

Comparison of closed system transfer devices for turnaround time and ease of use

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Abstract

Objective/purpose: The primary purpose of this study was to compare three closed-system transfer devices with differing mechanical interfaces for their suitability for adoption into our daily practice. The secondary purpose was to use the results of this study to support the selection of one of the closed-system transfer devices, which would suit both the pharmacy and nursing staff at our institution, furthermore promoting the enculturation of international recommendations into our clinical practice.

Study design/methods: The hazardous drug preparation process was observed and timed continuously from the moment the technician started compounding until the finished product was handed to the designated checker by raising hands. A self-administered, structured questionnaire was used for data collection looking at ease of use of each of the devices from the perspective of pharmacy technicians and nurses. The questionnaire contained an open-ended 10-point Likert-type scale of eight domains.

Results/key findings: An improvement in the compounding efficiency of hazardous drugs using PhaSeal™ ($n = 46$), ChemoLock™ ($n = 45$), and EquaShield® II ($n = 45$), when compared respectively against the historical control ($n = 86$), was statistically significant ($p < 0.001$). However, no statistically significant difference among the different closed-system transfer devices for preparation of hazardous drugs was observed in our study ($p = 0.1$).

In terms of ease of use, there was no difference in preference for ChemoLock™ and Equashield® II among the pharmacy technicians with both scoring a mean score of 10 with regard to implementation. While PhaSeal™ scored a mean score of 7.2. Among the nursing staff there was a slight preference for ChemoLock™ over Equashield® II with a mean score of 9.2 and 9, respectively with regard to the recommended product, while PhaSeal™ scored a mean score of 7.4. Both nursing staff and pharmacy technicians had a preference ChemoLock™, with a mean score of 10 and 9.6, respectively in terms of how easy was each device/system to use and overall impression for pharmacy technicians. This was followed by Equashield® II with a mean score of 9.8 and 8.6, respectively and then PhaSeal™ with a mean score of 7.2 and 6.6, respectively. Pharmacy technicians felt there were more steps, packaging and clutter when using PhaSeal® in comparison to the other devices. With Equashield® II, the estimation of clutter was higher than that of ChemoLock™ despite the number of packages being within a similar range.

Conclusion/recommendations: Our study found that with experienced staff, compounding of hazardous drugs with closed-system transfer devices can be as efficient as or even more so than with the traditional needle and syringe method. With the lack of statistically significant difference among the different closed-system transfer devices studied, in addition to the cost, ease of use was one of the factors that decided the products applicability in our institution.

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Introduction

The effectiveness of the closed-system transfer device (CSTD) in reducing surface contamination of hazardous drugs (HDs) is well established, with many large studies validating its effectiveness.^{1–8} These devices are known to improve the protective performance of primary engineering controls and are regarded as supplemental to these controls, they do not replace the protection offered by primary engineering controls.^{9,10}

Numerous guidelines to reduce the risk of HD exposure to healthcare professionals have been suggested by various international organisations.^{11–16} The voluntary nature of these guidelines, together with institutional apathy, means that the implementation is rarely met with vigour or enthusiasm by healthcare institutions. In a recent survey by the American Society of Health-System Pharmacists (ASHP) of US hospital pharmacy directors concerning their procedures for handling HDs, only 19.0% had conducted exposure monitoring (e.g., air sampling, wipe sampling) in the past 12 months to assess employee exposure to hazardous agents, and only 28.4% had conducted a formal gap analysis to identify and resolve potential areas of concern in the handling of HDs.¹⁷

Re-evaluation of the risks of environmental exposure to HDs prompted a new general chapter, USP <800> Hazardous Drugs—Handling in Healthcare Settings, which mandates the use of CSTDs for the administration of HDs to patients, and also recommends utilization of CSTDs for drug compounding.¹⁸ The intent and scope of USP <800> are much broader than some of the requirements found in the previous USP <797>, especially for HDs. The use of CSTDs as an additional safeguard against HD exposure is also recommended by the Occupational Safety and Health Administration (OSHA).¹⁹ Although USP is a scientific nonprofit organization, its standards such as USP <800> are enforced by a variety of local, state, and federal regulatory agencies in the USA and are also followed worldwide. In addition, accrediting bodies such as The Joint Commission survey for compliance with USP compounding standards in hospitals that receive its accreditation worldwide.

Since the publication of the consultation document of USP <800> in 2014, together with heightened awareness of handling of HDs, there has been renewed interest for using CSTDs. A 2017 survey of US hospital pharmacy directors showed overall 64.9% of hospital use CSTD for safe handling of HDs. The use of CSTDs

increased from 41.0% of hospitals in 2011 and from 50.3% of hospitals in 2014.²⁰ Of the hospitals that use CSTDs, 95.1% use CSTDs during the preparation phase of HDs, and 82.9% use CSTDs during HDs administration.²⁰ Lack of administrative support and the belief that the devices are too complicated to implement, in addition to the cost, were cited as reasons cited for not employing CSTDs.²¹ There is also a preconception among pharmacy administration that the introduction of the CSTDs increases the turnaround time. This conundrum has resulted in reluctance to adopt a CSTD by many healthcare institutions worldwide.²²

It is inevitable that as a result of the USP <800> which comes into effect in 1 December 2019 the uptake of CSTDs during drug preparation by pharmacy technicians and during drug administration by nursing staff is likely to change, with more nursing departments having access to CSTDs. Thus, carrying out a collaborative evaluation of CSTDs by multidisciplinary teams, to explore the various individual organisations' specifications, will enable vigorous clinical practice before a specific product is chosen. The involvement of the end users e.g. Pharmacy Technicians and Oncology Nurses is imperative in this evaluation, as a collaborative approach can lead to an efficient and seamless process of reducing inventory cost, training time and avoid duplication of work in evaluation of the CSTDs by different stake holders.²¹

The National Institute for Occupational Safety and Health (NIOSH) defines a CSTD as a “drug transfer device that mechanically prohibits the transfer of environmental contaminants into the system and the escape of hazardous drug or vapour concentrations outside the system.”¹¹ Though CSTDs are approved medical devices, unlike medicinal products, they lack detailed information from regulatory agencies about the design, efficacy, and limitations of each product.¹⁰

Of the CSTDs available, there are three broad classifications.²³ The first is a full containment, diaphragm-based system, similar to the systems used by PhaSealTM (the innovator product), SmartSiteTM VialShield, Halo[®] and a second-generation product from ICU medical, ChemoLockTM. The second can be broadly classified as a compartmentalized-based device, such as Equashield[®] I/II where there is no external additional piece to the system. The third is referred to as the air-cleaning technology device, such as OnGuard[®]/Tevadaptor[®]. CSTDs can be further subclassified according to the basic types of mechanical interfaces a device can have within itself. PhaSealTM, Equashield

I and II[®] are examples of devices that use a membrane-to-membrane mechanism with a needle. ChemoLock[™] is a classic example of a needleless mechanism, which forms a common fluid/vapour channel, basically without the use of a needle.²³

The primary purpose of this study was to compare three CSTDs with differing mechanical interfaces for their suitability for adoption into our daily practice. The three CSTDs evaluated had Food and Drug Administration's (FDA) 510(k) clearance, plus 2012 ONB product code as well as Food and Drug Administration (FDA) patient administration (FPA) applications (product code FPA).²⁴ The secondary purpose was to use the results of this study to support the selection of one CSTD, which would suit both the pharmacy and nursing staff at our institution, and encourage the enculturation of international recommendations into clinical practice. The study received ethics approval from the Office of Research Affairs of the corporate organization (Proposal # 2161095; ORA/0933/37).

Methods

At our institution, approximately 75,000 doses of sterile parenteral HDs are prepared each year, through manual compounding and using chemotherapy compounding robots.²⁵ The bulk of the data collection was carried out in the cancer Ambulatory Infusion Centre (AIC), where approximately 50% of all the organizational HDs are prepared daily (>175/day), in Class II biological safety cabinets (BSC) biological safety cabinets (BSC) located in a negative pressure clean room. The remainder of the data collection was carried out in the paediatric AIC, where approximately 20% of all HDs are compounded, in satellite pharmacies where 20% are prepared, and in a central inpatient sterile preparation room where 10% are prepared.

Prior to conducting the study, the company representatives of each CSTD were invited to train the staff in the technique of using each device with didactic lectures followed by interactive sessions, and hands on demonstration. The competency of the staff in using the CSTD was confirmed by the representatives of each company. The samples were provided free of charge by the company representatives with the full knowledge that it would be compared with other CSTDs. No representative from the company participated in any stage of the data collection.

The primary investigator studied the previous methodology,²⁵ from our historical control and adopted the timing process based on that to reduce variability in timing. The same observer timed all infusions for each individual so there could be no observer variability. Observations for the historical control took place at

various times on six randomly selected days without notifying the selected staff members in advance. Pharmacy technicians with experience in the aseptic preparation of compounded sterile products were selected to participate in the study. All had completed annual aseptic training courses. Antineoplastic medication doses prepared in intravenous (IV) syringes, and chemotherapy IV bags were included in the evaluation.

For the experimental arm of our study, five experienced pharmacy technicians and four experienced nurses' trialled all three CSTDs. The five pharmacy technicians were timed when fully garbed with Personal Protective Equipment (PPE) during the preparation of the HDs inside the BSC, and the four nurses were timed, fully garbed with PPE during the administration of the HDs. The preparation process was observed and timed continuously from the moment the pharmacy technician started compounding until the finished product was handed to the designated product checker. The data collection took place over three weeks, with the first week allocated to the PhaSeal[™], the second to Equashield[®] II and the third to ChemoLock[™]. The times were recorded on a data sheet for that specific chemotherapy preparation/administration, and the pharmacy and nursing staff were asked to fill out the rest of the sheet after simulations had been completed.

A self-administered structured questionnaire, adapted from Kicenuik et al.²⁶ with the author's permission, and inclusive of a new section for nurses (Supplementary Appendices 1 and 2), was used for data collection for ease of use (EOU) of each of the devices. The questionnaire contained an open-ended 10-point Likert-type scale of eight domains, including demographic data, for both nursing staff and pharmacy technicians. The standardized questionnaire was rated on a Likert-type scale to produce numbers that could be easily interpreted. Thematic coding was not used to collate the qualitative responses, nor did we set a minimum threshold to determine if a product was easy to use. Rather we chose the highest value recorded on the Likert-type scale when choosing the EOU of the CSTDs. In addition, the staff were not aware of any threshold prior to participating in the study.

Before data coding and entry, co-investigators reviewed and checked each questionnaire for completion, accuracy, and consistency. Analysis of the data was carried out using the Statistical Package for Social Sciences (SPSS) version 20 software package. The primary statistical analysis was descriptive in nature and included interquartile range, and median, and standard deviation (SD). Box-Whisker plots were used to show overall patterns, with spacing between the different parts of the box to indicate the degree of spread, any skew in the data, and any outliers, which

were plotted as individual points. Secondary analysis was performed using nonparametric tests for independent samples, with the Mann–Whitney test for two-sided independent samples at the 5% significance level for the comparison of the three CSTDs and the control.

In the adult infusion centre, the focus was on two regimens-ABVD (doxorubicin, bleomycin, vinblastine, and dacarbazine) and EC (epirubicin and cyclophosphamide), which were chosen because they contained IV piggyback, IV push (bolus) preparations, and the vials were either in powder form or solution. To ensure we gained enough samples, and that pharmacy technicians got hands on experience in using the devices, we also made some single preparations utilizing the CSTDs. In the paediatric infusion centre, the variety of medications prepared was much smaller, so all the cytotoxic medications compounded during the study day, utilized the CSTDs. Each week the same medications, predominantly cytarabine, vincristine, and cyclophosphamide, were compounded in similar doses. The compounding process itself was timed by a third party, following the same process as used in the AIC. The same individual timed every preparation used in the trial so there could be no observer variability. We measured three different products in real time within the two pharmacies using predominantly the same medications and the same regimens to ensure comparability. We also used the same pharmacy technicians to increase the reliability, not only

of the preparation times, but also to add validity to opinions on each device.

Results

A total of 136 preparations were recorded, 45 for PhaSeal™, 46 for Equashield®II and 45 for ChemoLock™. These preparations were recorded per medication, and the medications were timed in seconds. Figure 1 shows the preparation time of the HDs utilizing the CSTDs with 50 percentile (median), first quartile (25 percentile) and third quartile (75 percentile). Results show there was no statistically significant difference amongst the three different CSTDs for preparations of HDs ($p=0.1$). Outliers are plotted as individual circles and extreme outliers are plotted as individual stars for the CSTDs tested in Figures 1 to 4.

Figures 2 to 4 show compounding of HDs using PhaSeal™ ($n=46$), ChemoLock™ ($n=45$), and Equashield®II ($n=45$) against the historical control ($n=86$). In every case the time difference of the preparation of the HDs using the CSTD against the historical control was statistically significant ($p < 0.001$). The median preparation time for the sterile compounding of HDs was 76 s utilizing Equashield®II (SD 120.32), 80 s using ChemoLock™ (SD 64.76), and 122 s using PhaSeal™ (SD 129.98). ChemoLock™ had a lower minimum and maximum timing than the other two

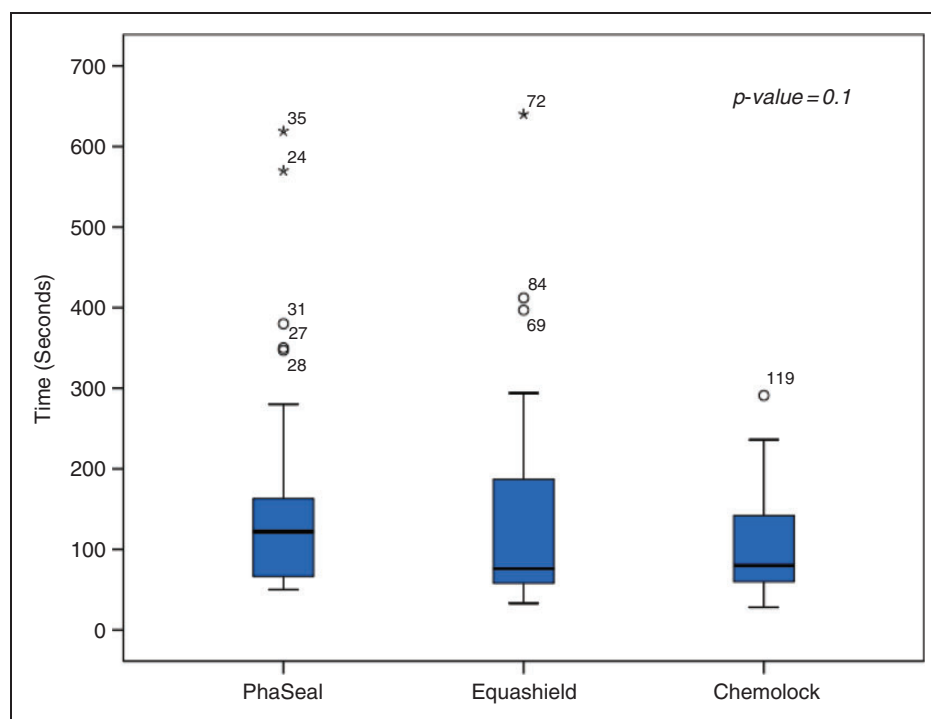


Figure 1. Box-whisker plot of compounding of HDs using different CSTDs ($n = 136$).

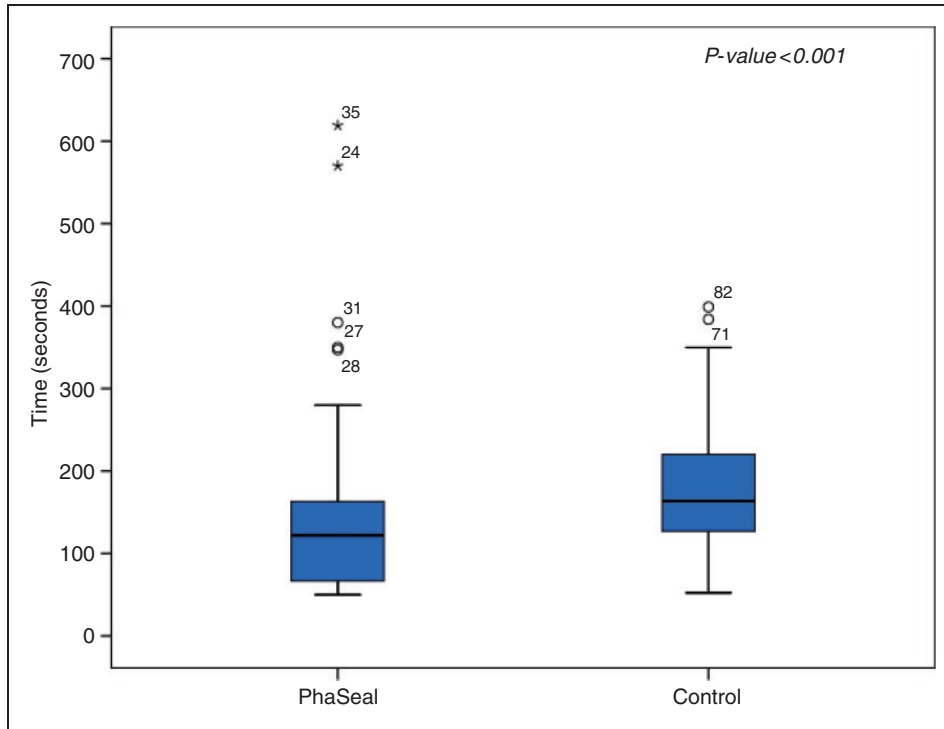


Figure 2. Box-Whisker of compounding of HDs using PhaSeal ($n = 46$) vs. control ($n = 86$).

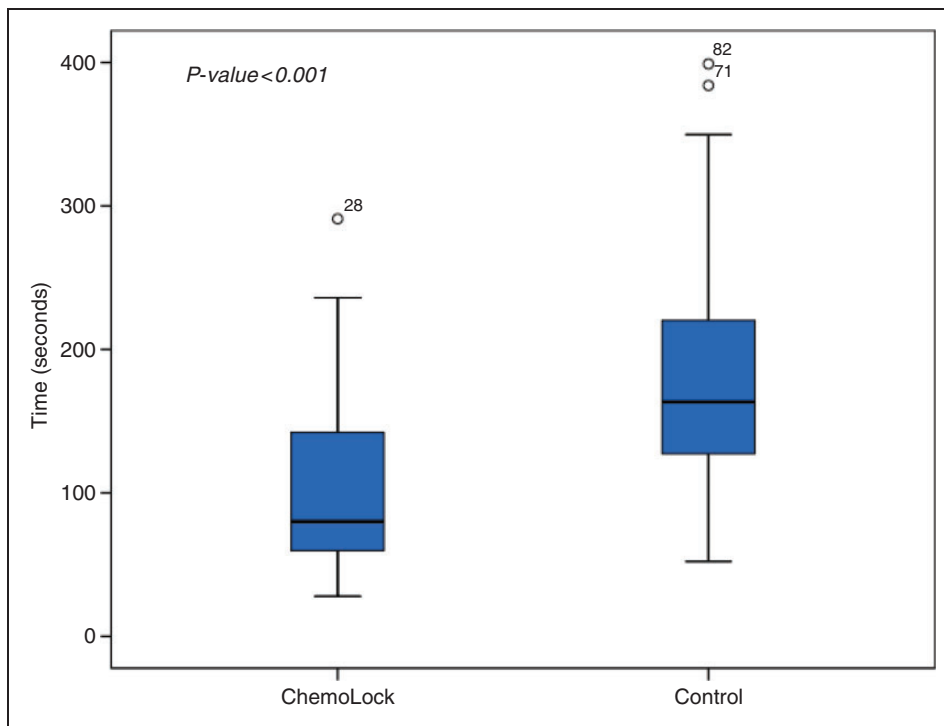


Figure 3. Box-Whisker of compounding of HDs using ChemoLock ($n = 45$) vs. control ($n = 86$).

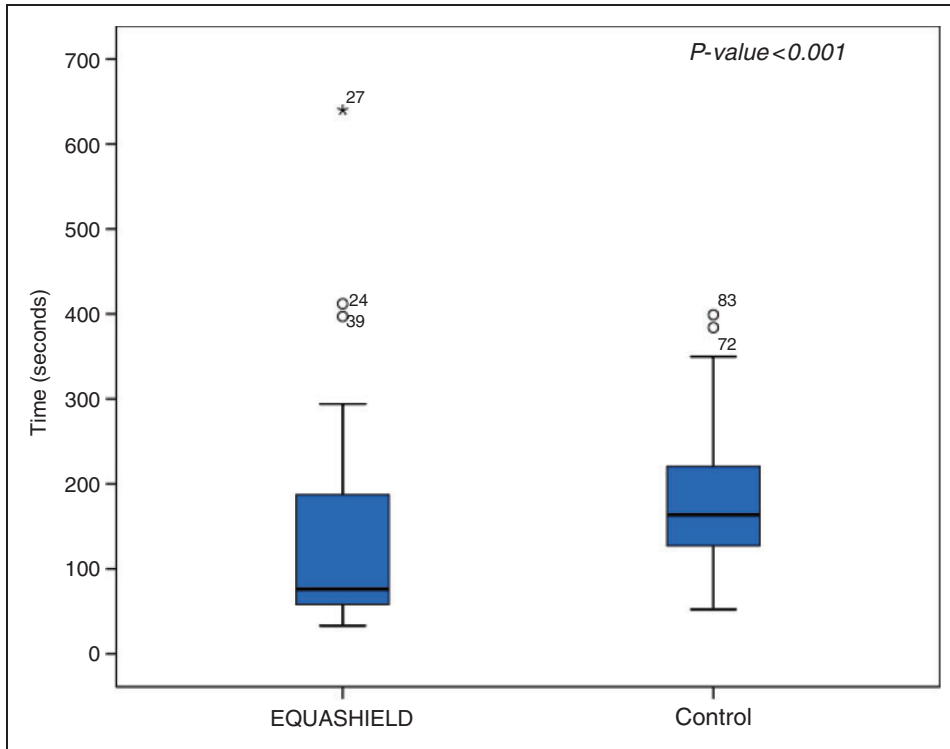


Figure 4. Box-Whisker of compounding of HDs using Equashield (N = 46) vs. control (N = 86).

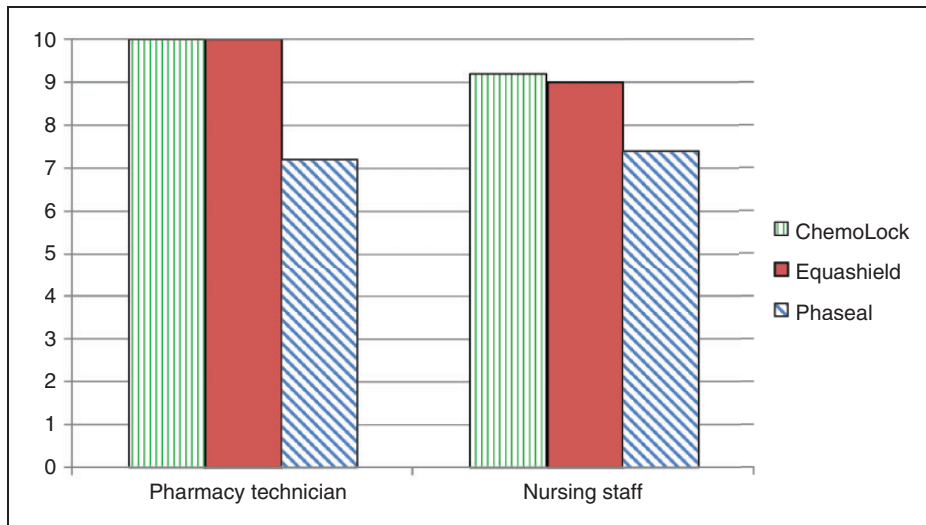


Figure 5. Mean values of the CSTD recommended by nursing staff/implementing by pharmacy technicians? 0: Bad; 10: Excellent.

products and only one outlier, the data were also much less spread out with this device.

Figure 5 shows the mean values recommended by nursing staff, and implementing of the CSTDs by pharmacy technicians. There was no difference in preference for ChemoLock™ and Equashield®II among the pharmacy technicians with both scoring a mean score of 10.

While PhaSeal™ scored a mean score of 7.2. Among the nursing staff there was a slight preference for ChemoLock™ over Equashield®II with a mean score of 9.2 and 9 respectively, while PhaSeal™ scored a mean score of 7.4.

Figure 6 shows nursing and pharmacy technicians' having a preference ChemoLock™, with a mean score

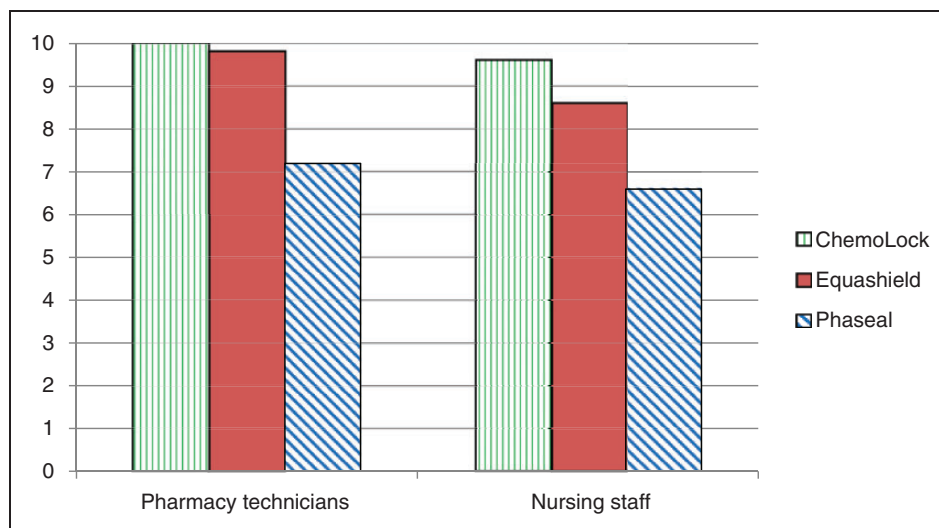


Figure 6. Mean values on how easy each device /system to use for nursing staff and overall impression of the CSTD for pharmacy technicians? 0: Bad; 10: Excellent.

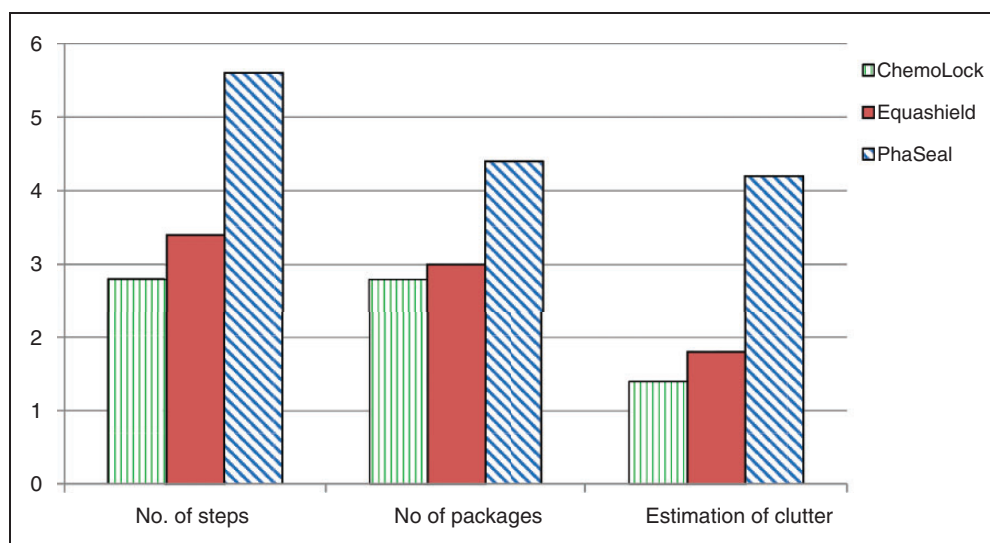


Figure 7. Mean values recorded from the Likert-type scale on factors affecting ease of use in pharmacy. Mean values recorded from the Likert-type scale.

of 10 and 9.6, respectively on how easy was each device/system to use for nursing staff, and overall impression of the CSTD for pharmacy technicians. This was followed by Equashield® II with a mean score of 9.8 and 8.6, respectively and then PhaSeal™ with a mean score of 7.2 and 6.6 respectively.

Figure 7 shows that the pharmacy technicians felt there were more steps, packaging and clutter when using PhaSeal® in comparison to the other devices. With Equashield® II, the estimation of clutter was higher than that of ChemoLock™ despite the

number of packages being within a similar range (two to three packages per compounding).

Discussion

Initially, the thought of pharmacy technicians having to juggle additional pieces of equipment for preparation of HDs was worrying; however, our study showed a statistically significant reduction in the median turnaround times of preparation of HDs using CSTDs, indicating it is more efficient and this is sound justification for

adopting the use of CSTDs into our practice. In fact, our study concurs with previous findings; that compounding with CSTDs can be as efficient as if not more efficient than compounding with the traditional needle and syringe method.²⁷

Although our results show variability in the time required for compounding using the three CSTDs evaluated, the lack of a statistically significant difference hindered the decision-making process. It would have been much easier to disregard a product that had a significantly negative impact on productivity compared to other CSTDs, making it a non-cost-effective/resource appropriate option. The differences in the mean preparation times and the number of outliers could be a reflection of how easily the product was to manipulate, the more outliers the greater variation in preparation time due to the number of pieces or variability of equipment needed.

EOU could be one of the factors that decided the products applicability especially if the costs of the CSTDs are competitive, as there is no significant difference between them when looking at efficiency. For the pharmacy technicians, the process of compounding can be impacted positively or negatively by packaging, clutter in the workspace, and adding or subtracting steps in an established process. We found that there were more steps when using the PhaSeal™ device in comparison to the other devices. With Equashield®II the estimation of clutter was higher than that of ChemoLock™ despite the number of packages being within a similar range. As reflected in the results, the additional steps required when utilizing the PhaSeal™ had a negative impact on the timings of the preparations. Others described more difficulty in learning how to use PhaSeal™ than other devices they tested, and the more numerous steps involved in operating the PhaSeal™ system, as an additional barrier to using this device.⁶

The technological advancements of CSTDs have led to improved design, and user-friendliness, giving them an advantage over the older generation CSTDs, which have neither changed in design or functionality since their conception. It is, therefore, not surprising that PhaSeal™, being the innovator CSTD, was perceived poorly in terms of EOU by both the nursing and pharmacy technicians. They indicated that the “push-turn-push” mechanism of PhaSeal™ was difficult to use at first. Other participants found PhaSeal™ more difficult to learn how to use, as well as having a greater number of steps.⁶

The three devices we studied had different safety mechanisms for ensuring the syringe couldn't be accidentally disengaged during compounding and administration. With Equashield®II, the syringe is bonded to the closed system and is purchased as a complete

package. Nurses, especially those with smaller hands, found the IV push administration very difficult to use as the ability to hold the plunger steady throughout administration was very tiring. Also because the closed system was already bonded to the syringe and the containment system used compartmentalisation, the syringes were much larger than those used to compound IV push medications normally.

Another attribute that varies between the three devices is the closing mechanism, and the risk it poses when administering HDs. Prior to the nurses beginning to push the HD via a syringe or start the infusion bag via an infusion pump, they need to know the connection is secure and there is no risk of leakage; this encourages confidence, and therefore products are often known by the mechanism they utilize for a secure connection. When using ChemoLock™, one nurse commented “I like the sound of the ‘click’, reassuring me that it's secure.” Another commented that the clicking noise is a positive attribute to the device, stating “it clicks on and off indicating good connection and release.” Equashield®II had two positive responses related to its closing mechanism, not specifically the “colour-to-colour, slide” alignment strategy, but that the equipment itself felt secure.

Those devices that utilize a “needle safe” approach rather than a “needle free” pose the risk that if the device malfunctions there is still a needle present and could cause needle stick injury. The ChemoLock™ does not involve any needles, increasing its safety for use, which is in line with many medical devices available today that are trying to reduce the use of needles, and thus, reduce the risk of needle stick injury. However, the mechanism behind the fluid flow, whether it involved a needle or was needle free, did not seem to have any impact on the participants' preference. In fact, there was no reference to any difference between the devices, and whether there was a needle inside the device did not impact on the pharmacy technicians' ability to manipulate the products as required. The two recommended systems utilized both fluid flow techniques; ChemoLock™ being a needle-free elastomeric double membrane system and Equashield®II a membrane to membrane with needle included.

There is a large variability in the manufacturers of HDs, which in turn means that the medication is often presented in different vial sizes with different neck specifications. We found it was difficult to connect both PhaSeal™ and Equashield®II devices securely to the vial neck of the Vinblastine used in the ABVD preparation, and this impacted negatively the pharmacy technicians' ability to withdraw all the medication from the vial. This also detracted from the security of the device, leading to the belief that when preparing this specific

drug, the system was not actually closed. The issues with selecting the appropriate sized device for the appropriate vial size also impacted on the pharmacists' ability to draw up the medication in an efficient manner. Within the PhaSeal™ and Equashield®II systems there are several different devices for use dependent on the size of the vial neck, which could lead to the belief that the system is more flexible and will cover a greater number of products. However, what was actually found during the study was that pharmacy technicians had to swap out different pieces of equipment when they did not fit properly. This was more evident in the PhaSeal™ trial week and is a possible explanation for the increased number of outliers associated with PhaSeal™ and Equashield®II, which weren't seen with ChemoLock™.

Within the ChemoLock™ system, there were only two vial devices which needed to be utilised. Most of the vials utilized the main vial spike, allowing access to vials having 20 mm/28 mm closures and an external balloon to equalize during reconstitution. The other spike used was designed specifically for small vials with a 13-mm closure. This device was utilized with the Vinblastine vials, which had caused issues with the other two CSTDs. With this solution to the vial neck issue, the pharmacy technicians could withdraw all the medication from the vial at the same time feeling the system was closed and secure; utilization of the entire vial of HD is a very important factor when choosing a suitable device. During the trial from the observers perspective, it was apparent that the ChemoLock™ system offered many more solutions to implementation issues, with some specific more difficult to utilize medications. This is a small but important factor when considering devices with such a large implementation cost. If the efficiency of the pharmacy technicians is negatively impacted because they have to find ways to overcome procedural difficulties, which the implementation of the CSTDs has produced, this in turn will be a false economy against the decrease in preparation time that has been shown against traditional procedures.

There are several limitations to this study. Firstly, it could be argued that the low number of preparations timed, the number of drugs prepared, and the limited number of pharmacy technicians and nurses involved in the study, does not provide sufficient statistical data to conduct a truly measurable trial and results may therefore be skewed. Secondly, as PhaSeal™ was the first CSTD tested, one might expect staff to become more experienced in the use of CSTDs as the trial proceeded, becoming better at using them by the time they got to the final product, resulting in faster use of the product. This could have skewed the results in favour of the CSTDs that were trialled later. Thirdly, the pharmacy

technicians' enthusiasm, in addition to their awareness of being observed, could have had an impact on their speed of work, since they were fully informed of the nature of the research.

Our study demonstrated that with experienced staff, compounding of HDs with a CSTD can be as efficient as if not more efficient than compounding with the traditional needle and syringe method. With the lack of a statistical significant difference amongst the different CSTDs studied, in addition to the cost, EOU was one of the factors that decided the products applicability.

Acknowledgments

The samples of CSTDs were provided to us by local sales representatives marketing the CSTDs in the country, with no obligation to purchase after our evaluation. In addition, they were informed of the purpose of our evaluation and gave permission for us to evaluate their product. They had no role whatsoever in conducting the research or writing the manuscript.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Supplementary material

Online supplementary data is available at <http://opp.sagepub.com/supplemental>.

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