Building a Business Case for a Central Sterile Compounding Pharmacy

UHC Pharmacy Financial Performance Committee

Introduction:

In view of recent catastrophic events involving national and regional sterile compounding pharmacies, many hospitals and systems have taken a step back to consider their options in preparing or purchasing these products. Recent UHC pharmacy surveys indicate that a majority of hospitals and pharmacy departments are considering in-sourcing opportunities for preparation of compounded sterile products (CSPs). In an attempt to assist the UHC pharmacy membership, the Financial Performance Committee established a project team in 2013 to analyze the feasibility and develop a business case for establishing a central sterile compounding pharmacy within hospitals and/or health systems. The purpose of this white paper is to report back on the findings and recommendations of this project team to the UHC membership.

Since September 2012, many hospital pharmacy departments have considered their options in preparing or obtaining CSPs for their patient populations. Due to the closure of large compounding/manufacturing pharmacies such as Ameridose and NECC in 2012, the capacity for manufacturing of sterile products has been significantly limited. This limited production in view of increased demand for sterile products has created a significant dilemma for many hospital and system pharmacy departments around the country. One option for the resolution of this issue is for hospital pharmacies to in-source preparation of CSPs by establishing a central sterile compounding pharmacy/facility for their hospital or health system.

Based upon UHC pharmacy surveys conducted this year, many hospital pharmacy departments reported the development of financial models and building a business case for setting up their own central compounding pharmacies. This project team has collected data and information from several UHC hospitals and system pharmacy departments in order to prepare a “best practices” model. This model will allow hospital pharmacies to evaluate their own circumstances and determine the feasibility of setting up their own central compounding pharmacy.

In January, 2013, the UHC Pharmacy Council Financial Performance Committee established a team to work on this project. This project team is known as the Central Sterile Compounding Pharmacy Team (CSCPT). Members of this team were identified and assigned as well as a team leader (see Appendix H). The purpose of this white paper is to report on the findings, recommendations and implementation tools that were developed by this team.

Project Charter

In March of 2013, the CSCPT met and developed a charter for this project . Included in this charter were the following key project components:

- Project description/problem statement
- Scope of the project
- Deliverables
- Proposed financial analysis process
- Potential project benefits

The primary deliverables to be developed by this project team included the development of a financial analytics tool and return on investment (ROI) calculator and recommendations pertaining to quality metrics or outcomes as these related to a centralized sterile compounding pharmacy. Other important aspects identified for this project were delineated by the team in the Project Charter.

Call for Information from UHC Pharmacy Council and Members

In April, 2013, a call for information on central compounding pharmacies was sent out to UHC Directors of Pharmacy. Information was received from several UHC hospital and system pharmacy departments pertaining to efforts to build a central compounding pharmacy. This information was reviewed and discussed by the team as a baseline for moving forward. Only a limited number of pharmacy departments reported making substantial progress in implementing their own central compounding pharmacies. Several of these pharmacy department directors were interviewed by the CCPT.

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During the course of the information collection phase of this project, several systems were identified as having conducted a detailed analysis of the central sterile compounding pharmacy concept. These systems included:

- Froedtert Health (Wisconsin)
- Greenville Health System (South Carolina)
- Lehigh Valley Health Network (Pennsylvania)
- University of Rochester Medical Center (New York)

Each of these systems' pharmacy departments had developed a business plan that justified implementation of a central sterile compounding pharmacy. Two examples of the business case proposals are included as Appendices F & G.

The business plan is generally developed in order to provide a factual, succinct and positive argument supporting implementation of the particular project identified. The business case proposal is generally used as a tool to bring to the hospital or system C-suite or administration to request approval for resources (space, capital funding, equipment and human resources) to support the project. Although business case formats may vary from one hospital or system to another, several of the common components of a business case include:

- Introduction/background/project history
- Strategic rationale
- Resources required (space, equipment, staff)
- Benefits vs. risks of the project (both to implement and not implement)
- Implementation timeline

Each of these various key components are included in one form or another in the two business case studies presented in this paper. The business case proposal should be limited to no more than four to five pages. A presentation on key points of the proposal can be even further limited to five to ten slides for presentation to a group or live meeting.

Development of a business case proposal is highly recommended by the project team as a valuable tool to define the project, identify benefits and provide detailed financial analysis for a central compounding pharmacy to be presented to the hospital or system administration for approval.

Organization of the Project Team and Work Process

Following the development of the project charter and request for information from the UHC pharmacy community, three sub-groups were established in order to investigate and develop recommendations in the following key areas:

- Financial analytics and ROI calculation
- Automation/technology options available currently on the market
- Quality assurance and metrics

This project team met on a regular (monthly) basis throughout 2013 in order to collect data, review and analyze existing/pending programs and develop the necessary tools to allow hospitals and pharmacy departments to conduct their own assessment. The remainder of this report will focus on the findings and recommendations of these three groups.

Group One – Financial Analytics and ROI

Financial analytics and ROI are an integral part of every well formed business case. As hospitals and health care systems across the nation are being asked to provide more services with less resources, financial analytics and ROI are major consideration factors for the C-suite. A successful business case should provide monetary justification for the compounding and, if possible, demonstrate the compounding center's ability to contribute to the overall financial sustainability and strategic plan of the organization.

The financial justification consists of four key components: define the current state, identify the investment required, project the future state, and calculate the ROI. Defining the current state requires identification of products that can potentially be produced by the compounding center and calculating the current operating costs. Consideration should be given to three product groups. Commercially sourced pre-mixed IVs are often associated with a significant premium for their ready-to-use convenience and should be reviewed for margin opportunity. Second, all other ience,duct groups. First, cts that can potentially be produced outsourced IV products, which likewise are associated with significant premiums and have recently been the spotlight of major quality concerns, should be identified. Finally, in-house manually compounded IV products should be reviewed for potential operational gains if compounded by the compounding center.

After the current state has been defined, the investment required should be thoroughly investigated and quantified. The major considerations in this section include but are not limited to: overhead, automation, and human capital. Information related to automation options will be covered in a later section. These three components will likely represent the majority of the investment required to complete the compounding center project. Likewise, these three components will directly impact the ROI for the project and will likely be the rate-limiting factor for the C-suite. Efforts should be made to keep this section as lean as possible without affecting the overall quality, safety and operations of the compounding center.

With all other factors known, the future state can be projected. In this section the operating costs of products identified for conversion to the compounding center are calculated. Care should be given to accounting practices to ensure that double cost accruing does not occur with costs accounted for the investment section of the financial justification. In the simplest form, the operational costs of the future state would be the cost of drug and supplies for the final IV products produced.

The final step in the financial justification involves the calculation of the ROI. The ROI is a common financial performance analytic used to evaluate the efficiency of an investment. The ROI will give the C-suite insight on the expectation of reclaiming the capital dedicated to the investment of the compounding center. The ROI can be simply calculated by the gain from the investment (in this case drug cost savings) minus the investment, divided by the investment. The ROI can be calculated over various periods of business; however, there is a growing trend among hospital or health system leadership to favor the short term. For this reason, it is recommended that both a three and five year ROI be presented.

Given the crucial contribution of financial justification to the business case, the financial analytics sub-group of CSCPT sought to provide the UHC membership with a tool to facilitate the gathering and calculation of the aforementioned information (see Appendix A). The presented financial justification tool is intended to give pharmacy leadership a thorough yet succinct overview of the financial feasibility of opening a compounding center. The tool is constructed in Microsoft Excel and contains three spreadsheets that cover the 4 key components of financial justification previous discussed. The first spreadsheet consists of 24 questions that can be answered in the space provided. The answers are used to auto populate and calculate both a three year and five year ROI on the ROI tabs of the workbook.

Group Two – Automation/Technology Analysis

A subgroup was formed to research the availability of automated technology that would be used in a Centralized Sterile Compounding Unit. The committee decided that chemotherapy compounding would not be a part of this assessment. The main focus of this section will be IV Automation, Tabletop Technology, and Repeater Pumps/Rapid Fill/Syringe Devices.

There are a limited number of vendors that sell IV Automation products. The three main producers of IV Automation are, Health Robotics IV Station™, Intelligent Hospital Systems (RIVA™), and Baxter Healthcare (IntelliFill™). In general, the estimated costs of acquiring such equipment can range from $750,000 to $1.5 million for the unit alone. The return-on-investment can be significant based on reduction in waste, improvements in medication safety, along with the redeployment of pharmacists and technicians to higher value activities. In addition, the return-on-investment should include the money saved from what would have been spent outsourcing these products.

A number of critical issues that need to be considered are space requirements, cleaning expenses, software integration/interfaces, and limitations of the equipment designs (e.g. not all robots can utilize ampoules, certain IV bottles, non-standard vials).

All of these vendors will provide a higher degree of accuracy compared to manual compounding processes. The automation provided in each of these units, allows for higher productivity with an associated reduction in labor, while operating throughout the day.

A compilation and comparison of the three vendors is available in Appendix B. Tabletop Technology is produced by five main vendors which includes Pearson Medical Technologies, Medical Packaging Inc., Euclid, Amerisource Bergen, and Pentapack (see Appendix C). The equipment supplied by these vendors offers an array of services for both solid and liquid dose packaging. In general, the estimated cost of purchasing solid dose packaging equipment can range from $12,000 to $135,000 for one unit. Additional costs and fees for service and supplies should also be considered when comparing vendors. Individual unit dose costs for solids range from $0.006 up to $0.0106. Individual unit dose costs for liquids range from $0.016 up to $0.1062.

When comparing software features a database source such as Gold Standard or First Databank is available for data integration with Medical Packaging, Inc., Amerisource Bergen, and Pearson Medical Technologies, LLC. Currently there is no networked version of software available on the market for multiple machines, but Pearson Medical Technologies, LLC has one in development. Packaging size options vary ranging in speed from 48 to 120 solid dose packages per minute. Each vendor also has customizable templates varying to different degrees regarding the fields, formats, lettering, and picture imaging.

From a service standpoint each company offers a one year limited warranty on the tabletop packager. Pearson Medical Technologies, LLC, offers a 24 hour telephone support service that can be purchased with their Annual Customer Agreement. For further comparison a product feature summary is available in Appendix C.

Additional equipment to consider purchasing for a compounding pharmacy includes Automated Syringe Fillers and Repeater Pumps. An automated syringe filler is designed for rapid batch filling, and labeling of sterile syringes. By including syringe fillers in your compounding pharmacy it allows for large batch preparation of a common use drugs such as Cefazolin syringes without disruption to the IV automation. Baxter currently has the RAPIDFILL Automated Syringe Filler available on the market that fills syringes in volumes up to 12 ml. Repeater Pumps are also necessary to include for reconstitution of drugs, and IV admixing and filling of bags. Repeater Pumps have a small footprint fitting within a standard hood or can be mounted on a stand. Repeater Pumps can also be purchased from Baxter. For any additional equipment purchased there will be ongoing supply costs to also factor into the budget.

Group Three – Quality Processes and Metrics

Quality Assurance: Sterility

A beyond use date (BUD) is assigned to all compounded sterile products (CSPs). The BUD is the time after which a CSP cannot be administered. The BUD is based on two factors: (1) the drug's chemical stability and (2) the drug's sterility - the BUD will always be whichever is shorter. USP Chapter <797> defines BUD based on sterility and drug compounding risk level (Table 1 below). End product sterility testing is required when the USP <797> BUD is exceeded.

Table 1: USP <797> Beyond Use Dates

Risk Level	Room Temperature	Refrigerated	Frozen
Immediate Use	1 Hour	N/A	N/A
Low with 12 hr or less BUD	12 hours or less	12 hours or less	N/A
Low	48 hours	14 days	45 days
Medium	30 hours	9 days	45 days
High	24 hours	3 days	45 days

Sterility Testing: Membrane Filtration versus Direct Inoculation

Sterility testing is required when the BUD exceeds USP <797> limits to ensure quality and safety. USP Chapter <71> sterility tests define two methods for sterility testing; direct inoculation and membrane filtration. For direct inoculation the sample is introduced directly into liquid media whereas membrane filtration multiple samples are filtered through one filter. Membrane filtration is the preferred method to test for sterility.

Quantity of Samples to Test

USP <71> provides recommendations for the minimum number of articles to be tested in relation to the number of articles in the batch (See Appendix D - Tables 2 and 3 abbreviated from USP <71>). Different CSP types have different test requirements for the quantity per container of a product as well as for the quantity per batch

Quality Assurance: Standard operating procedures

Standard operating procedures (SOPs) are required for every aspect of compounding, including each component of USP <797> and USP <71>. The more thorough and detailed the SOP, the less variability in a process. Examples of SOPs that will be needed for your facility include but are not limited to the following table. Additional guidance on quality assurance recommendations and SOPs are included in Appendix E.

SOP Examples	
General SOPs	Personnel qualifications Documentation practices
Environmental Monitoring	Viable Air Sampling Surface Sampling Particle Testing Airflow and Pressure differential Monitoring Temperature and Humidity Monitoring
Cleaning	Cleaning and Disinfecting (pharmacy, compounding areas, ante room, etc)
Training and Competency	Personnel Aseptic Media Fill Testing Hand hygiene and garbing Gloved fingertip sampling Orientation and training and competency evaluation General Conduct
Inventory storage	Inventory storage and handling
Compounding Processes	Stability and assignment of BUD Use of automation or compounding devices Non-automated compounding Sterility testing for BUD extension Quality release and final checks of CSP Labeling and packaging

Quality Assurance: Vendor Assessment

ASHP has created tools for assessing and choosing an outsourcing vendor. The outsourcing sterile products preparation contractor assessment tool is a good tool for assessing vendors that a hospital may continue to outsource to or use internally to validate their own compounding practices.

Building a Business Case for a Sterile Compounding Pharmacy

Several members of the CSCP Team have already completed an analysis of these major components to implement a central sterile compounding pharmacy. Part of their presentation to hospital/system administration included a business case proposal. Two examples of such a business analysis and plan are included in this paper in order to provide guidance and clarity on preparing such a report (see Appendices F & G). Key components of a business case include:

- Introduction/background
- Strategic rationale
- Resources needed

- Benefits vs. risks
    - Risks of opening a central compounding pharmacy
    - Risks of not opening a central compounding pharmacy
- Financial analysis
- Implementation timeline

Summary and Conclusions

Recent deleterious events involving large regional and national sterile compounding pharmacies have left an indelible mark on health systems, pharmacies and our patients. Bold and decisive steps must now be taken in order to restore patient safety, confidence and stability to our health systems and pharmacies. One such step that many hospital and system pharmacies are taking is to design and implement free standing sterile compounding pharmacies. This is a highly individualized decision-making process that must consider many factors not the least of which involve financial, automation/technology and quality assurance components.

A primary purpose of this white paper is to provide basic information for UHC members and others to assist in this decision-making process. This paper is not meant to be an "all inclusive" document covering this complex topic, but rather a basic guideline for pharmacists to follow to begin the evaluation and implementation process. Additional factors and detail may need to be evaluated by each hospital or system in order to develop the optimal end product for their specific patient population.

APPENDIX A –
Sterile Compounding Center Financial Justification Worksheet

APPENDIX B
IV Automation Summary

Vendors:

1. Health Robotics IV Station and IV Station Onco™
2. Intelligent Hospital Systems RIVA™
3. Baxter Healthcare IntelliFill™

In general, estimated cost for IV automation can range from $750,000 to $1.5 million for the unit alone. Researchers have demonstrated that IV automation for compounding reduces medication waste, improves patient safety, and allows for the reallocation of pharmacists and technicians to higher value activities.

Advantages:

- Reduces the risk of repetitive strain injury
- Provides a higher degree of accuracy than manual compounding
- Reduces the opportunity for contamination
- Improves productivity
- Improved documentation of compounding activities

Concerns to consider:

- Cost and space requirements are high
- High initial costs and expensive validation processes
- Limitations of the Robotics – (e.g. not all robots can utilize ampoules or IV Bottles)
- Software interfaces and integration

Intelligent Hospital Systems - RIVA™

- ISO class 5 compounding environment and ISO class 5 vestibules for loading inventory into storage carousels. Storage carousels hold the compounding supplies and drug vials.
- Contained air handling for sterile compounding can also be used for hazardous drugs (e.g. chemotherapy)
- RIVA prepares up to 50 doses per hour
- RIVA™ is equipped to safely measure very small doses. Highly sensitive scales weigh each preparation before and after every fluid addition.
- No human access to compounding area during compounding process
- Uses multi sizes of syringes and IV Bags
- Identifies drugs, diluents and final containers by barcode reader optical imaging. Also identifies vials by height and expected weight.

- Adjusts diluents and allows for serial dilutions
- Provides a detailed electronic audit trail with easy to create reports for verification, audit, and compliance
- Check weights of volume dispensed

Health Robotics IV Station™

- Automatic dosing of medications from their commercial containers (vials only, ampoules are not supported)
- Automatic reconstitution of powder drugs with appropriate diluents
- Identification of final containers (syringes, IV bags) with Bar-Code labels
- Handling of the preparation cycle within an ISO 14644-1 Class 5 air quality environment.
- Overnight sterility control by UV-C lamps
- Controlled access with real-time identification of authorized users by multiple ID / password credentials (optional support of common readers such as biometric face recognition, magnetic or RFID badge)

Baxter Healthcare IntelliFill™

- IntelliFill™ provides an ISO class 5 compounding area
- Automates preparations of small volume medications in 12 ml syringes for doses from 0.5 ml to 11.5 ml
- No human access to compounding location
- Drug cabinet holds up to 50 different drugs and multi-days inventory
- Fills and caps sterile syringes
- In reservoir mode, produces up to 600 syringes per hour and in patient specific mode, up to 70 syringes per hour
- Reconstitutes, multi-dose draw, serial dilution
- Completes weight check, bar code scan, and picture of vials
- Produces customized labels

APPENDIX C
Tabletop Technology Comparison Chart

	Pearson Medical Technologies, LLC	Medical Packaging Inc.	Euclid	Amerisource Bergen	Pentapack
Machine	**iPackRx**	**Auto-Print, Auto-Print Express 90**	**Cadet, Cadet Twin/s**	**FastPak**	**HP500, HP550**
Barcodes	States can do all barcodes: 2-D, Data Matrix, Aztec, Stacked, and Linear.	States can do all barcodes: 2-D, Linear, Matrix, Aztec, and Stacked.	Linear, 2D, and Aztec	2D and Linear	There are several software options but based on the selection all primary barcodes are available.
Inline Barcode Verification	Yes. Can use own scanners too.	No inline verification or read on product when finished.	Pill Camera is only to capture images of product at site level (no images are downloaded anywhere and can only import black/white images).	Horizontal feeder	This is an option using the software provided by PentaPack.
Server	Microsoft SQL Server - Currently have Express version and are exploring Enterprise version. Express version does not allow for any integration/interfacing capabilities.	Microsoft SQL Server.	Does have a SQL server built into it, but due to the number of labels all users use access database instead.	Microsoft SQL or VM	Stand alone PC.
Speed	48 packages per minute	60 packages per minute on Model 9300; 90 packages per minute on the Express 90 model.	Cadet = 60 per minute, Cadet Twins 1.5, 2x2 =120 per minute (difference in Cadet Twins is width 1.5, 2 with 2 as the most popular for Vitamin E)	80 packages per minutes	100 products per minute with batch size options from 20 to 5,000 units.
Package Size Options	4 package size options. Does not require a hardware change - automatic adjustment.	Variable (7 standard options), (8 disks, 6 special feed disks). Could add additional disks with the Express 90 and they work with the 9300 too.	8 disks, 4 chutes for Cadet, 9 disks/5 chutes for Twin - so only one package size template option.	Two standard options that allow for single tablet/capsules and fit easily within ADCs or a larger package that allows for multiple items (typically used in LTC.)	Can package liquid dose cups, suppositories, tablets, and capsules all in one machine. 5, 15ml for liquid, variable for tablet. The HP550 has a larger capacity and could do up to 40 ml liquid volume.

	Pearson Medical Technologies, LLC	Medical Packaging Inc.	Euclid	Amerisource Bergen	Pentapack
Database Source	m:Print software that uses Gold Standard with Premium, FDA with Basic	PakEdge software that uses First DataBank.	All machines use the same software but there is no database source and no interest from company in pursuing it.	First DataBank	
Printer	Thermal - no ribbon.	Thermal Transfer Ribbon.	Thermal Transfer Ribbon		Thermal transfer
Pill Feeder	Yes - intelliCount Universal Pill Feeder	Yes - Auto-Print Pill Feeder available for 9300 model only - not on the Express 90 model.	No Autofeeder	Yes - AutoPac is optional autofeeding device for runs of 600+ packages	Fixed manual feed tray for solids and Repeater pump for liquids.
Compatibility	Windows 7, 32 and 64 bit.	Windows 7, both 32 and 64 bit.	Windows 7, both 32 and 64 bit		Windows 7, both 32 and 64 bit
Data Backup	Yes - setup as on demand but can be scheduled.	Yes. Standalone PC and PC needs connected to internet. Can setup as on demand or schedule backup. Backup is only a text file and does not include any images.	Computer can be networked to be backed up every night on the network file.		
Features	Tall man lettering, drug images, unlimited templates, 5 customized fields, site specific pictures can be added, default expiration date can be individualized, can be setup for half tablets - Software modification to allow max length of 2" to 2.5' for package size.	Tall man lettering, variable length packaging up to 2x2, unlimited templates, customized fields, can run multiple systems from one screen and does have sequential numbering option. Group templates are not customizable and have 3 options currently - Verifier, Administrator, Tech or none. Can not add to or change these user group templates.	Tall man lettering, customizable fields, only one template in the software.		Thermal forming station to form blisters specific for the size / shape of the solid being packed. Multiple packing materials available based on need.
Crush Technology	Yes with pill drop detection sensor.	No Crush Technology	No Crush Technology	Yes - Horizontal feeder.	No

	Pearson Medical Technologies, LLC	Medical Packaging Inc.	Euclid	Amerisource Bergen	Pentapack
Liquid Machine	Currently in development with goal to have a product end of 1st quarter 2014. Pulled previous machine from market due to packaging materials.	Yes - FluidDose (22 units/minute). New FluidDose machine uses syringes in 10, 20, 30 ml size with a leur lock and tubing. No Baxa pump anymore. The screen is larger so calibration is easier and there are more pinch valves now on the machine.	Yes - Speedy Wet Cadet (32 units/minute) unless it's a cough syrup then it's about 12 units/minute.		Yes - all in one machine up to 15 ml and 40 ml based on the model, and uses a Baxa repeater pump.
Interface to ADM	No interface capabilities.	No interface capabilities.	No interface capabilities. Can export to excel file but it's strictly a stand alone device with a Microsoft Access database.		No interface capabilities.
Web features/multiple machines/sites	In development. Plan is to have networked version of mprint software.	Requires separate license for each site. (printer regulates the license). No networked version.	Requires separate stand alone equipment and individual machine formulary maintenance.		NA
Updates - how often, software/technology?	Have to purchase Annual Customer Support/Maintenance agreement to receive updates for both software and drug database.	Updates are automatic. PakEdge updates come separately from First Databank updates.	No database so rarely receive updates to either software or equipment.		
Lease Options	Yes - 12 to 84 months, deferred payment programs, and up to 9 months with no payments.	Leasing is an option.	No Lease Option.		No Lease Option.
Warranty	1 year limited.	1 year limited.	One year on parts and labor in plant. Customer still responsible for freight and shipping.		1 year on mechanical + electrical parts, no guarantee on wear, labor hours or travel costs.
Service Agreement	Includes 24 hr telephone support with purchase of Annual Customer agreement.	1 year free technical phone support to MPIs 800#.	No Service Agreement - can send machine in to get it fixed but then may receive refurbished model as permanent replacement. Some phone support is available as needed with separate fee.		

	Pearson Medical Technologies, LLC	Medical Packaging Inc.	Euclid	Amerisource Bergen	Pentapack
Cost per dose / Supply Costs	Class A Packaging. Cost per dose estimate is: 1.25" per pack =$0.0067 cost per UPD up to 2.00" per pack is $0.0108.	Cost per dose estimate is: For the Autoprint it's 0.01 total cost per dose. Fluiddose: Small Cups = $0.0962, Med Cups = $0.1012, and Large Cups = $0.1062.	Supplies are the same for the Cadet and Wet Cadet; however the Twins have different materials. Supplies have to be ordered from Euclid. Costs per dose estimate is: Cadet=$0.008, Twin=$0.0056, Twin2x2=$0.0066, Wet=$0.08		Solids = $0.006 Liquids = $0.016

APPENDIX D
Sterility Testing and Beyond Use Dating (BUD)/USP 71 Guidelines

Quality Assurance

Sterility

A beyond use date (BUD) is assigned to all compounded sterile products (CSP). The BUD is the time after which a CSP cannot be administered. The BUD is based on two factors the drugs chemical stability and the drugs sterility; the BUD will always be whichever is shorter. USP Chapter <797> defines BUD based on sterility and drug compounding risk level (Table 1). End product sterility testing is required when the USP <797> BUD is exceeded.

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Sterility Testing: Membrane Filtration versus Direct Inoculation

Sterility testing is required when the BUD exceeds USP <797> limits to ensure quality and safety. USP Chapter <71> sterility tests define two methods for sterility testing; direct inoculation and membrane filtration. For direct inoculation the sample is introduced directly into liquid media whereas membrane filtration multiple samples are filtered through one filter. Membrane filtration is the preferred method to test for sterility.

Quantity of Samples to Test

USP <71> provides recommendations for the minimum number of articles to be tested in relation to the number of articles in the batch (Table 2 and table 3 abbreviated from USP <71>). Different CSP types have different test requirements for the quantity per container of a product as well as for the quantity per batch.

Table 2: USP <71> Minimum Quantity to be Used for Each Medium

Table 2. Minimum Quantity to be Used for Each Medium	
Quantity per Container	Minimum Quantity to be Used (unless otherwise justified and authorized)
Liquids (other than anitbiotics)	
Less than 1 mL	The whole contents of each container
1–40 mL	Half the contents of each container, but not less than 1 mL
Greater than 40 mL, and not greater than 100 mL	20 mL
Greater than 100 mL	10% of the contents of the container, but not less than 20 mL
Antibiotic liquids	1 mL
Other preparations soluble in water or in isopropyl myristate	The whole contents of each container to provide not less than 200 mg
Insoluble preparations, creams, and ointments to be suspended or emulsified	Use the contents of each container to provide not less than 200 mg

Table 3: USP <71> Minimum Number of Articles to be Tested in Relation to the Number of Articles in the Batch

Table 3. Minimum Number of Articles to be Tested in Relation to the Number of Articles in the Batch

Number of Items in the Batch	Minimum Number of Items to be Tested for Each Medium (unless otherwise justified and authorized)[*]
Parenteral preparations	
Not more than 100 containers	10% or 4 containers, whichever is the greater
More than 100 but not more than 500 containers	10 containers
More than 500 containers	2% or 20 containers, whichever is less
✦*For large-volume parenterals*	2% or 10 containers, whichever is less
Antibiotic solids	
Pharmacy bulk packages (<5 g)	20 containers
Pharmacy bulk packages (≥5 g)	6 containers
Bulks and blends	See *Bulk solid products* ✦
Ophthalmic and other noninjectable preparations	
Not more than 200 containers	5% or 2 containers, whichever is the greater
More than 200 containers	10 containers
If the product is presented in the form of single-dose containers, apply the scheme shown above for preparations for parenteral use.	
Devices	
Catgut and other surgical sutures for veterinary use	2 % or 5 packages, whichever is the greater, up to a maximum total of 20 packages
✦Not more than 100 articles	10% or 4 articles, whichever is greater
More than 100, but not more than 500 articles	10 articles
More than 500 articles	2% or 20 articles, whichever is less ✦
Bulk solid products	
Up to 4 containers	Each container
More than 4 containers, but not more than 50 containers	20% or 4 containers, whichever is greater
More than 50 containers	2% or 10 containers, whichever is greater

[*] If the contents of one container are enough to inoculate the two media, this column gives the number of containers needed for both the media together.

Standard Operating Procedures

Standard operating procedures (SOPs) are required for every aspect of compounding, including each component of USP <797> and USP <71>. The more thorough and detailed the SOP, the less variability in a process. Examples of SOPs that will be needed for your facility include but are not limited to the following table.

SOP Examples	
General SOPs	Personnel qualifications Documentation practices
Environmental Monitoring	Viable Air Sampling Surface Sampling Particle Testing Airflow and Pressure differential Monitoring Temperature and Humidity Monitoring

Cleaning	Cleaning and Disinfecting (pharmacy, compounding areas, ante room, etc)
Training and Competency	Personnel Aseptic Media Fill Testing Hand hygiene and garbing Gloved fingertip sampling Orientation and training and competency evaluation General Conduct
Inventory storage	Inventory storage and handling
Compounding Processes	Stability and assignment of BUD Use of automation or compounding devices Non-automated compounding Sterility testing for BUD extension Quality release and final checks of CSP Labeling and packaging

APPENDIX E

Sterile Compounding Quality Assurance Spreadsheet/Checklist Document

APPENDIX F
Case Study – Building a Business Case for a Central Compounding Pharmacy/Greenville Health System Pharmacy Department (2013)

Compounding Pharmacy
Business Case
July 25, 2013

Introduction

In response to recent events involving national manufacturing pharmacies, the GHS Pharmacy proposes opening a central fill pharmacy for compounding and stocking a defined list of sterile and non-sterile products for use by the five campus pharmacies. This pharmacy will prepare low and medium risk sterile preparations. It will not prepare high risk preparations.

The bulk of preparations done in this pharmacy will be IV sterile preparations. These preparations are predominantly used for the more acute patients. Prefilled syringes used by the CRNAs during surgery represent a significant portion of the sterile preparations that will be provided from this facility.

The non-sterile products will be used throughout the system in all levels of care; adult and pediatric alike.

Examples of other drugs/preparations include IV antibiotics, OR syringes such as atropine, ephedrine and phenylephrine and epidural syringes and Oxytocin bags for pain management. These will also be used for inpatient or outpatient surgery.

These preparations will be dispensed by all of the GHS inpatient pharmacies for use on their campus.

The new pharmacy will eliminate, or significantly reduce, the need to outsource packing and preparation of products while providing the service at a significantly reduced cost. The use of robotics will improve patient safety by improving the accuracy and sterility of our intravenous preparations. The automation coupled with an extensive QA program will allow GHS to receive extended dating sufficient to ensure these products are available when and where they are needed.

The goal of this project is a hub and spoke distribution model for all campuses with improved patient safety, inventory control, and cost savings.

Strategic Rationale

The failure of New England Compounding Center (NECC) and Ameridose to safely prepare these products has had a severe and immediate impact on GHS forcing us to rethink our strategy for providing these preparations. Ongoing regulatory findings do not look favorable for these compounding pharmacies.

In addition, The Joint Commission standards require all preparations to be available in the most readily usable form and that compounding of sterile preparations by nursing should be eliminated. This requirement was strengthened in the 2013 Medication Management standards.

"Medications in patient care areas are available in the most ready-to-administer forms commercially available or, if feasible, in unit-doses that have been repackaged by the pharmacy or a licensed repackager. MM.03.01.01 EP10, MM.03.01.03 EP3. "

The use of the Robotic IV Automation (RIVA) system will allow the pharmacy to accommodate this requirement for the sterile preparations.

In addition, USP <797> guidelines[1] severely limit the beyond-use dates (BUD) of pharmacy compounded sterile preparations. Syringes prepared within an existing GHS pharmacy will receive a 30 or 48 hours room temperature BUD whereas syringes prepared by a properly designed and managed compounding pharmacy may receive up to a 60 day BUD. The use of Robotic IV Automation (RIVA) robots within the clean room ensures both the sterility and accuracy of the final product without the lot-to-lot variations caused by manual preparation. The combination of facility design, automation, and a QA program will allow for extended dating of these preparations and for storage in Omnicells for use by nursing and anesthesia immediately when needed.

Furthermore, the addition of the Pentapack repackager will allow the pharmacy to resume packaging oral products and expand the number of unit-dose liquids we are packaging and to replace many of the oral syringes currently being extemporaneously batch prepared in the Children's Pharmacy.

The ultimate goal of this project is to meet the needs of our patients. In the context of this proposal that need is measured by sterility and accuracy of our compounded sterile preparations and the availability of the products at the point of care. This proposal will meet both of those goals. The best option for GHS is for the pharmacy to prepare these products in a properly designed and managed pharmacy.

[1] Issued by U.S. Pharmacopoeia (USP), the <797> regulation governs any pharmacy that prepares "compounded sterile preparations" (CSPs).

Resources Needed

The primary components of the central fill pharmacy include:

- A 1000 sq ft USP <797> compliant clean room (ISO 7)
- Two Intelligent Hospital Systems RIVA robots to prepare sterile IV bags and syringes
- One 6' horizontal laminar air flow clean bench for manual sterile compounding
- A Pentapack HP500 unit-dose packaging system for unit-dose oral solids and liquids
- Areas for inventory receiving, storage, and quarantine
- Total square footage for the central fill pharmacy to equal 3000 sq ft located within MDC
- 3.0 technician FTEs and 1.0 of a pharmacist's FTE

Benefits vs. Risks

Benefits:

- Decreased dependence on and potential liability associated with using compounding manufacturers
- Assurance of the sterility and accuracy of the compounded sterile preparations needed for our patients
- Improved ability to adapt to shortages and back orders
- Improved compliance with standards requiring medications available in the most ready to administer form possible
- Decreased need for nursing to compound products in patient care areas
- Improved Beyond-Use Dating for pharmacy compounded sterile preparations. (Example: 30 days vs. 30 hours.)
- Centralized purchasing and oversight of the medications repackaged or prepared
- Improved packaging of unit-dose solid and liquid oral medications

Risks of not opening a central compounding pharmacy:

- Continued sterility and QA concerns associated with the use of compounding manufacturers
    - Examples: NECC, Ameridose, NuVision, and The Compounding Shop.
- Potential for the FDA to shut down or severely limit the compounding manufacturers' ability to provide compounded sterile preparations (CSPs)
- Concerns of increased regulations associated with product tracking
- Limitations on our ability to stock ready to administer products in the patient care areas
- Escalating Cost of outsourced products (sterile and non-sterile.)

Risks after opening a central compounding pharmacy:

- Potential change in regulations that limits the scope of the operation
- A failure of the QA plan

Ongoing savings will occur based on decreased production cost versus the cost of outsourcing. Additional savings will be seen by providing more options and a quicker response time for the pharmacy to accommodate drug shortages and back orders.

Implementation Timeline

Construction and licensure is estimated to take 3 months. After licensure, the pharmacy will immediately begin repackaging non-sterile products for use by the hospitals. At the same time, it will begin compounding sterile preparations with standard expiration dating (low volume batches) and will use these products for QA testing. Successful QA testing will allow the pharmacy to extend the dates. We anticipate 3 months of testing before we begin assigning extended dating to the sterile preparations.

Financial Analysis

See financial analysis attached.

APPENDIX G
Case Study – Building a Business Case for a Central Compounding Pharmacy/University of Rochester Medical Center Pharmacy Department (2013)

University of Rochester Medical Center
Robotic Sterile Product Manufacturing and Workflow Management
For a Central Sterile Compounding Pharmacy
Department of Pharmacy

Business Plan
December, 2012

Summary

In the wake of NECC Disaster and other compounding pharmacy issues, there were several immediate effects. Several large "outsource" compounding pharmacies were closed and the NYS Board of Pharmacy blocked the shipment of compounded products that were not "patient-specific." Multiple compounding pharmacies were inspected by FDA with many findings of poor practices and non-compliance with standards. Like most institutions, our medical center had outsourced multiple products to these operations (>50 line items at one hospital). We implemented an interim plan to insource the most critical of these items. For others we regressed to dispensing vials (e.g. in the Operating Rooms). Long-term, we need a plan to insource our compounded sterile products (CSP) to eliminate dependency on an unreliable outsourcing market. This plan will involve both technology and space to safely and efficiently address these needs.

Space will be addressed by building an off-site facility that meets or exceeds USP-797 standards for compounded sterile products. The facility will be designed with the capability of meeting cGMP standards in case the standards are revised in the future. We will establish standards and processes to assure high-quality production, storage and distribution of CSPs for medical center affiliated institutions. This includes the introduction of robotics and workflow management. The facility will operate in a fiscally responsible manner to reduce overall costs.

Technology

Robotic compounders for preparation of compounded sterile products (CSPs) have evolved significantly over the past 5 years, and are rapidly emerging as a valuable and cost-effective technology for medium to large hospitals. These devices represent a self-contained, totally automated, ISO 5 environment which meets all regulatory requirements and standards (USP 797, TJC, CMS, etc) for the preparation of ready-to-administer, labeled CSPs for adult and pediatric patients. In addition to preparation using precise gravimetric measurements, the robotic devices also have redundant mechanisms (bar code and digital image verification) to assure proper product selection and record both digital images and time-stamped documentation of the manufacturing process to provide a highly reliable audit trail. In addition, IVA workflow management technology can also incorporate these safety and quality standards for those products that are produced manually. Combining workflow technology with IVA Robotics offers a comprehensive solution to the high-risk process of sterile product manufacturing.

Like most automation, the robotic compounder is most efficient at doing batch production of single standardized products; however they are also capable of preparing single or small batches of custom solutions. This may represent sending high-risk, complex, error-prone solutions (e.g. NICU IV solutions) to

the robot. The robots are capable of preparing small volume CSPs, large volume CSPs and syringes, allowing considerable scope for potential batch production.

The return on investment is based upon the following components:

- In-sourcing several products that we currently outsource at a significant premium. This includes frozen antibiotic premixed solutions, epidural solutions, pre-mixed controlled substance infusions, electrolyte infusions, and other miscellaneous infusions (e.g. oxytocin, nicardipine, etc).
- Use of larger, cost-effective bulk vials in the production of batches of standard CSP products.

This return on investment is based upon a conservative estimate of the potential throughput of the devices (25 units per hour), and a limited potential selection of products to be managed on the robots. If the production capability of the robot is closer to the number quoted by the manufacturer, the ROI could be greater due to the ability to shift more products to the robots, and/or enhanced safety by preparing more custom products on demand.

The importance of moving towards insourcing CSP production using automation and workflow management has been recently highlighted by the closing of Ameridose by the FDA and the regulatory actions against PharMedium by the NYS Board of Pharmacy which has left our medical center without access to these outsourced products. The unpredictable nature of the future and the liability concerns of working with outsource compounding pharmacies makes it imperative that we develop a capacity to meet our needs internally.

The implementation does not involve complicated interface development. The information is transmitted to the robot software using a standard HL-7 interface, however this may require some build with eRecord/ISD resources involved. There is initial development and then on-going maintenance of the library of sterile products in the robot software. The robotics and IVA workflow management system work from the same software platform, avoiding the need to maintain multiple interfaces and libraries.

The potential advantages of implementing robotic manufacturing and automated workflow management of CSPs include:

- Cost savings of over $10,000,000 for a 5 year period. Considering the useful life of this technology exceeds 7 years, the projected annual savings increases substantially after year 5 although not part of the ROI.
- Enhanced safety due to reduction in the potential for human error, self-contained clean environment, redundant product verification, and integrated labeling process.
- A comparable level of quality and audit capabilities for both machine and manually produced doses of CSPs.
- Improved labeling of sterile products compared to current capabilities of eRecord.
- Audit capabilities that include digital image capture, product verification, time-stamped documentation of gravimetric measurements, etc.
- Greater internal control of CSP production that is less susceptible to price increases, manufacturing shortages or delays, and availability due to regulatory actions and recalls.

This proposal includes technician and pharmacist FTEs needed to maintain the operations of a central compounding facility taking into account NYS regulations regarding pharmacists to technician ratios and assuming a production schedule of 12 hours per day, 5 days per week. This includes set up, maintenance, and trouble-shooting of the robots; maintenance of product library in robot software; sterility testing

procedures and documentation for end-of-use dating verification; production and storage of products; and packaging and shipping to multiple facilities.

Product selection:

There are currently two leading vendors in this business sector: RIVA (Intelligent Hospital Systems) and Health Robotics. The Health Robotics products are smaller, less expensive per unit, and while requiring greater human interaction due to more limited storage capacity, have an estimated and observed throughput capacity similar to RIVA per device. Due to the lower cost per unit, we can include additional units (4) with greater overall throughput while also incorporating automated workflow management at a similar cost. In addition, Health Robotics includes both robotic production and manual workflow technology on the same platform. This provides a more comprehensive approach to safety and quality for CSP production. Therefore, it is recommended that we consider Health Robotics as the preferred vendor for implementation at our medical center.

Business Case:

	Year 1	Year 2	Year 3	Year 4	Year 5	Total
Annual Savings:						
Savings from Insourcing for Health System (approx 1100 beds)*	$1,983,474	$2,023,143	$2,063,606	$2,104,878	$2,146,976	$10,322,078
Annual Costs:						
Construction Costs (4000 sf facility renovation)	$1,200,000					
Equipement and Infrastructure	$160,000					
Robotics/Workflow Management Lease and support	$559,203	$559,203	$559,203	$559,203	$559,203	$2,796,015
Consumables/BUD Testing	$60,000	$61,800	$63,654	$65,564	$67,531	$318,548
Salary+Benefits for Technicians and Pharmacists	$763,483	$786,387	$809,979	$834,278	$859,307	$4,053,435
Real Property Rental	$108,000	$111,240	$114,577	$118,015	$121,555	$573,387
Misc (travel, telecom, office supplies, employee recognition, etc.)	$10,000	$10,300	$10,609	$10,927	$11,255	$53,091
Total Annual Costs	$2,860,686	$1,528,930	$1,558,022	$1,587,987	$1,618,850	$9,154,476
Incremental Margin	**($877,212)**	**$494,213**	**$505,584**	**$516,892**	**$528,126**	**$1,167,602**
Cummulative Margin		**($382,999)**	**$122,585**	**$639,477**	**$1,167,602**	

Assumptions:

- $60,000 estimate for BUD testing based on maximal testing estimate, will likely be lower once QA established.
- Salary and benefit increase of 3% per year
- 2% drug cost annual inflation rate
- Not included in cost savings is waste reduction based on annual wastage of pre-mixed frozen products (approximately $50,000 per year in potential additional savings).
- Lease of robotics/workflow management based on 5% interest rate

*Medications used in the cost savings evaluation:

Atropine 0.4 mg/mL 2.5 mL	Fentanyl 2mcg/ml-Bupiv 0.0625% bag	Midazolam 1 mg/mL 2 mL
Aztreonam 1gm bag	Fentanyl 2mcg/ml-Bupiv 0.1% bag	Midazolam 1mg/ml bag
Aztreonam 2gm bag	Fentanyl 2mcg/ml-Bupiv 0.125% bag	Morphine PCA
Calcium Gluconate 1gm	Fentanyl 50 mcg/mL, 2 mL	Neostigmine Methylsulfate 1 mg/mL, 5 mL
Calcium Gluconate 2gm	Fentanyl 50 mcg/mL, 5 mL	Nicardipine 20mg bag
Cefazolin 1gm bag	Glycopyrrolate 0.2 mg/mL, 5 mL	Oxytocin 30units bag
Cefazolin 1gm syringe	Heparin 100units/ml bag	Penicillin 2MU bag
Cefazolin 2gm syringe	Heparin 2 units/ml bag	Penicillin 3MU bag
Cefepime 1gm bag	Heparin 30 units/ml in NS bag	Phenylephrine 0.32mg/ml bag
Cefepime 2gm bag	Hydromorphone 0.2 mg/mL 10 mL	Phenylephrine HCl 100 mcg/mL 10 mL
Ceftriaxone 1gm bag	Hydromorphone PCA	Rocuronium 10 mg/mL 10 mL
Ceftriaxone 2gm bag	Ketamine HCl 10 mg/mL 5 mL	Succinylcholine Chloride 20 mg/mL, 5 mL
Clindamycin 600mg bag	levetiracetam 1.5gm/100ml bag	Vancomycin 1gm bag
Clindamycin 900mg bag	levetiracetam 1gm/100ml bag	Vancomycin 500mg bag
Ephedrine Sulf 5 mg/mL 10 mL	levetiracetam 500mg/100ml bag	Vancomycin 750mg bag
Epinephrine 1.6 mcg/mL 10 mL	Lidocaine 2% , 5 mL, PF	Vecuronium Bromide 1 mg/mL 10 mL
Epinephrine 5mg/250ml bag	Magnesium 1gm bag	Zosyn 2.25gm bag
Esmolol HCl 10 mg/mL, 10 mL	Magnesium 2gm bag	Zosyn 3.375gm bag
Famotidine 20mg bag	Magnesium 40gm bag	Zosyn 4.5gm bag
Fentanyl 20mcg/ml 100ml Bag	Methohexital 10 mg/mL 10 mL	

APPENDIX H
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