

Original Article

Compounding efficiency of Snap-N-Go vials compared to traditional sterile compounding techniques for vancomycin 1.5g and 2.0g

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Abstract. The current procedure for compounding vancomycin is an inefficient, time-consuming process that has been shown to result in more human error and leads to an overabundance of waste due to its short half-life after compounding. In an attempt to mitigate these inefficiencies, Pentec Health has developed a new medication formulation called Snap-N-Go™ to eliminate many of the unnecessary steps utilized by the traditional method. Their product may help to eliminate drug waste due to its longer half-life and may improve safety because the vial contains all the drug information on its label. This will assist the pharmacist in verifying exactly what the pharmacy technician used to compound the product in the cleanroom and potentially reduce administration errors at the patient's bedside. This study will primarily determine how much time can be saved by using Snap-N-Go™ versus traditional methods and compare the cost differences between the products used in each process.

Keywords: Snap-N-Go™, vancomycin, compounding, stability, cleanroom

Introduction

Compounding sterile products is a key responsibility of hospital pharmacies in providing a high volume of patients with intravenous (IV) medications. The current procedure for compounding vancomycin is a lengthy process that involves reconstituting lyophilized powder with sterile water, then drawing this solution into a syringe to be added to an IV fluid bag of normal saline. Because of the multitude of steps in this process, there have been numerous reports of medication errors due to inaccuracies and impurities despite additional regulations and guidelines to improve compounding practices [1]. According to an observational study done at five U.S. hospitals, the error rate for compounding IV admixtures is 9% [2]. Errors that occur throughout the compounding procedure include choosing incorrect ingredients, physical and chemical contaminants, and inappropriate compounding methods.³ Because of these ongoing issues, the need for further enhancement and optimization of sterile compounding processes at institutions is imperative to ensure patient safety. At Northwestern Memorial Hospital, 160 doses of vancomycin 1.5 g and 50 doses of vancomycin 2.0 g are batched each week. In addition to this process being lengthy and error-prone, the final product of vancomycin has limited variability in strength and a stability of only 48 hours at room temperature or 14

days refrigerated between 2-8°C. The amount of vancomycin that is wasted as a result of this stability is an average of 24 units of 1.5 g vancomycin and 42 units of vancomycin 2.0 g per quarter.

Pentec Health has developed a new medication formulation called Snap-N-Go™ in an attempt to resolve some of the deficiencies in the current sterile compounding procedure. This innovative product consists of a glass vial filled with dissolved medication and a cap that is compatible with multiple IV bag adapters including Vial-Mate™ and Mini-Bag Plus Containers™. To compound using this product, the vial is attached to an IV bag of normal saline without the need for additional reconstitution and is mixed into the normal saline solution at the time of administration. Since the initial solution is prepared in a 503B compliant facility, depending on the vial docking device used following the manufacturers recommendation on BUD's the vancomycin, for example, is 30 days at refrigerated temperature after docking in the appropriate ISO environment. Pentec Health claims it will also improve workflow efficiency, reduce waste, and decrease human errors. This study will attempt to determine the validity of these claims by comparing the traditional method of compounding vancomycin to compounding using the Snap-N-Go™ vials.

The purpose of this study is to determine the safety and

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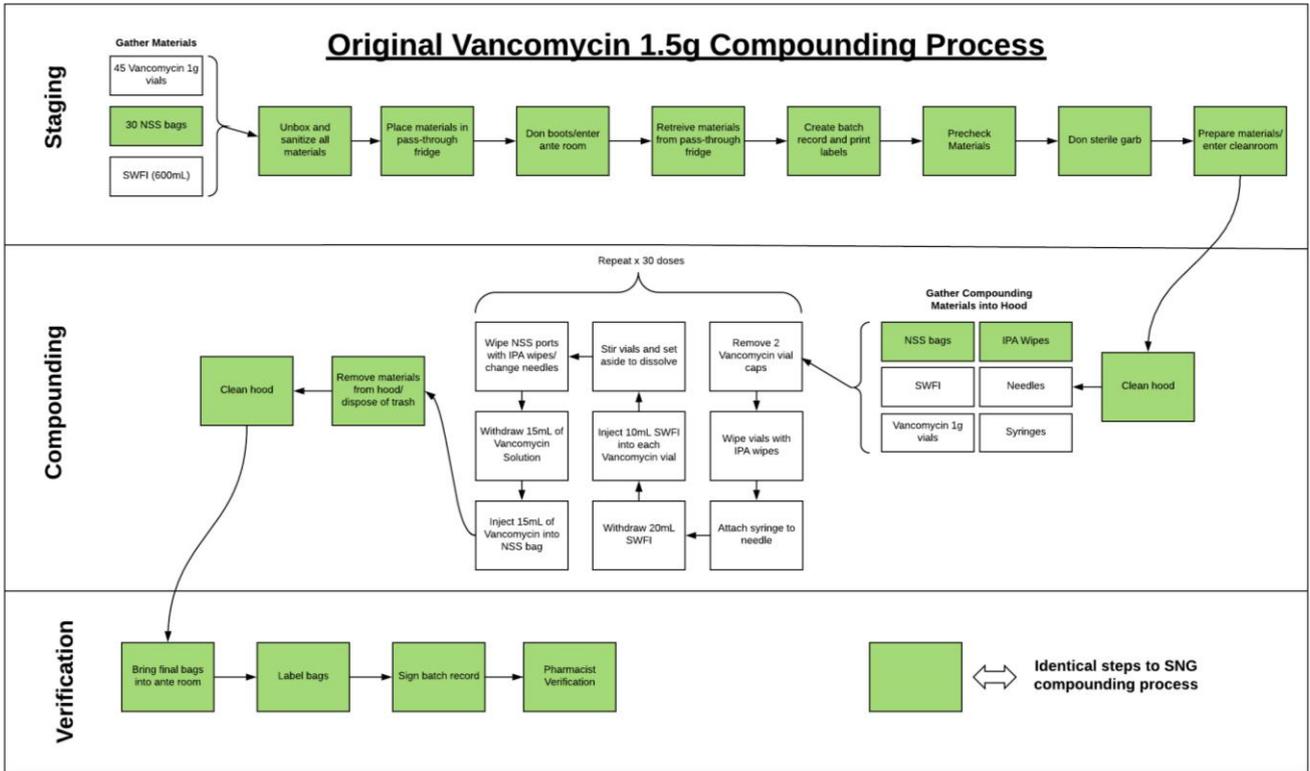


Figure 1 Traditional vancomycin 1.5 g compounding procedure. Outline of the staging, compounding, and verification steps taken to compound vancomycin 1.5 g using the traditional method of sterile compounding at Northwestern Memorial Hospital. NSS, normal saline solution; SWFI, sterile water for injection; IPA, isopropyl alcohol.

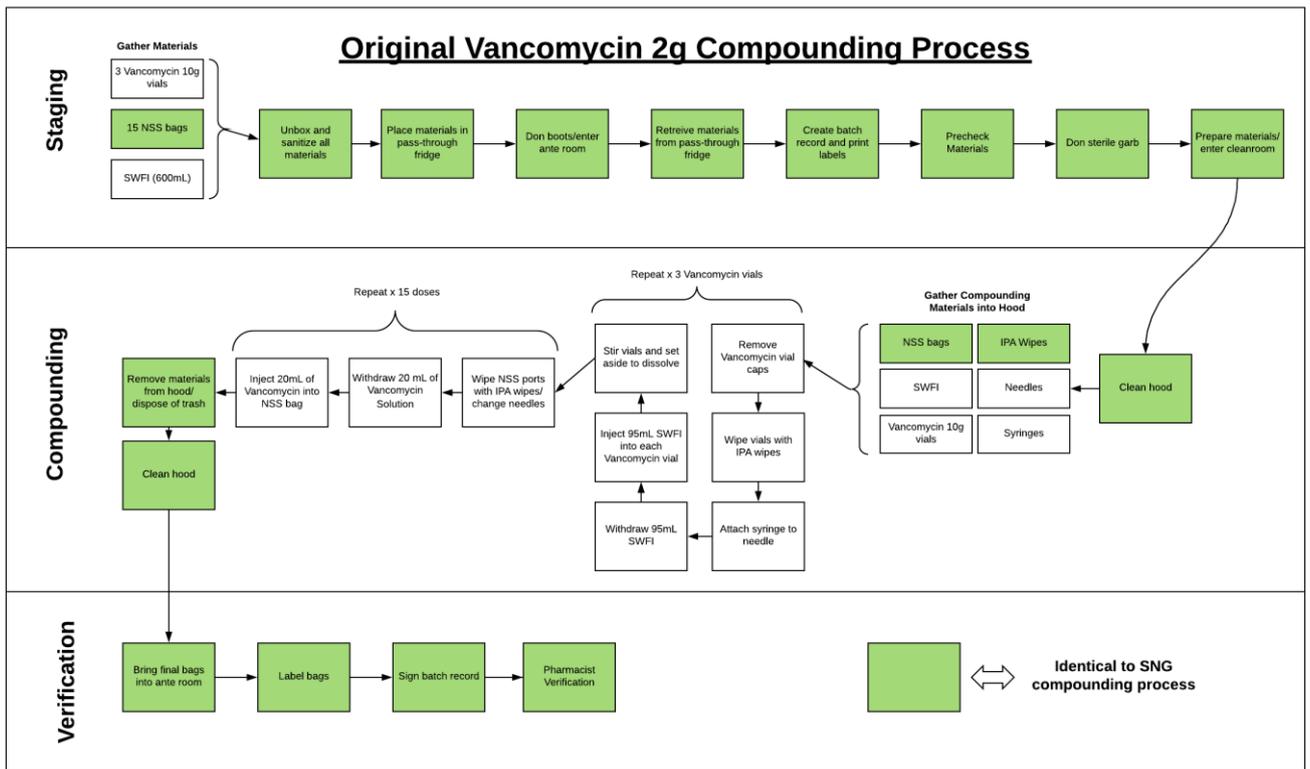


Figure 2 Traditional vancomycin 2 g compounding procedure. Outline of the staging, compounding, and verification steps taken to compound vancomycin 2 g using the traditional method of sterile compounding at Northwestern Memorial Hospital. NSS, normal saline solution; SWFI, sterile water for injection; IPA, isopropyl alcohol.

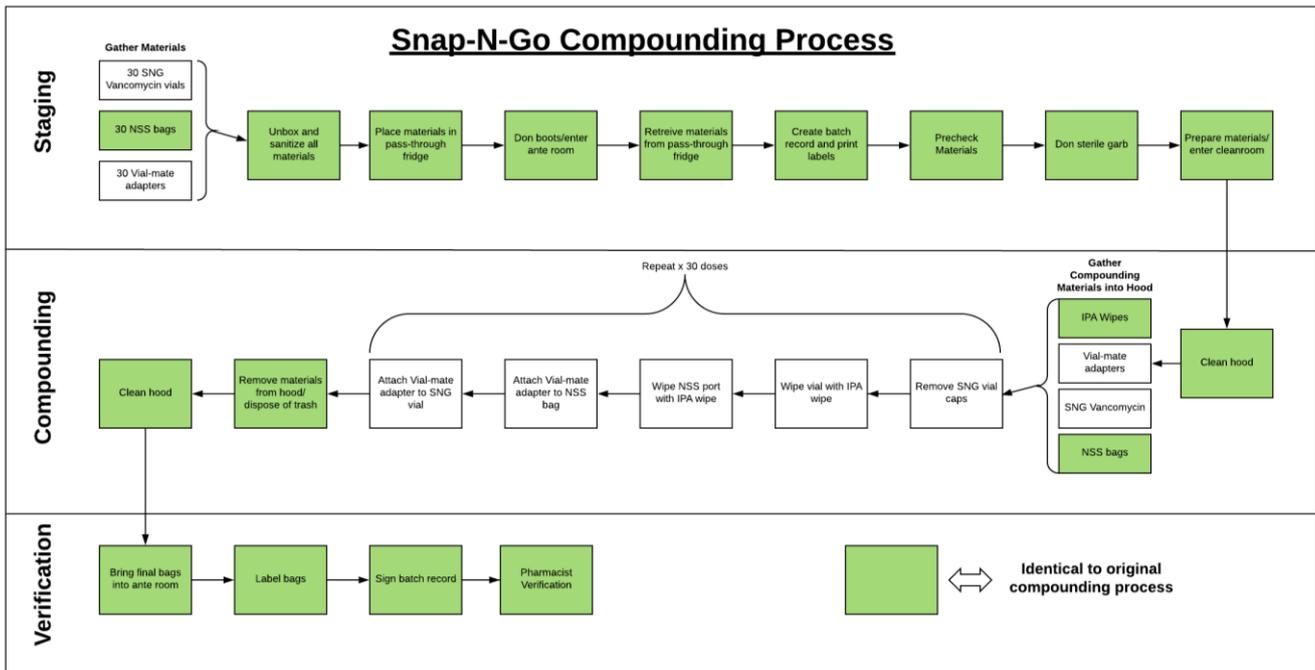


Figure 3 Snap-N-Go™ compounding procedure. Outline of the staging, compounding, and verification steps taken to compound vancomycin 1.5 g and vancomycin 2 g using the Snap-N-Go™ method of sterile compounding introduced by Pentec Health. SNG, Snap-N-Go; NSS, normal saline solution; SWFI, sterile water for injection; IPA, isopropyl alcohol.

efficiency of the Snap-N-Go™ compounding procedure compared to traditional compounding techniques.

Materials and Methods

We conducted this prospective study over the course of five days from April 2, 2018 to April 6, 2018 in the central pharmacy of Northwestern Memorial Hospital. All compounding was performed in an ISO class 5 laminar airflow workbench located within an ISO class 7 cleanroom.

On day one of the study, pharmacy technicians were observed in order to analyze their current procedure for compounding vancomycin. A workflow diagram was developed to map each step taken in the process and divided into three main categories: staging, compounding, and verification.

Each step in the traditional procedure was timed on days two and three. An observer from Pentec Health recorded the times to compound 30 doses of vancomycin 1.5 g and 15 doses of vancomycin 2.0 g using vials of lyophilized powder. Three pharmacy technicians were timed during the compounding stage. Each technician compounded ten doses of vancomycin 1.5 g and five doses of vancomycin 2.0 g. Vancomycin 1.5 g IV bags were made by reconstituting 1.0 g vials of vancomycin and adding the contents of one-and-a-half vials to a 500 mL fluid bag of normal saline. Vancomycin 2.0 g IV bags were made by reconstituting a 10 g vial of vancomycin and distributing the contents over five 500 mL fluid bags of normal saline. The 1.0 g vials of vancomycin were used to better illustrate the usual practice of compounding individualized doses at community hospitals, while the 10 g vials represented the routine compounding procedure of

larger hospitals that batch multiple doses of vancomycin at a time. The vancomycin lyophilized powder was reconstituted using sterile water for infusion. The details of each procedure is seen on the workflow diagrams, Figure 1 and Figure 2.

On days four and five, the observer timed the technicians and pharmacist following the same procedure as days two and three, but utilizing the Snap-N-Go™ reconstituted vials of vancomycin instead. Each technician compounded 10 doses of vancomycin 1.5 g and 5 doses of vancomycin 2.0 g by attaching the Snap-N-Go™ vials to 500 mL normal saline IV bags with Vial-mate™ adapters.

The primary endpoint was the time to compound vancomycin using lyophilized powder vials compared with Snap-N-Go™ vials to compare the efficiency of each process. Secondary endpoints included technician and patient safety, amount of waste produced, and dissolution times of medication.

Statistical analysis

The primary analysis was designed to show whether the Snap-N-Go™ method was significantly faster than the standard approach for compounding vancomycin. The sum of reconstitution and compounding times using lyophilized powder were compared with the entire time duration of compounding the Snap-N-Go™ vials. One-way ANOVA was performed to test the null hypothesis between multiple independent variables (1.5 g traditional, 2.0 g traditional, 1.5 g SNG, and 2.0 g SNG) and a continuous dependent variable of time to compound. The null hypothesis was that no significant difference exists in the time it takes to compound using traditional vials vs SNG vials. A student t-test was then used to compare the continuous outcomes

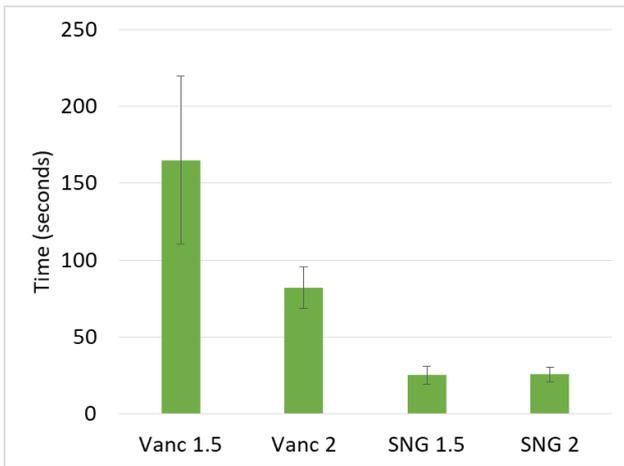


Figure 4: Average time to reconstitute and compound.

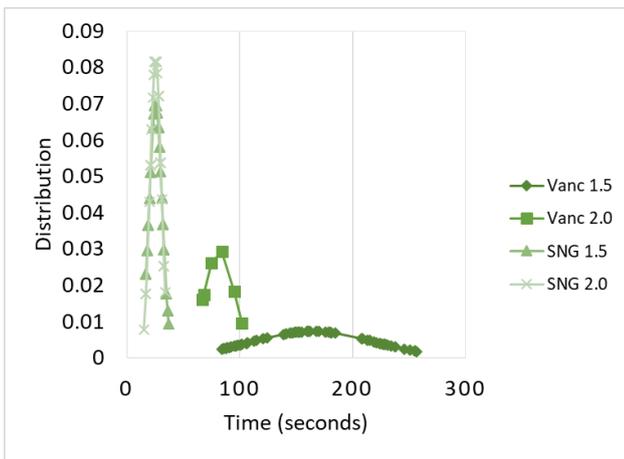


Figure 5: Distribution of compounding time.

between the two 1.5 g vials (traditional vs SNG) and also between the two 2.0 g vials (traditional vs SNG). This test was two-sided with a p value of 0.05 set to determine significance. Additionally, a 95% confidence interval was calculated to analyze the difference of means between both groups. Data analysis was conducted using Excel 2016. was two-sided with a p value of 0.05 set to determine significance. Additionally, a 95% confidence interval was calculated to analyze the difference of means between both groups. Data analysis was conducted using Excel 2016.

Results

One-hundred-and-twenty doses of vancomycin 1.5 g and 60 doses of vancomycin 2.0 g were compounded. All doses were evenly distributed between the traditional compounding technique and the Snap-N-Go™ method. Two of the three pharmacy technicians remained active for the full duration of the study. The same pharmacist verified all doses of vancomycin and the observer from Pentec Health recorded all times. The shortest time to reconstitute and compound 1.5 g vancomycin (n = 60) using the

TABLE 1
ONE-WAY ANOVA SUMMARY

| Groups | Count | Sum | Average | Variance |
|----------|-------|------|-------------|-------------|
| Column 1 | 60 | 9894 | 164.9 | 2977.074576 |
| Column 2 | 30 | 2449 | 81.63333333 | 180.516092 |
| Column 3 | 60 | 1531 | 25.51666667 | 32.79632768 |
| Column 4 | 30 | 766 | 25.53333333 | 23.70574713 |

TABLE 2
ANOVA DATA

| Source of variation | SS | df | MS | F | P-value | F crit |
|---------------------|-------------|-----|-------------|-------------|----------|-------------|
| Between Groups | 699345.1833 | 3 | 233115.0611 | 223.5813288 | 8.70E-60 | 2.655938877 |
| Within groups | 183504.8167 | 176 | 1042.641004 | | | |
| Total | 882850 | 179 | | | | |

lyophilized powder vial was 84 seconds and the longest time was 257 seconds, with the average being 165 seconds (SD = 54.6). For the 2.0 g dose of vancomycin (n = 30), the shortest time to reconstitute and compound each dose was 67 seconds and the longest was 102 seconds, with an average of 82 seconds (SD = 13.4). The fastest time to compound Snap-N-Go™ was 17 seconds for vancomycin 1.5 g vials (n = 60) and 15 seconds for the vancomycin 2.0 g vials (n = 30). The longest compounding times for Snap-N-Go™ were 37 seconds for vancomycin 1.5 g vials (n = 60) and 34 seconds for vancomycin 2.0 g vials (n = 30). Twenty-six seconds was the average time to compound both the Snap-N-Go™ vancomycin 1.5 g (SD = 6) and 2.0 g vials (SD = 4.9). The average time for the lyophilized powder vials to completely dissolve in solution was 282 seconds (SD = 70.1) for the 1.0 g vials and 530 seconds (SD = 285) for the 10 g vials. Both Snap-N-Go™ doses, 1.5 g and 2.0 g, needed one Snap-N-Go™ vial, one Vial-mate™ adapter, and one 500 ml NS bag. Compounding vancomycin 1.5 g with the lyophilized powder vials required an average of 2 needles, 4 alcohol swabs, and 1 syringe per dose. Compounding vancomycin 2.0 g with the lyophilized powder vials required an average of 1 needle, 3 alcohol swabs, 2 syringes, and 1 vented spike per dose.

The one-way ANOVA found an F-observed value (223.58) that was larger than the F-crit value (2.66) so we rejected the null hypothesis and determined that a significant difference in mean compounding time existed between our independent variables. An independent-samples t-test was then conducted to compare overall process times between the Snap-N-Go™ and original compounding methods based on which strength was compounded. A statistically significant difference in the vancomycin 1.5 g procedure time was found between the original lyophilized powder vials and Snap-N-Go™ vials, $t(118) = 19.68, p = 6.21 \times 10^{-28}$. There was also a significant difference in the process times for vancomycin 2.0 g Snap-N-Go™ vials and original lyophilized powder vials, $t(58) = 21.61, p = 2.11 \times 10^{-22}$. The vancomycin 1.5 g Snap-N-Go™ vials averaged 139 seconds faster to compound than the original lyophilized powder vials, 95% CI [129,150]. The average compounding time of the vancomycin 2.0 g Snap-N-Go™ vials was 56 seconds faster than the

lyophilized powder vials, 95% CI [54, 59].

The mean number of seconds taken to reconstitute and compound using the traditional sterile compounding technique and the Snap-N-Go method. Dissolution times were omitted from this data because they did not affect the overall time required to compound (technicians were able to compound additional doses while waiting for complete dissolution of medication). Compounding times differed between the vancomycin 1.5 g, vancomycin 2.0 g, and SNG vials, but were similar between SNG vials of differing strengths. Vancomycin 2.0 g took less time to compound than vancomycin 1.5 g because it was compounded as a batch dose rather than individual doses.

The distribution follows a standard bell curve for each method used to compound vancomycin. A wider distribution is observed using the traditional method due to the skill level required and differences between technicians performing the compounding. The narrow distribution observed for the SNG vials indicates that skill level is less of a factor in the speed of compounding vancomycin and all technicians were able to compound using this technique significantly faster than the traditional method. F (observed) > F -crit so we rejected the null hypothesis that there is no significant difference between the time it takes to compound vancomycin 1.5 g and 2.0 g using the traditional sterile compounding method and the SNG method.

Discussion

Throughout the course of this research we found that the time to compound Snap-N-Go was significantly faster than the lyophilized powder. The difference in compounding times between the two groups would be even more significant if dissolution times were included, but they were reported separately because it was observed that pharmacy technicians typically complete other tasks while waiting for the contents to dissolve. However, this increases the risk for human error when vials are left in the hood unsupervised.

One limitation of this study are the differences between technicians who performed the compounding. Technicians were selected to participate based on when they were scheduled to work in the cleanroom throughout the study week. This lack of consistency may have altered compounding times due to differences in their skill level and compounding methods, thus weakening the internal validity. Another limitation is that the study participants were not blinded to the fact that they were being timed. This could have altered the speed at which they compounded vancomycin compared to a regular work day. The longest times of the doses made with lyophilized powder were delayed due to coring of the vials in which additional vials were required from outside of the cleanroom.

We observed an inherent safety feature of the Snap-N-Go™ product in that it allowed the pharmacist to verify exactly what was compounded together. When verifying doses made with lyophilized powder, the accuracy in strength and ingredient used relies solely on the technician preparing the product. Premanufactured vials removes this

potential error and allows for accuracy even before the final verification by the pharmacist.

The IV solution of vancomycin has a short stability of 14 days when refrigerated and two days at room temperature, causing many doses to go unused before expiring and creating more waste. The Snap-N-Go™ product provides an additional benefit with its prolonged stability of one month, by potentially decreasing the amount of product wasted.

The main disadvantage of Snap-N-Go™ is its cost. A secondary cost analysis was run, although the pricing data varies and is exclusive to each institution. Nonetheless, Snap-N-Go™ appeared to be more expensive as a cost per dose in this particular study. Although the price of Snap-N-Go™ may vary with different contracts and medications, the overall cost still seems to be higher with supplies and labor factored in as compared to high volume batching.

Another inconvenience is the inability to batch a large volume of single doses using one multi-dose vial. Using a multi-dose vial, such as the 10 g lyophilized powder vial, can potentially reduce waste when a large number of doses are compounded. However, we found that an equivalent number of doses is compounded more quickly using the Snap-N-Go™ vials versus the 10 g multi-dose vials. Snap-N-Go™ comes in six strengths including 0.75 g, 1.0 g, 1.25 g, 1.5 g, 1.75 g, and 2.0 g for ease of use in compounding, which is especially beneficial for smaller hospitals requiring individual doses as needed.

Future studies for Snap-N-Go vials should be conducted using a larger sample size of product and uniformity between the pharmacy technicians performing the compounding. Other studies should also be conducted to determine the most efficient adapter to be used with Snap-N-Go™ vials, whether it be Vial-Mate™ or Mini-Bag Plus Containers™. The ease of use during administration has yet to be determined and could also be included in future studies.

Conclusion

Snap-N-Go™ vials have been shown to significantly increase efficiency while also enhancing the stability and safety of compounding vancomycin. Snap-N-Go™ comes at a greater initial monetary cost, but may be of more value to certain institutions based on their needs. Some of this cost is recovered by utilizing fewer materials to compound and allowing more time for pharmacy technicians to accomplish additional tasks. The larger cost appears to be most beneficial for smaller institutions, as most do not have the patient capacity necessary for batching large doses of vancomycin. Furthermore, smaller institutions have less personnel and time to complete the lengthy standard compounding process required to make individual doses.

Conflict of interest

The authors declare no conflicts of interest.

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