would become increasingly important if future researchers investigate novel seal geometries, expanding beyond the industry-standard chevron.

This study was executed in a simplified environment, without the stresses of the operating room, and the simulated medical devices do not necessarily represent those used today. As a result, investigating the effect of medical device in opening behavior under more realistic circumstances would be ideal to understand its effects on contamination rates.

APPENDICES

APPENDIX A Consent forms and flyers

Title: Reducing levels of contamination through package redesign and opening technique

Principal Investigators:
Dr. Laura Bix, School of Packaging, Michigan State University 517-355-4556
Dr. Tamara Bush, Mechanical Engineering Department, Michigan State University 517-353-9544

Secondary investigator:
Paula Perez, Grad. Student, Michigan State University, 517-775-9505

To participate in this research you must:

- be at least 18 years old
- have no known history of skin condition (e.g. eczema, latex allergy, etc.)
- have a history of employment as a healthcare professional with experience in aseptic presentation to sterile fields or be a healthcare student who has had practical experience with aseptic technique
- be willing to be videotaped presenting devices to a simulated sterile field

Purpose of the research:
You are being asked to participate in a research study, which investigates the effect of two factors on device contamination: (1) medical pouch design and (2) opening technique. The experiment will take no more than one hour to complete. By doing this research, we hope to develop packaging which eliminates contamination by making the process of opening and dispensing devices easier for health care professionals.

What you will do:
We will ask you to fill out some basic demographic information (age, gender, etc.) and information about your work history.

We will ask you to wear a pair of gloves and a lab coat (to help protect your clothes from the coating that will be applied to packages which simulates contamination). We will video tape you while you open pouches/packages and transfer the devices inside (tongue depressors) to a table in front of you. We will be asked you to open a total of twenty-four packages and change your gloves between each trial.

All pouches and gloves will be coated in Glitterbug®, which will serve as our simulated contaminant. The Glitterbug cream is not visible unless ultra violet light is shined on it. Glitterbug cream is meant to be used directly on the skin as a lotion and is frequently used to teach proper technique for hand-washing. This substance will not be placed directly on your skin in this experiment.

After you have opened each pouch and presented the contents, we will analyze the tongue depressors to determine if any traces of contaminant are visible. From these experiments we

hope to develop better packaging that helps health care professionals transfer the medical devices within them without contacting non-sterile surfaces.

Benefit
Although there is no direct benefit to you for participating in this research, it is our hope that the data gathered can be used to understand the interface between healthcare professionals and packaging in order to create designs that will facilitate presentation of contents to the sterile field.

Risk
The Glitterbug cream may cause irritation in small segments of the population or staining of clothing. To minimize this risk, Glitterbug will not be applied directly to the skin, but to gloves and packages that that you interact with. To minimize the risk of staining, we ask that participants wear a lab coat. We will be taping the sterile transfers and recording whether or not devices were transferred sterilely. It is possible that you could be identified while opening. To minimize the likelihood of this occurring, written data is only being tracked by subject number, even the research team cannot tie results to a specific individual. Additionally, we will make every attempt to record only the opening process (faces will not be included in the video). In the event that you move and your face is included, it will be obscured post-hoc.

Privacy & confidentiality
Your confidentiality will be protected to the maximum extent allowable by law. All information about subjects will be tied to a subject number and you will not be identifiable by name (even to the research team). Information collected during this study will be stored in a password protected computer in room 159 of the Packaging Building or in 114 of the same building. Research records will be accessible only to authorized researchers and members of MSU HRPP (Human Research Protection Program) at MSU. Occasionally, publications ask for raw data sets associated with published work. In the event that these are requested, they would be furnished to the journal (de-identified). Records will be kept for a minimum of three years after the closing date of the project.

Your rights to participate
Participation is voluntary. Refusal to participate will involve no penalty or loss of benefits to which you are otherwise entitled. You may discontinue participation at any time without penalty or loss of benefits to which you are otherwise entitled. You may change your mind at any time and withdraw. You may choose not to answer specific questions or to stop participating at any time.

As part of this research study, all subjects are required to be videotaped. However, you have an option of allowing your video tape for public viewing in presentations of the study results or not. If you agree that your video tape may be used for public viewing, we will give you a yellow or green sticker, if not, you will be given a red sticker. The sticker will be attached to your lab coat during all research activities. Video tapes not used for presentations will be destroyed upon completion of the data analysis.

Costs and Compensation
There is no cost for being in this study. In exchange for your participation, you will be given $40 cash.

The right to get help if injured
If you are injured as a result of your participation in this research project, Michigan State University will assist you in obtaining emergency care, if necessary, for your research related injuries. If you have insurance for medical care, your insurance carrier will be billed in the ordinary manner. As with any medical insurance, any costs that are not covered or in excess of what are paid by your insurance, including deductibles, will be your responsibility. The University's policy is not to provide financial compensation for lost wages, disability, pain or discomfort, unless required by law to do so. This does not mean that you are giving up any legal rights you may have. You may contact *Dr. Laura Bix*, MSU, 517-355-4556, ext. 153 or Tony Trier 989-860-6346 with any questions or to report an injury.

Contact Information
If you have concerns or questions about this study, such as scientific issues, how to do any part of it, or to report an injury, please contact the researcher, Dr. Laura Bix, Laura Bix 517-355-4556; 153 Packaging Building East Lansing MI 48824 bixlaura@msu.edu.

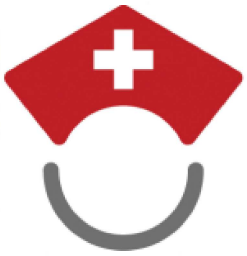
If you have questions or concerns about your role and rights as a research participant, would like to obtain information or offer input, or would like to register a complaint about this study, you may contact, anonymously if you wish, the Michigan State University's Human Research Protection Program at 517-355-2180, Fax 517-432-4503, or e-mail irb@ora.msu.edu or regular mail at Olds Hall, 408 West Circle Drive #207, MSU, East Lansing, MI 48824.

Documentation of Informed Consent
I voluntarily agree to allow the researchers to use my video footage taken during the course of the experiment for educational and conference presentation(s) relating to the research results.

☐ Yes ☐ No Initials_____

Your signature below means that you voluntarily agree to participate in this research study.

_____ _____
Signature Date
You will be given a copy of this form to keep.



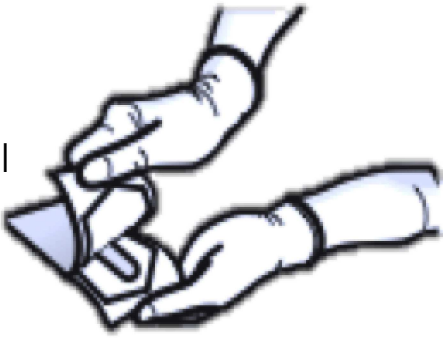
PARTICIPANTS NEEDED FOR A RESEARCH STUDY AT MSU SCHOOL OF PACKAGING

To Participate:

- ✓ Be 18 years or older.
- ✓ have a history of employment as a healthcare professional and have experience on aseptic presentation
- ✓ Have no history of skin condition (e.g. latex allergy, eczema, etc.
- ✓ Be willing to be video recorded.

You will be asked to:

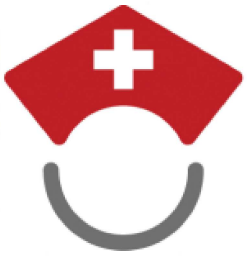
Put on a pair of gloves and a lab coat (provided by the research team). We will then ask you to present packages into a simulated sterile field (this will be filmed). Experiment takes 45 min!



For your participation in this study, subjects will be paid

$40 CASH.

Schedule an appointment with Paula Perez, the PhD student on charge of performing the study. **: (517)-775-9505, e-mail: perezper@msu.edu**



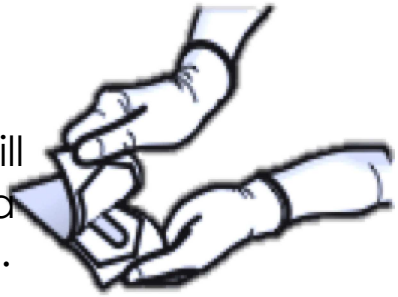
PARTICIPANTS NEEDED FOR A RESEARCH STUDY AT MSU SCHOOL OF PACKAGING

MICHIGAN STATE

To Participate:

- ✓ Be 18 years or older.
- ✓ have a history of employment as a healthcare professional and have experience on aseptic presentation
- ✓ Have no history of skin condition (e.g. latex allergy, eczema, etc.
- ✓ Be willing to be video recorded.

You will be asked to:



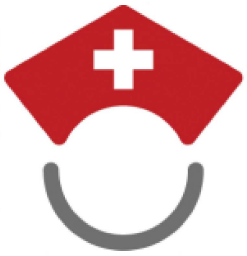
Put on a pair of gloves and a lab coat (provided by the research team). We will then ask you to present packages into a simulated sterile field (this will be filmed). Experiment takes 45 min!

For your participation in this study, subjects will be paid $40 cash.

Schedule an appointment with Paula Perez, the PhD student on charge of performing the study **: (517)-775-9505, e-mail:** perezper@msu.edu

Location: Sparrow Center for Research and Innovation.

Subjects are allowed to participate during NON-WORKING HOURS only.

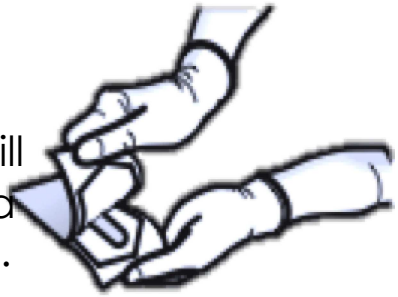


PARTICIPANTS NEEDED FOR A RESEARCH STUDY AT MSU SCHOOL OF PACKAGING

To Participate:

- ✓ Be 18 years or older.
- ✓ have a history of employment as a healthcare professional and have experience on aseptic presentation
- ✓ Have no history of skin condition (e.g. latex allergy, eczema, etc.
- ✓ Be willing to be video recorded.

You will be asked to:



Put on a pair of gloves and a lab coat (provided by the research team). We will then ask you to present packages into a simulated sterile field (this will be filmed). Experiment takes 45 min!

For your participation in this study, subjects will be paid $40 cash.

Schedule an appointment with Paula Perez, the PhD student on charge of performing the study **: (517)-775-9505, e-mail:** perezper@msu.edu

Location: Baker College

APPENDIX B Demographic information and data collections sheets

Demographic Information

A. General

1. Subject #_____
2. Age _____
3. Sex: ☐ Female
   ☐ Male
   ☐_____
4. Profession: ☐ Nurse
   ☐ RN
   ☐ RNFA
   ☐LPN
   ☐CNA
   ☐_____
   ☐Certify Surgical Technologist (CST)
   ☐Certify Surgical First Assistant (CSFA)
   ☐xs_____
   ☐Doctor
   ☐General Practitioner
   ☐Specialist

B. Education

1. Highest level completed: ☐High school
   ☐ Associate
   ☐Bachelor
   ☐Graduate
   ☐Other: _____

C. Experience

1. Years of experience in nursing or any healthcare related field:_____
2. Years of experience on aseptic technique: _____

3. Work setting _____

Data Collection Sheet

Subject #: _____

Handedness: ☐Left ☐Right ☐Ambidextrous

Seal Geometry

Pouch Treatment	Contamination: Circle: Yes / No				Comments
	Side 1		Side 2		
GEO1G1 1	YES	NO	YES	NO	
GEO1E1 2	YES	NO	YES	NO	
GEO2E1 3	YES	NO	YES	NO	
GEO1E2 4	YES	NO	YES	NO	
GEO1G2 5	YES	NO	YES	NO	
GEO2G2 6	YES	NO	YES	NO	
GEO2G1 7	YES	NO	YES	NO	

GEO2E2 8	YES	NO	YES	NO	

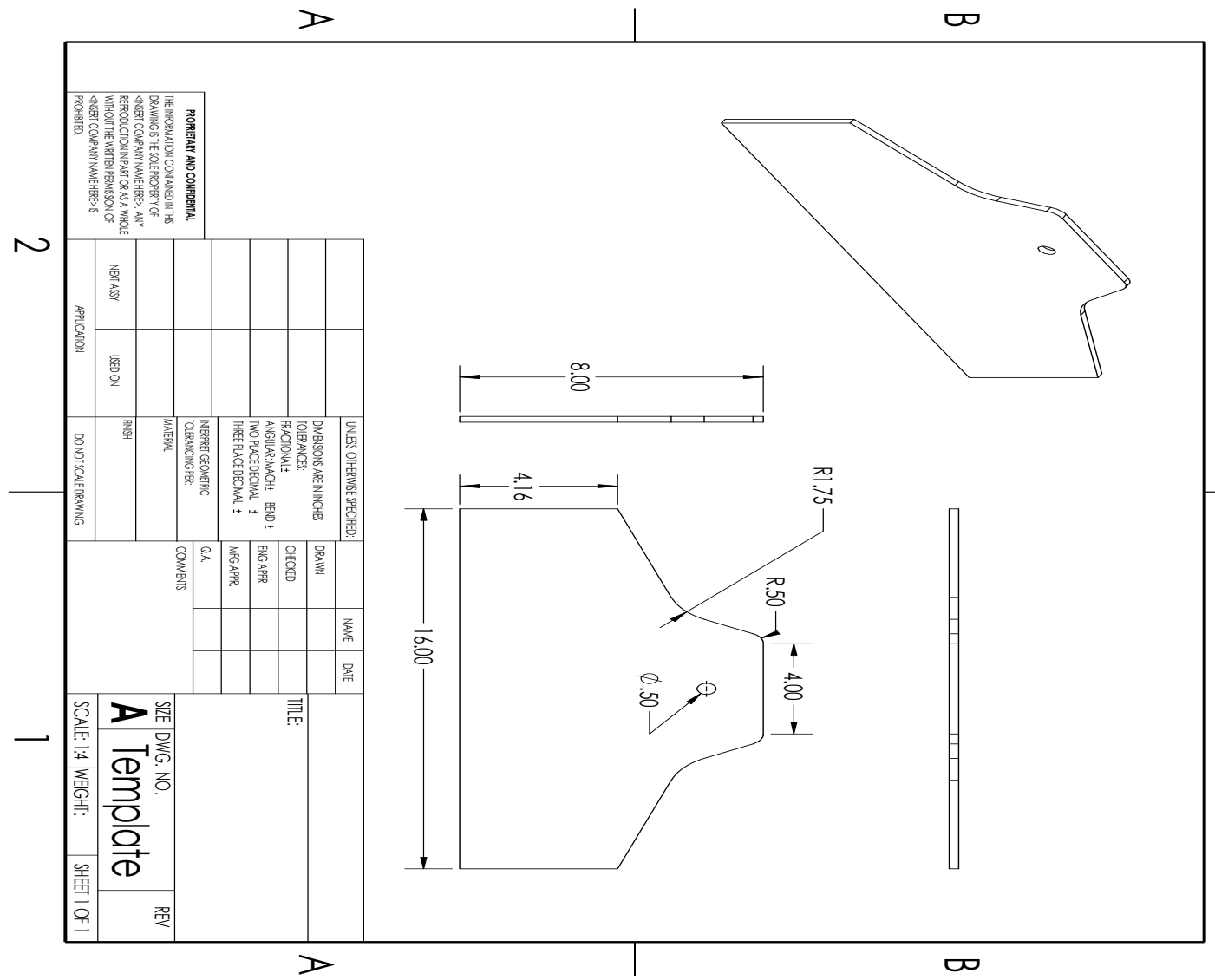
Untrained

Pouch Treatment	**Contamination: Circle: Yes / No**				**Comments**
	Side 1		**Side 2**		
IN1 9	YES	NO	YES	NO	
STD2 10	YES	NO	YES	NO	
IN1 11	YES	NO	YES	NO	
MOD1 12	YES	NO	YES	NO	
STD1 13	YES	NO	YES	NO	
OUT2 14	YES	NO	YES	NO	
IN2 15	YES	NO	YES	NO	
MOD2 16	YES	NO	YES	NO	

Trained

Pouch Treatment	Contamination: Circle: Yes / No				Comments
	Side 1		Side 2		
STD2 9	YES	NO	YES	NO	
OUT1 10	YES	NO	YES	NO	
IN1 11	YES	NO	YES	NO	
STD1 12	YES	NO	YES	NO	
MOD1 13	YES	NO	YES	NO	
OUT2 14	YES	NO	YES	NO	
IN2 15	YES	NO	YES	NO	
MOD2 16	YES	NO	YES	NO	

APPENDIX C Tab template drawing



APPENDIX D Matlab codes

Chevron style-Even distribution

```
function [sw]= TriangleFunction(y)

if (y>5.19)
    sw = 0;
end
if (4.75<y)&&(y<=5.19)
    sw = 2*(sqrt(45^2-(y+35.26)^2)-19.71);
end
if (0<y)&&(y<=4.75)
    sw = 2*(sqrt(45^2-(y+35.26)^2)-19.71)-2*(sqrt(44.61^2-(y+35.26)^2)-19.72);
end
if (0<y)&&(y<=0)
    sw = 16-2*(sqrt(44.61^2-(y+35.26)^2)-19.72);
end
if (-9.81<y)&&(y<=0)
    sw = 16-15.21;
end
if (y<= -9.81)
    sw = 0;
end


Y = (-9.81:0.01:5.20);

W = repelem(0,length(Y));
for i=1:length(Y)
   % determine width of larger triangle W=[width,y-coordinate]
   W(i) = TriangleFunction(Y(i));
   % subtract width of smaller trriangle if possible
end


Ynew = Y + 9.81;
subplot (2,2,4)
plot(W,Ynew)
xlim ([0 20])
ylim ([0 20])
title('Seal Width Graph')
xlabel('Width of Sealant (in)')
ylabel('Height (in)')

[v,T,vT]=xlsread('GEOTG.xlsx');
x=v(:,1);y=v(:,2);
subplot (2,2,3)
xlim ([0 20])
ylim ([0 20])
plot(x,y)
title('Chevron Style-Even Distribution')
xlabel('Width of Sealant (in)')
ylabel('Height  (in)')
```

Chevron style-Abrupt change

```
function [sw]= TriangleFunctionE(y)

if (y>5.19)
```

```
    sw = 0;
end
if (4.75<y)&&(y<=5.19)
    sw = 2*(sqrt(45^2-(y+35.26)^2)-19.71);
end
if (1.96<y)&&(y<=4.75)
    sw = 2*(sqrt(45^2-(y+35.26)^2)-19.71)-2*(sqrt(44.61^2-(y+35.26)^2)-19.72);
end
if (1.57<y)&&(y<=1.96)
    sw    =    2*(sqrt(45^2-(y+35.26)^2)-19.71)-2*(sqrt(44.61^2-(y+35.26)^2)-
19.72)+7.5;
end
if (0<y)&&(y<=1.57)
    sw = 2*(sqrt(45^2-(y+35.26)^2)-19.71)-2*(sqrt(44.61^2-(y+35.26)^2)-19.72);
end
if (0<y)&&(y<=0)
    sw = 16-2*(sqrt(44.61^2-(y+35.26)^2)-19.72);
end
if (-9.81<y)&&(y<=0)
    sw = 16-15.21;
end
if (y<= -9.81)
    sw = 0;
end


Y = (-9.81:0.01:5.20);

W = repelem(0,length(Y));
for i=1:length(Y)
   % determine width of larger triangle W=[width,y-coordinate]
   W(i) = TriangleFunctionE(Y(i));
   % subtract width of smaller trriangle if possible
end

Ynew = Y + 9.81;
subplot (2,2,4)
plot(W,Ynew)
xlim ([0 20])
ylim ([0 20])
title('Seal Width Graph')
xlabel('Width of Sealant (in)')
ylabel('Height (in)')
[v,T,vT]=xlsread('GEOT.xlsx');

x=v(:,1);y=v(:,2);
xlim ([0 20])
ylim ([0 20])
subplot (2,2,3)
plot(x,y)
xlabel('Width of Sealant (in)')
ylabel('Height (in)')
```

Round style-Even distribution

```
function [sw]= RoundFunction(y)

if (y>5.02)
    sw = 0;
end
if (4.63<y)&&(y<=5.02)
    sw = 2*sqrt(8.96^2-(y+3.93)^2);
```

```
end
if (0.09<y)&(y<=4.63)
    sw = (2*sqrt(8.96^2-(y+3.93)^2))-(2*sqrt(8.56^2-(y+3.93)^2));
end
if (0<y)&(y<=0.09)
    sw = 16-(2*sqrt(8.56^2-(y+3.93)^2));
end
if (-10.03<y)&(y<=0)
    sw = 16-15.21;
end
if (y<= -10.03)
    sw = 0;
end


Y = (-10.03:0.01:5.03);

W = repelem(0,length(Y));
for i=1:length(Y)
   % determine width of larger triangle W=[width,y-coordinate]
   W(i) = RoundFunction(Y(i));
   % subtract width of smaller trriangle if possible
end

Ynew = Y + 10.03
figure
subplot (2,2,2)
plot(W,Ynew)
xlim ([0 20])
ylim ([0 20])
title('Seal Width Graph')
xlabel('Width of Sealant (in)')
ylabel('Height (in)')

[v,T,vT]=xlsread('GEORG.xlsx');
x=v(:,1);y=v(:,2);
subplot(2,2,1)
plot(x,y)
[v,T,vT]=xlsread('GEORG.xlsx');
x=v(:,1);y=v(:,2);
subplot(2,2,1)
xlim ([0 20])
ylim ([0 20])
plot(x,y)
title('Round Style-Even Distribution')
xlabel('Width of Sealant (in)')
ylabel('Height (in)')
```

Round style-Abrupt change

```
function [sw]= RoundFunctionE(y)

if (y>5.02)
    sw = 0;
end
if (4.63<y)&&(y<=5.02)
    sw = 2*sqrt(8.96^2-(y+3.93)^2);
end
if (1.74<y)&&(y<=4.63)
    sw = (2*sqrt(8.96^2-(y+3.93)^2))-(2*sqrt(8.56^2-(y+3.93)^2));
end
```

```
if (1.35<y)&&(y<=1.74)
    sw = (2*sqrt(8.96^2-(y+3.93)^2))-(2*sqrt(8.56^2-(y+3.93)^2))+7.5;
end
if (0.09<y)&&(y<=1.35)
    sw = (2*sqrt(8.96^2-(y+3.93)^2))-(2*sqrt(8.56^2-(y+3.93)^2));
end
if (0<y)&&(y<=0.09)
    sw = 16-(2*sqrt(8.56^2-(y+3.93)^2));
end
if (-10.03<y)&&(y<=0)
    sw = 16-15.21;
end
if (y<= -10.03)
    sw = 0;
end


Y = (-10.03:0.01:5.03);

W = repelem(0,length(Y));
for i=1:length(Y)
   % determine width of larger triangle W=[width,y-coordinate]
   W(i) = RoundFunctionE(Y(i));
   % subtract width of smaller trriangle if possible
end

Ynew = Y + 10.03
figure
subplot (2,2,2)
plot(W,Ynew)
xlim ([0 20])
ylim ([0 20])
title('Seal Width Graph')
xlabel('Width of Sealant (in)')
ylabel('Height (in)')

[v,T,vT]=xlsread('GEOR.xlsx');
x=v(:,1);y=v(:,2);
xlim ([0 20])
ylim ([0 20])
subplot (2,2,1)
plot(x,y)
xlabel('Width of Sealant (in)')
ylabel('Height (in)')
title('Round Style-Abrupt Change')
```

BIBLIOGRAPHY

BIBLIOGRAPHY

AAMI Human Factors Engineering Committee. (2009). *Human factors engineering - design of medical devices*.

Allegranzi, B., & Pittet, D. (2009). Role of hand hygiene in healthcare-associated infection prevention. *Journal of Hospital Infection*, *73*(4), 305–315. http://doi.org/10.1016/j.jhin.2009.04.019

AORN Recommended Practices Committee. (2006a). Recommended practices for maintaining a sterile field. *AORN Journal*, *83*(2), 402–416. http://doi.org/10.1016/S0001-2092(06)60171-3

AORN Recommended Practices Committee. (2006b). Recommended Practices for the Care and Handling of Specimens in the Perioperative Environment. *AORN Journal*, *83*(3), 688–699. http://doi.org/10.1016/S0001-2092(06)60197-X

AST Education and Professional Standards Committee. (2008a). *AST Standards of Practice for Handling and Care of Surgical Specimens*.

AST Education and Professional Standards Committee. (2008b). *AST Standards of Practice for Surgical Drapes Introduction*.

ASTM. (2017). F17 - Standard Terminology Relating to Primary Barrier Packaging. http://doi.org/10.1520/C0071-12.2

Berns, T. (1981). The handling of consumer packaging. *Applied Ergonomics*, *12*(3), 153–161. http://doi.org/10.1016/0003-6870(81)90004-1

Bhalla, A., Pultz, N. J., Gries, D. M., Ray, A. J., Eckstein, E. C., Aron, D. C., & Donskey, C. J. (2004). Acquisition of Nosocomial Pathogens on Hands After Contact With Environmental Surfaces Near Hospitalized Patients. *Infection Control and Hospital Epidemiology*, *25*(2), 164–167.

Bix, L., & de la Fuente, J. (2010). Medical Device Packaging in Yam (ed.) Wiley Encyclopedia of Packaging Technology (3rd ed., pp. 713–727). Hoboken, NJ, USA: John Wiley & Sons, Inc. http://doi.org/10.1002/9780470541395.ch12

Boyce, J. M., & Pittet, D. (2002). Guideline for Hand Hygiene in Health-Care Settings. Recommendations of the Healthcare Infection Control Practices Advisory Committee and the HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force. *Morbidity and Mortality Weekly Report*, *51*(RR-16), 1–45. http://doi.org/10.1086/503164

Cai, J. (2012). *Perceptions of medical device packaging used by operating room personnel*. (Master Thesis). Michigan State University, East Lansing, MI.

Canty, L. A., Lewis, R., & Yoxall, A. (2012). Investigating openability of rigid plastic containers with peelable lids: The link between human strength and grip and opening forces. *Proceedings of the Institution of Mechanical Engineers, Part C: Journal of Mechanical Engineering Science*, *227*(5), 1056–1068. http://doi.org/10.1177/0954406212457729

Carayon, P., Wetterneck, T. B., Rivera-Rodriguez, A. J., Hundt, A. S., Peter Hoonakker, Holden, R., & Gurses, A. P. (2013). Human factors systems approach to healthcare quality and patient safety, *45*(1), 14–25. http://doi.org/10.1016/j.apergo.2013.04.023

Centers for Disease Control and Prevention. (2003). Guidelines for Environmental Infection Control in Health-Care Facilities. Retrieved from https://www.cdc.gov/infectioncontrol/pdf/guidelines/environmental-guidelines.pdf%5Cnhttp://www.cdc.gov/hicpac/pubs.html

Centers for Disease Control and Prevention. (2016). *National and State Healthcare Associated Infections Progress Report*.

Chen, K.-H., Chen, L.-R., & Wang, Y.-K. (2014). Contamination of medical charts: an important source of potential infection in hospitals. *PloS One*, *9*(2), e78512. http://doi.org/10.1371/journal.pone.0078512

Chun, H. K., Kim, K. M., & Park, H. R. (2015). Effects of hand hygiene education and individual feedback on hand hygiene behaviour, MRSA acquisition rate and MRSA colonization pressure among intensive care unit nurses. *International Journal of Nursing Practice*, *21*(6), 709–715. http://doi.org/10.1111/ijn.12288

Collins, A. S. (2008). Preventing Health Care - Associated Infections. In R. G. Hughes (Ed.), *Patient Safety and Quality: An Evidence-Based Handbook for Nurses: Vol. 2* (pp. 547–575). Rockville, MD: U.S. Department of Health and Human Services. Retrieved from https://archive.ahrq.gov/professionals/clinicians-providers/resources/nursing/resources/nurseshdbk/nurseshdbk.pdf

Crick, B., Chua, S., Canty, J., & McCullough, K. (2008). Potential for contamination of orthopaedic implants using individually wrapped screws. *ANZ Journal of Surgery*, *78*(4), 266–268. http://doi.org/10.1111/j.1445-2197.2008.04433.x

Dalstrom, D. J. (2008). Time-Dependent Contamination of Opened Sterile Operating-Room Trays. *The Journal of Bone and Joint Surgery (American)*, *90*(5), 1022. http://doi.org/10.2106/JBJS.G.00689

de la Fuente, J. (2013). *Usability of Tabs in Semi-Rigid Packaging*. (PhD Dissertation). Michigan State University, East Lansing, MI.

De Oliveira, A. C., & Gama, C. S. (2014). Evaluation of surgical glove integrity during surgery in a Brazilian teaching hospital. *American Journal of Infection Control*, *42*(10), 1093–1096. http://doi.org/10.1016/j.ajic.2014.06.021

Dietze, B., Rath, A., Wendt, C., & Martiny, H. (2001). Survival of MRSA on sterile goods

packaging. *Journal of Hospital Infection*, *49*, 255–261. http://doi.org/10.1053/jhin.2001.1094

Ducel, G., Fabry, J., Nicolle, L., Girard, R., Perraud, M., Pruss, A., … Vanhems, P. (2002). *Prevention of hospital-acquired infections*. *World Health Organization*. Retrieved from http://www.who.int/csr/resources/publications/drugresist/en/whocdscsreph200212.pdf?ua=1

Emerson, C. B., Eyzaguirre, L. M., Albrecht, J. S., Comer, C., Harris, A. D., & Furuno, J. P. (2012). Healthcare-Associated Infection and Hospital Readmission. *Infection Control and Hospital Epidemiology*, *33*(6), 539–544. http://doi.org/10.1086/665725.Healthcare-Associated

European Commission. (2010). *Medical Devices: Guidance document - Classification of medical devices*.

European Commission. (2017). Medical Devices Regulation (MDR) Final approved, *2017*(178), 1–566.

Fagon, J.-Y., Chastre, J., Hance, A. J., Montravers, P., Novara, A., & Gibert, C. (1993). Nosocomial Pneumonia in Ventilated Patients: A Cohort Study Evaluating Attributable Mortality and Hospital Stay. *The American Journal of Medicine*, *94*(March), 281–288.

Fallis, A. . (2013). AST Standards of Practice for Creating the Sterile Field. *Journal of Chemical Information and Modeling*, *53*(9), 1689–1699. http://doi.org/10.1017/CBO9781107415324.004

FDA. (2011). Applying Human Factors and Usability Engineering to Optimize Medical Device Design. *FDA Guidance for Industry*, (301), 1–37. http://doi.org/10.1177/1071181311551334

Food and Drug Administration. (2014). Is the Product a Medical Device? http://doi.org/10.1016/0026-0576(95)93949-0

Food and Drug Administration Amendments Act of 2007 (2007). United States. Retrieved from https://www.gpo.gov/fdsys/pkg/PLAW-110publ85/pdf/PLAW-110publ85.pdf

Fortunato, N. (2000). *Berry & Kohn's Operating Room Technique* (9th ed.). St. Louis: Mosby.

Gastmeier, P., Stamm-Balderjahn, S., Hansen, S., Nitzschke-Tiemann, F., Zuschneid, I., Groneberg, K., & Ruden, H. (2005). How outbreaks can contribute to prevention of nosocomial infection: analysis of 1,022 outbreaks. *Infection Control and Hospital Epidemiology*, *26*(4), 357–361. Retrieved from http://www.jstor.org/stable/10.1086/502552

Ghantoji, S. S., Sail, K., Lairson, D. R., & Dupont, H. L. (2010). Economic healthcare costs of Clostridium difficile infection : a systematic review. *Journal of Hospital Infection*, *74*(4), 309–318. http://doi.org/10.1016/j.jhin.2009.10.016

Gibson, J. (1977). The Theory of Affordances. In Perceiving, Acting, and Knowing : Toward an

Ecological Psychology, Shaw R, Bransford (eds). Hillsdale, NJ, USA: Lawrence Erlbaum Associates.

Gibson, J. (1979). *The Ecological Approach to Visual Perception*. Boston, MA, USA: Houghton Mifflin.

Goetz, W. (2003). Curl in Multilayer Pa / Pe Film. *Tappi*, *77*(4), 148.

Greco, G., Shi, W., Michler, R. E., Meltzer, D. O., Ailawadi, G., Hohmann, S. F., … Gardner, T. J. (2015). Costs associated with health care-associated infections in cardiac surgery. *Journal of the American College of Cardiology*, *65*(1), 15–23. http://doi.org/10.1016/j.jacc.2014.09.079

Guo, Y. P., Wong, P. M., Li, Y., & Or, P. P. L. (2012). Is double-gloving really protective? A comparison between the glove perforation rate among perioperative nurses with single and double gloves during surgery. *American Journal of Surgery*, *204*(2), 210–215. http://doi.org/10.1016/j.amjsurg.2011.08.017

Han, C. D., Kim, J., Moon, S. H., Lee, B. H., Kwon, H. M., & Park, K. K. (2013). A Randomized Prospective Study of Glove Perforation in Orthopaedic Surgery: Is a Thick Glove More Effective? *Journal of Arthroplasty*, *28*(10), 1878–1881. http://doi.org/10.1016/j.arth.2013.05.007

Hopper, W. R., & Moss, R. (2010). Common Breaks in Sterile Technique: Clinical Perspectives and Perioperative Implications. *AORN Journal*, *91*(3), 350–367. http://doi.org/10.1016/j.aorn.2009.09.027

Jencks, S. F., Williams, M. V., & Coleman, E. A. (2009). Rehospitalizations among Patients in the Medicare Fee-for-Service Program. *New England Journal of Medicine*, *360*(14), 1418–1428. http://doi.org/10.1056/NEJMsa0803563

Johnson, N. B., Hayes, L. D., Brown, K., Hoo, E. C., & Ethier, K. A. (2014). *CDC National Health Report : Leading Causes of Morbidity and Mortality and Associated Behavioral Risk and Protective Factors — United States , 2005 – 2013* (Vol. 63).

Kassarjian, O. (2011). *Effects of hole size, pressure differential and secondary packaging on microbial ingress of sterile medical device trays*. (PhD Dissertation). Michigan State University, East Lansing, MI.

Keates, S., & Clarkson, J. (2004). *Countering design exclusion, an introduction to inclusive design*. London: Springer-Verlag London Ltd.

Kramer, A., Schwebke, I., & Kampf, G. (2006). How long do nosocomial pathogens persist on inanimate surfaces? A systematic review. *BMC Infectious Diseases*, *6*(130), 1–8. http://doi.org/10.1186/1471-2334-6-130

Kyne, L., Hamel, M. B., Polavaram, R., & Kelly, C. P. (2002). Health Care Costs and Mortality Associated with Nosocomial Diarrhea Due to Clostridium dificile. *Clinical Infectious*

Diseases, *34*(3), 346–353. Retrieved from http://www.jstor.org/stable/4461866

Liebmann, A., Schreib, I., Schlözer, R. E., & Majschak, J.-P. (2012). Practical Case Studies: Easy Opening for Consumer-Friendly, Peelable Packaging. *Journal of Adhesion Science and Technology*, *26*(20–21), 2437–2448. http://doi.org/10.1163/156856111X599544

Magill, S. S., Edwards, J. R., Bamberg, W., Beldavs, Z. G., Dumyati, G., Kainer, M. A., … Fridkin, S. K. (2014). Multistate Point-Prevalence Survey of Health Care–Associated Infections. *New England Journal of Medicine*, *370*(13), 1198–1208. http://doi.org/10.1056/NEJMoa1306801

Minckley, B. (1969). A Study of Practices of Handling and Opening Suture Packets in the Operating Room. *Nursing Research*, *18*(3), 267–270.

Moghimi, B. N., Kim, S., & Park, S. (2016). Assessing of Flexible Packaging Integrity: Using the Aerosolization Bacteria. *Packaging Technology and Science*, *29*, 135–143. http://doi.org/10.1002/pts

Morris, B. A. (2003). Reducing Curl in Multilayer Blown Film: Experimental Results, Model Development, and Application to a Cereal Liner Film. *Journal of Plastic Film and Sheeting*, *19*(1), 31–54. http://doi.org/10.1177/875608703038032

Morris, B. A. (2016). *The Science and Technology of Flexible Packaging: Multilayer Films from Resin and Process to End Use* (1st ed.). Cambridge, MA: Elsevier.

Narins, B. (2013). *The Gale Encyclopedia of Nursing and Allied Health*. (J. Longe, Ed.) (3rd ed.). Detroit, Mich: Gale. Retrieved from http://msulibraries.summon.serialssolutions.com/2.0.0/link/0/eLvHCXMwhV1LSwMxEB4KIogefOITc_JWyWub5CjiqjehiuClJJvk1G4FPXjytzcTs9vWS48hISGvmfkm800ABL-lw38ywevYxMiYE5Vuog5VZWVjopAuGmsc-vc_7vhbLV_Gqh5A9ydil8QRYf2sgMbeeZEUGR8Z9jsWBg2kkTJ4qp-LuZ4lcdK9UqnM50rAwS

Norman, D. A. (1988). *The Psychology of Everyday Things*. New York: Basic Books.

Norman, D. A. (1999). Affordance, Conventions, and Design. Interactions. *Interactions*, 38–43. http://doi.org/https://doi.org/10.1145/301153.301168

Norman, D. A. (2013). *The Design of Everyday Things* (Revised an). New York: Basic Books.

Oake, N., Taljaard, M., van Walraven, C., Wilson, K., Roth, V., & Forster, A. J. (2010). The Effect of Hospital-Acquired Clostridium difficile Infection on In-Hospital Mortality. *Archives of Internal Medicine*, *170*(20), 1804–1810.

Parush, A., Parush, D., & Ilan, R. (2017). *Human Factors in Healthcare: A Field Guide to Continuous Improvement*. (R. M. Baecker, Ed.)*Synthesis lectures on assistive, rehabilitative, and health-preserving technologies #11*. Morgan & Claypool. http://doi.org/10.2200/S00753ED1V01Y201701ARH011

Percival, S. L., Suleman, L., Vuotto, C., & Donelli, G. (2015). Healthcare-associated infections, medical devices and biofilms: risk, tolerance and control. *Journal of Medical Microbiology*, *64*, 323–334. http://doi.org/10.1099/jmm.0.000032

Phillips, N. (2016). *Berry & Kohn's Operating Room Technique - E-Book*. Elsevier Health Sciences. Retrieved from https://books.google.com/books?id=xSOKCwAAQBAJ

Plester, D. W. (1973). The Effects of Radiation Sterilization on Plastics. *Sterilization Technology*, 141–52.

Pokrywka, M., & Byers, K. (2013). Traffic in the Operating Room: A Review of Factors Influencing Air Flow and Surgical Wound Contamination. *Infectious Disorders - Drug Targets*, *13*, 156–61.

Rello, J., Ollendorf, D. A., Oster, G., Vera-Llonsch, M., Bellm, L., Redman, R., & Kollef, M. H. (2002). Epidemiology and Outcomes of Ventilator-Associated Pneumonia in a Large US Database. *CHEST*, *122*(6), 2115–2121. http://doi.org/10.1378/chest.122.6.2115

Richards, M. J., Edwards, J. R., Culver, D. H., & Gaynes, R. P. (2000). Nosocomial infections in combined medical-surgical intensive care units in the United States. *Infection Control and Hospital Epidemiology*, *21*(8), 510–515. Retrieved from http://www.jstor.org/stable/10.1086/501795

Rowlands, J., Yeager, M. P., Beach, M., Patel, H. M., Huysman, B. C., & Loftus, R. W. (2017). American Journal of Infection Control Video observation to map hand contact and bacterial transmission in operating rooms. *American Journal of Infection Control*, *42*(7), 698–701. http://doi.org/10.1016/j.ajic.2014.02.021

Rubin, R. J., Harrington, C. A., Poon, A., Dietrich, K., Greene, J. A., & Moiduddin, A. (1999). The Economic Impact of Staphylococcus aureus Infection in New York City Hospitals. *Emerging Infectious Diseases*, *5*(1), 9–17.

Rutala, W. A., & Weber, D. J. (2008). *Guideline for Disinfection and Sterilization in Healthcare Facilities*.

Safdar, N., Crnich, C. J., & Maki, D. G. (2001). Nosocomial Infections in the Intensive Care Unit Associated with Invasive Medical Devices. *Current Infectious Disease Reports*, *3*, 487–495. http://doi.org/10.1007/s11908-001-0085-5

Schultz, J. K. (1978). Is flipping supplies an acceptable practice in the OR? *AORN Journal*, *28*(5), 912–916.

Scott, R. D. (2009). *The direct medical costs of healthcare-associated infections in U.S. hospitals and the benefits of prevention*. Retrieved from http://www.cdc.gov/hai/pdfs/hai/scott_costpaper.pdf

Severin, J. E. (2006). *The Effect of Pressure Differential on Microbial Penetration of a Sterile Medical Device Tray*. Michigan State University, East Lansing MI.

Severin, J., Bix, L., Linz, J., Gilliland, D., & Lockhart, H. (2007). A New Methodology for Whole-Package Microbial Challenge Testing for Medical Device Trays. *Journal of Testing and Evaluation*, *35*(4), 100869. http://doi.org/10.1520/JTE100869

Sherman, M. (1998). *Medical device packaging handbook*. (M. Sherman, Ed.) (2nd ed.). New York: Marcel Dekker, Inc.

Siegel, J. D., Rhinehart, E., Jackson, M., Chiarello, L., & the Healthcare Infection Control Practices Advisory Committee. (2007). *2007 Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Health Care Settings*. Retrieved from http://www.cdc.gov/infectioncontrol/pdf/guidelines/isolation-guidelines.pdf

Simmers, L. M. (2008). *Introduction to Health Science Technology* (2nd ed.). Clifton Park, NY: Cengage.

Smith, E. B., Raphael, I. J., Maltenfort, M. G., Honsawek, S., Dolan, K., & Younkins, E. A. (2013). The effect of laminar air flow and door openings on operating room contamination. *Journal of Arthroplasty*, *28*(9), 1482–1485. http://doi.org/10.1016/j.arth.2013.06.012

Smith, G., Vindenes, F., Keijzers, G., & Rando, A. (2009). Potential for infection in orthopaedic practice due to individually packaged screws. *Injury*, *40*(2), 163–165. http://doi.org/10.1016/j.injury.2008.06.024

Song, X., Bartlett, J. G., Speck, K., Naegeli, A., Carroll, K., & Perl, T. M. (2008). Rising Economic Impact of Clostridium difficile – Associated Disease in Adult Hospitalized Patient Population. *Infection Control and Hospital Epidemiology*, *29*(9), 823–828. http://doi.org/10.1086/588756

Spruce, L. (2017). Back to Basics: Sterile Technique. *AORN Journal*, *105*(5), 478–487. http://doi.org/10.1016/j.aorn.2017.02.014

Stone, P. W. (2009). Economic burden of healthcare-associated infections: an American perspective. *Expert Review of Pharmacoeconomics & Outcomes Research*, *9*(5), 417–422. http://doi.org/10.1586/erp.09.53.Economic

Technical Committee ISO/TC 198. (2006a). *ISO 11607-1: Packaging for terminally sterilized medical devices—Part 1: Requirements for materials, sterile barrier systems, and packaging systems*.

Technical Committee ISO/TC 198. (2006b). *ISO 11607-2 Packaging for terminally sterilized medical devices—Part 2: Validation requirements for forming, sealing and assembly processes*.

Trier, T. (2013). The role of medical device pouches as a source of indirect contamination and potential infection contributor. In *Healthcare Packaging Immersion Event (HcPIE)*. East Lansing, MI.

Trier, T. (2016). *Aseptic Technique and Packaging: A Study of Potential Contamination Pathways During the Usage of Sterile Packaging in an Operating Room Context*. (PhD Dissertation). Michigan State University, East Lansing, MI.

Trier, T., Bello, N., Bush, T. R., & Bix, L. (2014). The role of packaging size on contamination rates during simulated presentation to a sterile field. *PLoS ONE*, *9*(7). http://doi.org/10.1371/journal.pone.0100414

Trier, T. M. (2012). *An Investigation of the Effect of Pouch Size on Hand Repositioning and Contamination of a Medical Device*. (Master Thesis). Michigan State University, East Lansing, MI.

Umit, U. M., Sina, M., Ferhat, Y., Yasemin, P., Meltem, K., & Ozdemir, A. A. (2014). Surgeon behavior and knowledge on hand scrub and skin antisepsis in the operating room. *Journal of Surgical Education*, *71*(2), 241–245. http://doi.org/10.1016/j.jsurg.2013.08.003

von Eiff, C., Jansen, B., Kohnen, W., & Becker, K. (2005). Infections Associated with Medical Devices Pathogenesis , Management and Prophylaxis. *Drugs*, *65*(2), 179–214.

Weinstein, R. A. (1991). Epidemiology and control of nosocomial infections in adult intensive care units. *The American Journal of Medicine*, *91*(Supplement 3B), 179S–184S. Retrieved from http://www.sciencedirect.com/science/article/pii/0002934391903666%5Cnhttp://linkinghub.elsevier.com/retrieve/pii/0002934391903666%5Cnhttp://www.ncbi.nlm.nih.gov/pubmed/1928162

Wilcox, M. H., Cunniffe, J. G., Trundle, C., & Redpath, C. (1996). Financial burden of hospital-acquired difficile infection Clostridium. *Journal of Hospital Infection*, *34*, 23–30.

Winder, B. (2006). *The Design of Packaging Closures. In Packaging Closures and Sealing Systems*. (T. N. W. B, Ed.). Oxford, UK: Blackwell Publishing, Ltd.

Yambrach, F. (2010). Package-Integrity in the Sterile Disposable Healthcare Products in Yam (ed.)Wiley Encyclopedia of Packaging Technology (3rd ed., pp. 851–859). John Wiley & Sons, Inc. http://doi.org/10.1002/9780470541395.ch15