White Paper on Hospital Pharmacy Unit-Dose Acquisition and the Case for the Third-Party Repackaging Option

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Abstract

Our research team from the Center for Innovation in Healthcare Logistics (CIHL) was asked to develop better logistical strategies for securing medications in unit-dose form to support the best practice of barcode-enabled point-of-care (BPOC) administration. To aid us in our research, a CIHL strategic partner, the VHA hospital network, was utilized to provide in-depth background on hospital pharmacy strategic, tactical and operational methods. One of the pharmacy directors from the VHA network was able to also provide specific, case-study data. Together we designed and administered a survey to provide a more complete view of the landscape [12]. This white paper discusses the current state-of-practice, including the options available for securing medications in unit-dose form, as well as the options available for repackaging in the pharmacy. We then discuss the third-party repackaging option, including its positives and negatives. Our overall recommendation is to work towards the third-party option and so we discuss the challenges that need to be overcome for this to become a widespread practice. Finally, the impact of current and expected pedigree requirements on this issue are discussed.
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White Paper on Hospital Pharmacy Unit-Dose Acquisition and the Case for the Third-Party Repackaging Option

Preamble

This paper was written to provide a comprehensive view of hospital pharmacy unit-dose acquisition. The team consisted of three faculty researchers and two graduate students in the Center for Innovation in Healthcare Logistics (CIHL) at the University of Arkansas, a member-directed research center formed with the mission of, “seeking healthcare supply chain and logistic innovations that put the right materials in the hands of caregivers when and where they are needed.” The CIHL faculty and students all have industrial engineering backgrounds. To assist the CIHL researchers, a CIHL strategic partner, the VHA hospital network, was utilized to provide in-depth background on hospital pharmacy strategic, tactical and operational methods. In particular, an advisory group of five pharmacy directors (four within VHA and one from the Veterans Administration system) was established. Our group also administered a survey of pharmacy directors to obtain general results on the state-of-practice. The survey yielded 91 responses that were diverse across geographical location, hospital size, and use of information technology and repackaging practices [12]. And finally, one of the pharmacy directors from the VHA network was able to also provide specific, case-study data to our more general survey results.

1. Introduction and Current State-of-Practice

In hospitals, medication errors occur during every step of the medication administration process, but they occur most frequently during the prescribing and administering stages [1]. In fact, “when all types of errors are taken into account, a hospital patient can expect on average to be subjected to more than one medication error each day” [1].

A hospital’s medication dispensing process is one potential source of error and can result in adverse drug effects. A study published in 2006 [6] focused on the identification of errors across four areas of the dispensing process: automated dispensing cabinets (ADCs) fill, controlled substance fill, first dose fill (for less common medications not routinely stored in ADCs), and cart fill. The study found that ADC fill had the highest number of errors, a significant finding given the widespread use of ADCs.

One way to prevent some types of medication errors is to administer medications in unit-dose packages since this ensures that the medication name, dosage, and other characteristics are available to the administering professional (typically, a nurse) right until the time the medication is administered. As a result, administering medications in unit-dose packaging is not only considered a best practice, but is also near universal in its application, with millions of unit-dose medications dispensed in hospitals and health systems daily [19].
Barcode technology represents a promising solution to at least some medication dispensing errors, offering several advantages. Barcode technology saves time, improves accuracy, and is capable of identifying rare events, something for which human beings are not proficient [6]. Using barcode technology has the potential to reduce the errors associated with the incorrect medication, incorrect strength, and incorrect dosage. Another advantage of using barcode technology is that it can assist the hospital in the identification of medications not current in the hospital medication dictionary. Medications not listed in the dictionary cannot be scanned during the medication distribution processes [5]. A study on medication dispensing errors before and after implementing barcode technology revealed that barcode technology in the pharmacy compares favorably with other patient safety interventions [16]. Given the high volume of medications dispensed in a hospital, even small reductions in errors will result in significant improvements in patient safety.

Unfortunately, not all hospitals employ the use of barcode technology. One of the reasons is because the cost of adopting barcode technology is substantial. However, a study conducted to evaluate the cost-benefit ratio of such an investment found that barcoding eventually pays for itself within a 5- to 10-year time horizon [13]. As the study noted though, “whether the implementation of a barcode-assisted medication-dispensing system is successful or not ultimately depends as much on the implementation as on the system itself, both of which can introduce errors.”

In order to further improve patient safety, some hospitals are implementing barcode-enabled point-of-care (BPOC) systems. In such a system, medications are administered in barcoded unit-dose packages and these systems require that patients wear a barcoded bracelet. When a nurse administers the patient’s medications, he or she must first scan the barcode on the medication and then the patient’s wristband. These systems help ensure that the right medications reach the right patient at the right time by allowing barcodes on a patient’s ID wristband to be checked against medication packaging and the physician’s orders [2].

In contrast to unit-dose packaging, the best practice of BPOC systems is not universal, with only approximately 13% of hospitals today implementing such a system [12] (a similar result was reported at a recent conference [20]). The primary-cited roadblock is in terms of information systems and infrastructure on the floor needed to read the barcoded medications and patient wristbands. However, the roadblock that is not cited, but is observed, is related to nurse buy-in, or the lack thereof, due to insufficiently-designed systems that can make the nurses’ jobs more difficult and time consuming. With these roadblocks acknowledged, and eventually addressed, we believe that BPOC will continue to increase in application (our survey indicated that 58% of the respondents are in the planning stages of BPOC [12]). Thus, our focus is on securing medications in unit-dose form.

The term “medications” is a broad term, used to cover a variety of final forms and administration protocols: oral solids, liquids, creams and balms, injectables, IVs, etc. And according to our survey of hospital pharmacy directors [12], 85% of them prefer to acquire all pharmaceuticals in unit-dose form directly from the manufacturer. Such sentiment was supported by a ruling of the U.S. Food and Drug Administration (FDA), which became
effective on April 26, 2004 requiring that all drug and biological products sold to hospitals incorporate barcodes on their labels [2]. Drug manufacturers must place a barcode on the “immediate container” of the product, which is generally the smallest unit of packaging. Therefore, if pharmaceutical manufacturers supply unit-dose medications, each unit-dose must have a barcode. The barcode must contain the medication’s 10-digit National Drug Code (NDC) number. This number uniquely identifies each medication by drug name, strength, and manufacturer. This ruling was aimed at making unit-dose systems widely adopted, but unfortunately it does not require that manufacturers set the smallest unit of packaging at the unit-dose level. Moreover, the barcode that is placed on the package may be unreadable by the pharmacy’s system.

In 2004 only about a third of all medications were available from the manufacturer in barcoded unit-dose packages [2]. And after the FDA ruling went into effect in 2003, this number has since increased. For example, in our survey of hospital pharmacy directors, more than half acquire at least 60% of their medications in unit-dose form from the manufacturer [12]. Even with these increases in availability, hospitals are repackaging more, with a 2002 survey conducted by the American Society of Health-Systems Pharmacists (ASHP) finding that 70% of health-system pharmacy directors said they have had to increase repackaging [15]. A study by the Institute for Safe Medication Practices confirms this finding, stating that 75% of respondents reported availability problems with unit-dose packaging of both new and established brand-name oral-solid products [10]. Part of this may be a response by pharmaceutical manufacturers to curtail some unit-dose packaging efforts, especially for those medications that have a larger retail (rather than clinical care) demand.

Therefore, given that hospital pharmacy directors need barcoded unit-dose medications, and these needs are increasing, some repackaging will be required to achieve their goals of increasing patient safety. We next discuss the options available for doing so.

2. Repackaging Options Available

The option preferred by 85% of hospital pharmacy directors [12] is to purchase medications directly from the manufacturer in unit-dose form. This method has the characteristics of having the highest level of quality and tends to be least labor and infrastructure intensive for the hospital. In addition, the packaging is typically sized to the medication and there is also a significant level of convenience associated with purchasing and delivery through established wholesaler/distributor relationships. Unfortunately, not all medications are available in barcoded unit-dose packages and some that do not have readable barcodes. When this option is not available (or the premium associated with it is too expensive), pharmacy directors then have two main options: (1) repackage the medication themselves or (2) work with an external agent other than the manufacturer to acquire the medication in unit-dose form.
2.1 Internal Repackaging

Repackaging the medication within the pharmacy has the advantages of flexibility, a low per unit labor and supply expense, and a great deal of control. The disadvantages are that this option typically involves investment in equipment for repackaging (which is space-consuming), the packaging is of a “one-size-fits-all” model (so, it is large), as well as knowing that the process will be conducted by employees not necessarily trained in industrial pharmacy practices.

The three basic repackaging process technology choices within the pharmacy include: manual, semi-automated and automated. A manual process typically uses little more than a device to seal the packaging. Manual labor is used for the repackaging and relabeling process. With a semi-automated process, a device for repackaging and relabeling is automatically controlled, but the induction of medications is performed manually. And finally, with an automated process, the induction of medications, repackaging and relabeling are all automated. In theory, with further discussion later, the three processes follow the typical cost-benefit trade-off of a higher investment in capital for a decreased level of labor.

2.2 External Repackaging

Working with an external agent other than the manufacturer to acquire the medication in unit-dose form has the advantages of freeing clinically-trained pharmacists and pharmacy technicians to work on clinical issues, knowing that the repackaging operations will be performed by staff that are trained in industrial pharmacy practices. Removing this operation from the pharmacy also frees up space in a typically space-constrained pharmacy. The disadvantages of this option include increased coordination and possible delays, as well as less flexibility and control. The per-unit cost for this service is also a potential concern.

The two basic partnering arrangements include: a large wholesaler/distributor that buys in bulk and repackages for sale or a third-party repackager that receives the hospital’s medications and repackages them before sending them to the pharmacy. (There is another arrangement of contracting with a third-party to conduct on-site packaging at the hospital, but this arrangement is not common, with only 2% of the survey respondents [12] currently using this practice. Moreover, this practice merely shifts responsibility, so its advantages and disadvantages are covered by other discussions.) The wholesaler/distributor arrangement most closely resembles directly purchasing from the manufacturer, but hospital pharmacy directors noted concerns about the intermittent availability of medications, costs and packaging characteristics of this arrangement. The third-party repackager arrangement has the advantage of the repackager always working with “your medications” (we provide a more extensive discussion of this topic later).

2.3 Summary

In general, as compared to the hospital pharmacy, the manufacturer is least likely to mislabel or mispackage unit-dose medications. The medications repackaged by a third-party repack-
ager tend to fall in between the two groups. This characterization is due to the stringent FDA Code of Federal Regulations (CFRs) and the Current Good Manufacturing Practices (CGMPs) that pharmaceutical manufacturers are subject to [14]. Third-party repackagers are subject to a portion of the CFRs, like packaging, labeling, cleaning, and training, but they are not put through the same inspection as the manufacturer [14]. Also, third-party repackagers are trained in industrial processes, whereas that is not the hospitals’ core competency. In addition, the hospital pharmacy’s repackaging is regulated only under state regulatory agencies [14] and therefore varies by the state of operation.

In the next two sections we further explore the internal and external options. Before doing so, we reiterate that the core of the research team consists of industrial engineers educated on pharmaceutical practices and issues by a select group of hospital pharmacy directors. Our findings are also supported by a survey of hospital pharmacy directors [12]. In all cases, it was made clear to us that the purpose of unit-dose packaging is patient safety and so our mindset was to examine solutions that decrease cost only when system safety is maintained or improved.

3. Repackaging in the Hospital Pharmacy

In this section we describe the repackaging process for a hospital pharmacy when conducted by hospital personnel. We also discuss the technology options for repackaging, focusing on the repackaging of oral solids due to the fact that the technology for oral solid repackaging has been utilized the longest.

3.1 The Process and the Options for Repackaging Technology

When medications are repackaged in the hospital pharmacy, the basic flow of the medications is as follows. First, the medications are received in bulk from the pharmacy’s wholesaler/distributor. After performing an audit of the order, the bulk medications are stored until needed. In general, the repackaging of the medications is postponed since the useful life of the medication is reduced based on FDA regulations when the medication is repackaged.

Once the medications are repackaged into unit-doses, they are typically combined with the medications that were procured in unit-doses. This inventory is then used to support the pharmacy’s unit-dose medication distribution process. There are two main models for this process: cart-less and cart-fill. In both systems, unit-dose medications are stored on the hospital floor in a medication cart or cabinet (e.g., Pyxis). The primary difference between the two models is seen in the sorting scheme of the medication cart. In a cart-less system, available medications are sorted by medication types, while in a cart-fill system they are sorted by patients. Restocks to both systems are made by the central pharmacy. Numerous safety and quality checks are implemented in the system so that a nurse can only access medications that are on a patient’s daily requirements and were electronically approved by a pharmacist.
In general, hospitals are striving for a cart-less model, as it keeps the most commonly-used medications close to the patient. Doing so allows for a shorter response time when a physician changes the prescription for the patient and removes the complexity of specifying medications by patient that are prescribed on an “as needed” (PRN) basis. Also, because medications are stored by medication types, if a patient’s prescription does change, returned medications are not an issue. The main disadvantage with a cart-less system is that not all medications can typically be stored in the carts due to capacity issues. Therefore, a nurse must locate these doses from multiple other locations which requires extensive effort from both the nursing and pharmacy staffs. Also, because drawer space utilization is important in this model, it is ideal to have smaller unit-dose packages than most fully automated systems can produce.

In a cart-fill system, carts are filled in a central pharmacy with each patient’s daily prescribed medications organized together. Therefore, there is a separate location for each patient’s prescribed medications. Under this system, the pharmacy receives the physician’s medication order form, which the pharmacist then reviews and checks for any problems. After the pharmacist approves the medication order, a technician picks the needed doses for a specific period of time, typically the next 24 hours and places them in a cart sorted by patient. If a cart-fill system is used, fully-automated systems can reduce the manual operations of picking a patient’s daily medications by processing orders as they appear on the unit-dose cart fill list and producing a strip of individually packaged unit-dose medications for each patient. The downfall to a fully-automated system with a cart-fill system is there is not a good process in place for return medications. The filled medication cart is delivered to the hospital floor and typically can only be accessed by authorized pharmacy and nursing personnel. This system allows the pharmacy to dispense only the number of doses needed by individual patients. The primary disadvantage to this system is the labor-intensity and inefficiency of the process. Every 24 hours a technician must pick all medications needed during the next 24-hour period and place them in the appropriate patient-specific drawer in the medication cart. There is substantial duplication in this system when unused medications due to changes in the patient’s prescriptions are returned to the pharmacy. Also, PRN medications will likely need to be double-handled. Because medications are stored by patients and not medication type, the size of the unit-dose package does not tend to be an issue.

In pharmacies that utilize an automated repackager, the order fulfillment process is a manual process for those medications received in unit-doses and then combined with the output of the repackager. In those cases where the hospital employs a cart-fill system the automated repackager can reduce the labor involved not only in the repackaging process, but also this fulfillment process. That is, although labor is also reduced in the fulfillment process in a cart-less system, the labor savings is more significant in a cart-fill system.

As mentioned previously, the basic technology options for repackaging in the pharmacy are manual, semi-automated and an automated repackager. The manual option is characterized by various sealing technology methods, with the equipment available for hundreds of dollars. For liquids and powders, the manual option is the most prevalent, as there are not many automated (or semi-automated) systems available to repackage medications in these
forms.

The semi-automated option typically manifests itself in what are referred to as table-top unit, consisting of a rotary table, an automated sealer and labeler, and a manual induction process. The equipment for such a system runs in the thousands of dollars (e.g., Euclid tabletop units are available for approximately $18,000). In a semi-automated system, the actual packaging process is automated, but the retrieval of medications and monitoring processes are not. A technician is required to retrieve the appropriate bulk medication, fill the machine, and monitor the process. In addition, the system needs to be manually cleaned in order to prevent cross contaminations of medications.

The automated packager option consists of a set of canisters, where each canister holds one medication and is specific to the physical characteristics of the medication. The medications travel down a common chute to the packaging and labeling units (note that because of this common chute, medications that would contaminate other medications, or be contaminated by them, cannot utilize an automated repackager). The equipment for such a system runs in the hundreds of thousands of dollars (e.g., a SafetyPak from OmniCell costs approximately $200,000). Also, worth noting, the primary vendors of these systems (McKesson, Omnicell and Talyst) all utilize the same technology by a Korean company, JVS, varying only the computer interface. These machines are not always able to hold all of the unit-dose formulary and therefore some manual or semi-manual systems may still need to be in place. Also, until a new canister is procured for a new medication (and it is recommended by the manufacturer that each canister be custom-made), the medication must be repackaged in some other fashion. These systems are typically equipped with extensive reporting capabilities, inventory management tools, and/or are integrated in with additional pharmacy workflow automation (like a carousel system), which can help lower costs of expired medications and on-hand inventory. Also because the bulk medications are stored inside a machine, fully-automated machines tend to reduce the amount of space required to store medications and the cost of pilfered medications. In all of the hospitals that we have visited that employed such a technology, the utilization of these machines were a few hours in a day. From our survey, 28 of the 32 respondents employing this technology (88%) reported utilizing the systems only four or less hours per day [12]. Therefore, the extremely high infrastructure cost is often times hard to justify given such low utilization. Also, many pharmacy directors had issues with automated repackager unreliability, as well as the maintenance and upkeep of the technology.

3.2 The Requirements for Repackaging

The requirements for repackaging vary with hospital size or activity levels, as well as the percentage of medications acquired in unit-dose form. That is, as hospital size or activity levels increase or the percentage of medications acquired in unit-dose form decreases, the requirements placed on a repackaging system increase. For example, using typical results from [12], for a 200-bed hospital that averages 11.4 doses per patient per day and acquires 70% of its medications in unit-dose form, 684 doses would require repackaging daily. Likewise, a 500-bed hospital that averages 10.8 doses per patient per day and acquires 75% of its
medications in unit-dose form, would need to repackage 1,350 unit-doses daily.

For the 200-bed hospital employing the semi-automated repackaging option, its repackaging system may only consist of a table-top unit and less than one full-time equivalent (FTE), whereas the 500-bed hospital may be choosing between two table-top units with four FTEs versus an automated repackager with one FTE.

It is worth noting that repackaging liquids and powders is even more labor intensive than their oral solid counterparts and many hospitals struggle with producing these unit-doses internally.

3.3 Summary

As one can see, repackaging in the hospital is characterized by a system that is either manually-intensive (for the manual or semi-automated options) and utilizes more employees than the FTE-count would indicate (due to the high activity levels needed for short periods of times each day) or a less labor-intensive system that requires a significant investment in technology with typically low utilization of at most four hours of operation per day. From an outside perspective (that is shared by many that work in pharmacies), this is not ideal. Thus, in the next section we consider the strategy of partnering with a third-party repackager.

4. Partnering with a Third-Party Repackager

In the previous section we discussed the process of repackaging within a hospital pharmacy. In this section we present the process of securing unit-dose medications when the hospital partners with a third-party repackager. Overall, one would think that the process is the same, with only the party involved in the repackaging changing. However, there are a few, critical differences in the process when conducted by a third-party repackager.

4.1 The Process

Whether a third-party repackager is used or the medications are repackaged in-house, under both strategies, the medications are purchased from a wholesaler/distributor. However, in the third-party repackager option, the medications are directly mailed to the repackager (as opposed to the hospital) in most cases (thus, at no time does the third-party repackager own the inventory). Therefore, in order to efficiently use a third-party repackager, the hospitals wholesaler/distributor must be able to provide “bill-to, ship-to” ordering.

Once the medications have arrived at the repackager, the repackaging operations at the third-party location differ from in-house repackaging in the following critical ways:

First, dedicated production facilities with specialized production suites are utilized at a third-party repackager, which enhances quality by controlling for the risk of product mix-ups, cross contamination, and staff interruptions/distractions.
Second, the staff is dedicated to repackaging. This difference has implications relative to staff training, staff performance, and the monitoring of staff performance.

Third, due to the volume and multiple customers it serves, the third-party repackager typically uses technology-based solutions to retrieve the information on the incoming medications (versus manual key-stroke entry, like in most hospitals), which will reduce errors.

Fourth, again due to volume for the multiple customers it serves, some third-party repackagers use sophisticated production software with extensive checks and validations (e.g., biometrics and drug databases for identification and handling information) that permits the repackager to pinpoint the location of a specific order to a machine and production worker at any time.

Fifth, the automated repackager technology discussed earlier is not used at third-party repackagers because the third-party keeps all inventory separate (i.e., one hospital’s medications are never mixed with another hospital’s medications). When a third-party repackager repackages a medication, they repackage the entire quantity and never hold inventory of medication in an “open, but not being processed,” state. Now, that is not to say that third-party repackagers do not have automated repackagers; some do. But the key difference with these automated repackagers and the ones used in a hospital is that there is no inventory storage unit. And likewise, the technology we observed is not designed with a common chute. Therefore, there are no cross-contamination issues like in the automated repackagers used at a hospital because the unit at the third-party is cleaned between each change of medication. And, as a side note, a unit of this type that we observed (PentaPak, specially manufactured in Belgium for one repackager) was also able to vary the packaging size by medication, which is a feature the automated repackagers we saw installed at a hospital pharmacy did not have. And recall that flexible packaging size has advantages in stocking medical carts or ADCs.

In general, due to the fact that the repackager is focused on repackaging, utilizing their equipment at higher rates, and requiring new equipment more frequently, the repackager will always be a step or more ahead of hospitals and their staff in terms of equipment and training available.

On the processing similarity side, all repackagers employ table-top and manual units for the repackaging for at least some of the oral solids, as is the case in most hospital pharmacies. The difference that we saw in practice was that where hospitals tended to completely wash the unit only between repackaging some medications, the third-party repackagers washed the unit between all medication repackaging with table-top units.

With respect to the quality of the repackaged product, there are three, main quality advantages the repackager can legitimately claim:

1. The repackagers employ cGMPs [8]. This can lead to small impacts in the process (e.g., the segregation of work; a worker at a repackager is working on one repackaging lot
at a time instead of multiple, as is typical in a hospital pharmacy) to large ones (e.g., the routine testing of equipment; moisture permeation testing on packaging and foil occurs weekly instead of only when problems are identified, as is typical in a hospital pharmacy).

2. Additional quality control checks are performed on the output of the process. Repackagers, since they are a third-party, keep one unit of each lot (referred to as a reserve or retention sample) and hold the unit in inventory for a year after the medication’s expiration date for bioavailability and bioequivalence testing [7]. One repackager we interviewed conducted in-production testing/sampling (e.g., verification of the 25th dose — the 25th dose has to pass an inspection before the process will continue). Also, the third-party repackagers stay abreast of medication recalls and notices, passing this information onto the hospitals they service, providing another quality check in the system.

3. The repackagers must be registered with the FDA. The registration process states that cGMPs have been established and have processes that work to ensure compliance. When the FDA visits, the inspectors verify and validate the above by reading the standard operating principles (SOPs) and then observing the operations, inspections, record keeping, etc., first-hand. These visits are unannounced and are typically of a multi-day length.

Once the medications are repackaged by a third-party, they are prepared for shipment to the corresponding hospital pharmacy. The shipments are delivered via a priority parcel delivery service (e.g., UPS, FedEx, DHL), arriving the next morning after repackaging. The hospital then receives the medications through its normal receiving and induction process (i.e., with other medications that wholesalers/distributors ship in unit-dose form).

4.2 The Comparison

Now that we have provided an overview of both options for obtaining medications in unit-dose form, highlighted the differences between the two options in terms of process quality, we compare them in terms of the two highest-rated concerns from [12]: turn-around time and costs.

A discussion on a third-party repackager’s turn-around time requires discussion on the timeline associated with the internal and external repackaging options. It is typical for a hospital pharmacy to process a repackaged medication over two days. Namely, the bulk medications arrive on Day 1, the medications can be repackaged on Day 2, and then the repackaged medications are available for orders on Day 3. Note that this entire schedule can be compressed to same-day, when needed. For an external option, the bulk medications arrive at the repackager on Day 1 and are repackaged that day, arriving at the hospital on Day 2 and made available for orders on Day 3. Note that this entire schedule can be compressed to two days, when needed. So, the difference in terms of timing is up to one day when the repackager promises same-day processing and up to two days when the repackager
promises two-day processing. And when weekends are considered, the internal option affords even more flexibility when that is needed (although most hospitals noted that they did not typically repackage on the weekends).

Another easy-to-quantify difference is the per-unit and additional shipping charges associated with the third-party repackaging options. In terms of oral solids, the charge ranges from $0.03–$0.07 per unit, with additional shipping charges of typically $9 per case (where a case may have 5,000–7,000 unit-doses). Thus, the total charge may run about $0.06 per dose. Third-party repackagers do have economies of scale that allow them to capitalize expensive technologies that small hospitals may not be able to afford [18]. This per unit charge has to be balanced against the purchasing of technology that the hospital would not normally need under the external partnership option, the labor involved in repackaging, and the additional staff that would be needed to check the process (note that the units themselves must be checked in either option from the hospital’s point-of-view; a point that was emphasized repeatedly by our collaborating pharmacy directors). In addition, outsourcing unit-dose packaging may eliminate the need for physical remodeling within the hospital and may result in a reduction in inventory [17]. This balance, from a strictly financial point-of-view, rarely favors the internal option when all aspects of the process are considered [13, 21], especially for anything other than very large pharmacies.

A hybrid model to note here is when a group of hospitals, typically part of the same network, pool their requirements so that they can take advantage of the volume and efficiencies of an external supplier, all the while maintaining a tighter degree of control as in the internal option. This strategy is used, with noted success, by HCA’s hospitals in TN [11] and Mercy Hospitals in the AR, OK, MO, KS and TX area [3]. Note that in this model, the central hospital repackager typically holds inventory of a core set of medications and so the automated repackagers utilized in a hospital pharmacy are viable options, with a typically higher utilization.

The above hybrid model leads to the final model: the wholesaler/distributor turned repackager model. That is, many of the large medication wholesaler/distributors will supply some unit-dose medications that they have themselves repackaged. For example, Cardinal, McKesson and Morris & Dickson were identified in [12] as being used in this capacity by at least one survey respondent. From the hospital’s point-of-view, in theory, this is the next-best option than buying direct from the manufacturer in unit-dose packaging. However, every hospital pharmacist we discussed this with indicated that they did not view this as the best option since the wholesalers/distributors charge too much for this service, the package size did not vary by medication (i.e., it tended to be too large), and more importantly, medications were frequently unavailable. Therefore, we do not fully consider this option in the remainder of our analysis.

4.3 State of the Repackaging Industry

The third-party repackaging industry is small and has not matured, with little market penetration. The companies listed in Table 1 represent all known third-party repackagers with some capability and interest in this market where websites could be found (repackagers
Table 1: Known Third-Party Repackers, Dec., 2008.

<table>
<thead>
<tr>
<th>Repackager</th>
<th>Website</th>
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<tbody>
<tr>
<td>Ameridose</td>
<td><a href="http://www.ameridose.com">www.ameridose.com</a></td>
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<td>American Health Packaging</td>
<td></td>
</tr>
<tr>
<td>Choice Rx, Inc.</td>
<td><a href="http://www.healthpack.com">www.healthpack.com</a></td>
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<td>Macron Packaging Systems</td>
<td><a href="http://www.choiceRx.com">www.choiceRx.com</a></td>
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<td>Murfreesboro Pharma Nursing Supply PDRx</td>
<td><a href="http://www.macronunitdose.com">www.macronunitdose.com</a></td>
</tr>
<tr>
<td>Redwood unit-dose</td>
<td><a href="http://www.unitdosesupply.com">www.unitdosesupply.com</a></td>
</tr>
<tr>
<td>Regional Service Center (RSC)</td>
<td><a href="http://www.pdrx.com">www.pdrx.com</a></td>
</tr>
<tr>
<td>Sandhills Packaging, Inc.</td>
<td><a href="http://www.redwoodunitdose.com">www.redwoodunitdose.com</a></td>
</tr>
<tr>
<td>Shamrock Medical Solutions Group</td>
<td><a href="http://www.unit-dose.com">www.unit-dose.com</a></td>
</tr>
<tr>
<td>Unit Dose Solutions, Inc.*</td>
<td><a href="http://www.sandhillspackaging.com">www.sandhillspackaging.com</a></td>
</tr>
<tr>
<td>Atlantic Biologicals*</td>
<td><a href="http://www.medsolgroup.net">www.medsolgroup.net</a></td>
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<td>Atlantic Biologicals*</td>
<td><a href="http://www.unitdoseinc.com">www.unitdoseinc.com</a></td>
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<tr>
<td>Atlantic Biologicals*</td>
<td><a href="http://www.atlanticbiologicals.com">www.atlanticbiologicals.com</a></td>
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</tbody>
</table>

*A strategic partnership exists between these two companies.

that were identified in [12], but no additional information could be found include: MedPrep (Pittsburgh) and Vibranta, Inc. (Miami)).

However, if one defines a fully-capable repackager as one that can repackage oral solids, liquids, etc., and will do so for medications purchased from any licensed provider, then only three (Regional Service Center, Shamrock, and Unit Dose Solutions/Atlantic Biologicals) are fully-capable repackers at the time of this writing. The observations of best practices noted above were based on visits and additional information from RSC and Shamrock, with Shamrock the third-party repackager that has the specialized equipment and software packages identified above and thought to be state-of-the-art.

4.4 Summary

Since most hospitals repackage their own medications, the following is a generalized, but widely-held — and somewhat inconsistent — position. Nearly all hospitals would rather purchase all medications in unit-dose form (since manufacturers are experts at this), but when they are not available, they would rather repackage the medications themselves, not fully trusting a third-party repackager (who typically employs better processes than they do). As one hospital pharmacy director put it, “it won’t be the third-party company’s name in the paper when we have a problem, it will be my hospital’s name.” Additionally, the fact that the statement would be just as true if inserting “pharmaceutical company” for “third-party company,” did not sway his opinion. Which goes to the largest challenge that the third-party repackaging industry faces, to raise that level of trust. In the next section we will continue this discussion.

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5. Moving Forward: How to Drive Towards a Better Third-Party Repackaging Industry

In this section of the paper we first present our overall recommendation: due consideration should be given by hospital pharmacies to partnering with a third-party repackager. Then, since most hospitals are currently not partnering with a third-party repackager, we present a set of concerns that must be satisfied before a hospital should choose to follow this recommendation. Finally, we present our thoughts on what hurdles need to be overcome before the third-party repackaging industry will achieve widespread market penetration.

5.1 Our Overall Recommendation: Partner with a Third-Party Repackager

As stated previously, our overall recommendation is that due consideration should be given by hospital pharmacies to partnering with a third-party repackager. We arrive at this recommendation through our system-wide evaluation of the current state-of-practice related to repackaging practiced at most hospital pharmacies. What we found is that most repackaging efforts performed at a hospital are labor-intensive, with approximately two-thirds having chosen to use either manual or semi-automated systems [12]. The repackaging efforts are performed by pharmacy technicians, many of which were never trained in industrial pharmacy practices. As a result, the process is both costly and requires a system with double-, triple-, and sometimes quadruple-checking of their work. From an industrial engineering perspective, we note that quality cannot be inspected into a process; that is, the process itself must be designed to ensure quality since manual inspection itself is not fail safe.

Of the third of the hospital pharmacies that use an automated repackager, they do so because they either believe or have been told that the automated repackager will improve patient safety because it is, “a more reliable system.” However, we can state that all but one of the automated repackagers we have seen in practice or heard related to us directly, are considered failures. Many of the pharmacy directors we met with would, “get rid of the repackager,” if they deemed that possible due to a wide variety of quality-related issues (no medication packaged, multiple medications packaged into one unit, crushed and broken medications, sever lack of technical support, etc.). Very similar sentiments were expressed in a recent report by KLAS [9].

In short, the repackaging efforts at the hospital are being performed at cross purposes with the intent of unit-dose administration of medications. That is, the point of unit-dose administration is to increase patient safety by reducing medication-related errors. However, if the repackaging process itself produces medication packaging errors, these are very likely to be passed along to the patient [6]. As one pharmacy director put it, “it used to keep me up at night realizing that we were introducing medication errors with our in-house system.” Thus, our recommendation is that a hospital pharmacy should give due consideration to partnering with a third-party repackager. We define how that repackager should be evaluated next.


5.2 Evaluating a Third-Party Repackager

Our interactions with hospital pharmacies has lead us to the following criteria upon which to evaluate a third-party repackager:

1. First, and foremost, an evaluation of the process that ensures quality throughout. In particular, beyond a third-party repackager utilizing cGMPs, there should be processes in place that the hospital recognizes as processes that they themselves are not utilizing.

2. Turn-around time is critical to the availability of medications. The “drop-shipment method” of a hospital pharmacy ordering from their wholesaler/distributor and then having the wholesaler/distributor directly ship to third-party repackager provides the opportunity for the repackager to repackage the same day that the medications are received. With expedited parcel delivery available in most locations, this will translate into a one-day delay in most cases. This turn-around time appears to be acceptable as long as assurances can be supported that the repackager will perform the repackaging operations within one day of receipt.

3. Repackaging capability is a critical element in acceptance, since most repackaged medications will ultimately be stored in multiple locations within a hospital (pharmacy shelves, carousel system, robotic system, medication cabinets on the floor, etc.). The most-sophisticated repackager that we visited was able to specify the size of the packaging to a greater degree than any in-hospital operation that we have visited. Also implicit in this criteria is the readability of the resulting 1D- or 2D-barcode applied by the repackager.

4. Another aspect of repackaging capability is in terms of the physical state of the medication. Not all third-party repackagers could handle all forms (oral solids, liquids in cups, syringes, etc.). However, some third-party repackagers can handle forms that some hospitals cannot. A full-scale move to a third-party will require that the repackager is technically competent in many repackaging technologies and forms.

5. The “upcharge” for repackaging is another factor that needs to be considered. While the sentiment was expressed by numerous pharmacy directors that the first three items above were more critical, the upcharge for repackaging is also evaluated relative to the cost of repackaging in the pharmacy (ranges on this value were $0.05–$0.10 for oral solids and more for other medication forms). Although pharmacy directors would like the upcharge to be as low as possible, they understand that the repackagers are performing a critical service and a business model that allows the third-party repackagers to prosper is necessary. Ranges on the “acceptable” upcharge were from $0.08–$0.20/unit for oral solids (and more for other medication forms). At present, most hospitals also must pay the shipping charges from the third-party repackager to their hospital.

We believe the above evaluation criteria are straightforward and reasonable. In exchange for output that is more error-free (based on a higher-quality system), the hospital directors
are willing to pay an upcharge that slightly exceeds their current operating costs as long as the repackaged product itself (packaging, barcodes, etc.) is of the same or better quality and the turn-around time is 1–2 days. In addition to the above increased quality of the product, hospital pharmacy directors also believe they will benefit in terms of having pharmacists and pharmacy technicians spending more of their time performing tasks they are trained in doing (which correlates well with job satisfaction and retention).

If the decision is made to partner with a third-party repackager it is still ultimately the responsibility of pharmacy directors for making decisions that provide their patients with high-quality, contaminate-free products even if these products are provided by an outsourcing vendor [4]. Many of the same concerns that exist for outsourcing IV admixture products would be the same for outsourcing medication repackaging. Therefore, it behooves pharmacy directors to take the necessary steps to truly understand the quality of the services provided by these outsourcing vendors [4]. Before entering into any partnership with a drug repackager, the pharmacy director should send an RFI (Request for Information) to each eligible vendor to solicit the following information:

- Licensure and certifications
- Description of repackaging processes
- Quality control processes
- Samples of packaging and labeling
- Barcode capabilities
- List of customer references

Once the RFI process has been completed, the pharmacy director should conduct an on-site audit review of any potential repackaging partners. The purpose of this audit visit is to receive a first-hand view of the facility, meet key leadership and management staff, conduct an on-site record review, and observe the process in person. As part of the site audit visit, the pharmacy director should review the facility’s SOPs, staff training and competency assessment records, quality control records and procedures, quality assurance and quality improvement documents, summary of any actions by regulatory agencies, and any customer complaints and their resolution. The pharmacy director should also tour the facility and check for overall cleanliness, tour inventory areas (including drug preparation areas), distribution areas and product quarantine areas, making sure that there are designated areas for each function. The director should also check building security, room temperature monitoring, refrigerator/freezer temperature monitoring, as well as the security provided for controlled drugs. As part of the audit, the pharmacy director should ask to see all the records for any particular product that has been repackaged recently.

Prior to finalizing the audit, the pharmacy director should ascertain what records will be provided to the hospital from the repacker and how frequently they will be provided. In addition, the director should reach an agreement with the repacker’s leadership team on
how frequently on-site audits will occur. Both of these last steps are critical to help ensure that the hospital pharmacy will receive the highest-quality products from the third-party repackaging partner.

5.3 Hurdles for the Third-Party Repackaging Industry

Our survey of pharmacy directors [12] provided some insight into their concerns with partnering with a third-party repackager. In decreasing order of concern, cost, turnaround/order fulfillment time, quality, product offerings, and insufficient barcode capabilities were the top responses. And with respect to acceptable turnaround time, 25% selected “1 day” as their response, 34% selected “2 days,” 39% selected “3–5 days,” and 2% selected “> 5 days” [12]. Additional feedback is available in the full survey report [12].

Interestingly, the primary consideration in choosing a third-party repackaging partner, product quality, was not the top-rated response in our survey. This implies that product quality was not a “concern” for some pharmacy directors due to their current (positive) experience. But that is not to say that product quality is not the primary consideration and that the quality of the repackaging process will not face a significant evaluation. More than one pharmacy director in our study group remains skeptical that an outside organization will meet this hurdle since they know their current process (complete with multiple inspections in the system) so well and do not always see the improvements a third-party repackager can add. Moreover, it is very difficult to imagine an outside organization caring as much, and having as much at stake, as the hospital pharmacy director. However, since third-party repackagers are competing for business, they do have an incentive to strive for quality [18]. In all cases, a significant amount of time and evaluation has to be invested into the relationship since although the third-party repackager is likely to be held liable in the case of a medication error, the hospital will likely not be viewed without fault. This step of the process will require site visits to the repackager, which will likely involve interviewing multiple members of the repackagers staff. Additionally, the pharmacy director will expect continuous quality reports that detail any problems and the corrective actions taken.

To assist the repackagers in overcoming this hurdle, the pharmacy directors in our study group mentioned steps like meeting FDA requirements (like manufacturers) or establishing an independent accreditation body, who, in addition to specifying initial and on-going requirements, would be directed to perform site visits to ensure compliance. One of the pharmacy directors mentioned that he/she would be more willing to partner with a repackager that had on staff an industrial engineer responsible for continuous process improvement.

5.4 Summary

Currently, we found that less than 10% of hospital pharmacies are working with a third-party repackager [12]. However, the hospital pharmacies surveyed indicated they would consider doing so if issues surrounding cost, turnaround time, and quality were addressed [12]. This is a tremendous opportunity for the third-party repackaging industry if they are able to overcome the hurdles we outlined. Our prediction is that with increased adoption of this
practice both quality and cost will improve; thus, benefiting all participants of the healthcare system.

6. Impact of Pedigree

All of our thoughts on repackaging are based on the current state of the industry. However, in this section we briefly mention an issue that is very much on the minds of many in the medication distribution industry: electronic “pedigree” (or e-pedigree). We then discuss how e-pedigree is likely to impact the case for third-party repackers.

Primarily in an attempt to help protect patients from counterfeit medications, the state of California has issued a mandate that all prescription drugs must have an electronic “pedigree.” Other states have begun to institute similar mandates. The California legislation requires that each prescription medication be uniquely identified and electronically tracked at the lowest unit of distribution through the distribution system, from the point of manufacture through wholesalers/distributors to its final transaction in a pharmacy.

Some of the implications of the e-pedigree mandate is that each organization involved in the “chain of custody,” will be required to add their information to the e-pedigree — up to the point that the medication reaches the organization that dispenses it. For example, the manufacturer, wholesaler, and third-party repackager (if there is one) would need to add their information to the e-pedigree, but the hospital would not. In addition, at each step where the unit size has changed, the smaller units will need to be uniquely identified relative to the other units. Therefore, wherever the bulk quantity of medication is transformed to unit-dose quantities, that party is responsible for assigning unique identification numbers to the unit-dose quantities — again, except for the pharmacy, which will not be required to do so if they are the organization that repackages the medication.

The e-pedigree mandate presents a number of challenges and requires numerous changes to the current practices in the pharmaceutical supply chain. For example, manufacturers must have the ability to create a unique identifier for all prescription drugs in the smallest unit of sale so that they can be tracked. This means that, for example, each manufacturer-produced unit-dose must each receive an RFID tag or 2-dimensional barcode; the one-dimensional barcodes currently required by the FDA do not offer the ability to track medications at the item level, and most manufacturers currently lack the technological infrastructure required to produce these unique identifiers. Another challenge is that every party in the supply chain — for example wholesalers, distributors, third-party repackers — must have the infrastructure to read these unique identifiers. They must then add that they were a part of the chain of custody for these medications. One of the third-party repackers we interviewed already had this capability and was occasionally asked to utilize it today.

Because some of the manufacturers, wholesalers/distributors and repackers in the healthcare supply chain currently lack the infrastructure and processes required to comply with the California e-pedigree standards, the implementation of these requirements has been delayed from 2009 to 2011 to allow time to make such changes. Many believe that the target of 2011 is still ambitious, but most believe this will eventually be recognized as a national
The impact the mandate will have on the position we advocate in this paper is somewhat dependent on the processes and practices in place at individual hospitals. For example, let us consider a hospital that is currently working with a third-party repackager and implementing BPOC. For this hospital, after e-pedigree is implemented, they now will have a method to track individual doses down to the patient administration level. For this increased level of information, they will need to track medications coming into the hospital at unit-dose levels, as well as tracking the administration of medications at this level. This will (likely) require new scanners and software for automatic identification (i.e., linear barcode scanners to either 2D-barcode scanners or passive RFID readers). Given the sheer volume of unit-dose medications that enter the hospital pharmacy, a technology like RFID that does not require line-of-sight for identification is more attractive from the hospital perspective. Of course, due to the cost of RFID tags, those packaging or repackaging into unit-dose quantities will prefer 2D-barcodes.

And now, let us consider a hospital on the other end of the scale with respect to BPOC and other “best practices.” If this hospital is typical, it will receive approximately 80% of its medications in unit-dose quantities. The mandate will require them to verify receipt and check all incoming medications (in unit-dose or bulk form). The remaining 20% of their medications they will continue to repackaging themselves. According to the mandate as currently written, they will not be required to uniquely identify the medications they repackaging. And given that this hospital is currently not implementing BPOC, there is no increase in technology needed at the hospital due to repackaging (but, as noted above, every hospital will be required to be able to read the e-pedigree upon receipt). To this hospital, they will not necessarily take advantage of the e-pedigree in day-to-day operations, but the cost of medications is likely to increase, especially if RFID is the standard identification practice, and new infrastructure investments will need to be made. Thus, this hospital will pay many of the costs, but may not see significant benefits.

So, we see as a theme increased cost, but also the opportunity to provide additional information that may have a positive impact on system safety. However, due to the manner in which the mandate is currently written, it is also possible that an unintended outcome is realized. That is, what is to say that manufacturers will continue to produce medications in unit-dose quantities. Remember that they currently do so for approximately 80% of the medications on the market. But since it would be in both their financial interest (by only uniquely identifying a bottle versus the individual doses) and at least the short-term financial interests of the vast majority of hospitals that are not implementing BPOC (since there will be no cumbersome identification process at the unit-dose level upon receipt of the medications), there will be pressure to halt this practice. Only time will tell how the competing forces of short-term economics and long-term system safety will be resolved.
7. Conclusions

We conclude by stating that our overall recommendation of pharmacy directors should give due consideration to partnering with third-party repackers will not be universally accepted. In fact, we are sobered by the fact that the American Journal of Health-System Pharmacy published a special issue on outsourcing pharmaceutical services in January, 1997, with many of the articles advocating or providing support for the practice. On the other hand, the co-author of our paper that is a pharmacy director is an advocate for this practice after re-evaluating the third-party repacker industry after his negative assessment appeared in 2006 [5]. We believe that many other pharmacy directors will arrive at a similar conclusion if they were to do so as well. The Center for Innovation in Healthcare Logistics (CIHL) will continue to have an interest in this topic. Contact information and additional information on CIHL can be found at: cihl.uark.edu.

Acknowledgments

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References


