Academic Medical Center | Patient Safety Organization
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Patient Safety Alert: Pharmacy Compounding Safe Practice Recommendations

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Introduction

In follow-up to its first Medication Safety Task Force (MSTF) Collaborative, the Academic Medical Center Patient Safety Organization (AMC PSO) held an additional convening session. Key opinion leaders from member regional pharmacies and health care centers gathered to discuss best practices regarding compounding sterile preparations and patient safety, which had been generated directly from a MSTF held earlier in the year. Presentations and discussions were specifically held outlining detailed procedures for auditing and selecting vendor compound pharmacies, the most current patient-safety technologies, and standards for those who maintain an in-house compounding pharmacy and liability issues regarding general drug safety for practitioners and health care organizations.

Background

In the United States health care system, independent compounding pharmacies have long-established relationships with health care organizations by providing the organization's patients with such customized products as individualized chemotherapeutic agents, medication formulations, and doses that are not available commercially, preparations free of preservatives dyes and allergens, and diagnostic agents for practitioners and researchers (Drazen, Curfman et al. 2012). Over the last twenty years, multiple, well-publicized incidents of infectious microbes found in products synthesized by compounding pharmacies, however, have created a patient-safety crisis of faith among clinicians and health services providers towards these vendors (CDC. 2002; Drazen, Curfman et al. 2012; Kainer, Reagan et al. 2012). Patient safety is not the only looming concern for practitioners and their affiliated organizations when partnering with compounding pharmacies: the issue of medical liability is also a very real risk. An examination of recent lawsuits filed following large-scale medical product injuries reveals that physicians who prescribe defective drugs or administer substandard medical devices are frequently named in the ensuing litigation (Gallegos A, 2013). For example, both prescribers and manufacturers were named in lawsuits surrounding such products as fentanyl patches produced by Alza Corporation and Janssen Pharmaceutical Products, breast implants created by Dow Corning Corporation, and epidural steroids compounded by the New England Compounding Center. One retrospective study examining breast implant lawsuits (O'Brien C, 1999) detailed how plaintiffs used individual legal claims against doctor-defendants to push these physicians into quick and lower monetary settlements so larger, and more expensive, future lawsuits against the manufacturers could be financed. Plaintiffs have also won recent combined lawsuits against physicians and manufactures over medication and medical device malfunctions (Gallegos A, 2013):

- In 2012, a jury ordered a physician and manufacturer to pay $5.5 million to a mesh-implant plaintiff. Jurors found the manufacturer 60% at fault and the surgeon 40% at fault. Multiple lawsuits regarding flawed mesh implants are currently in motion.
- Another 2012 jury verdict awarded a patient $7.5 million dollars from her doctor and a manufacturer after she acquired frostbite from a cold-therapy medical device.
- In 2011, a physicians group paid $3.7 million dollars to the family of a patient who died after being administered a fentanyl patch. The family sued the doctors for negligence in prescribing the patch. Dozens more lawsuits regarding defective fentanyl

patches are currently active, naming both manufacturers and prescribers.

Issues of Vulnerability

In cases of defective medications, particularly those that are compounded, negligence is one of the most common claims used against prescribers. Here, legal arguments against a physician are typically built around the assertion that the physician breached the standard of care, as he or she knew or should have been aware that the pharmacy was not meeting applicable standards in compounding the medications. A second common legal argument suggests that physicians should be aware that certain medications should not be compounded, but instead, directly obtained from a manufacturer (Gallegos A, 2013). Additional claims made against doctors in cases of tainted medications include: failure to alert patients that a drug is foreseeably dangerous, failure to test compounded drugs, failure to sterilize and failure to enact quality control.

Physicians can also be sued under product liability laws, even though they did not manufacture the medication believed to cause harm. This typically occurs either in blanket lawsuits, where all parties along the chain of a product are named, or when a physician has been determined to be a "seller" of a product, rather than simply using the drug, or device, in question to provide a medical service.

Assessing the Quality of Outsourced Compounding Pharmacies

Before any health care organization or practitioner engages with a compounding pharmacy, there are a number of steps the organization or prescriber can take with the vendor to ensure patient safety and reduce their risk of liability. This includes actions to fully vet the potential supplier, such as requesting documentation of compliance with local state and federal manufacturing guidelines, and an on-site validation audit and comprehensive review of the facility.

PRE-AUDIT

First, it is important that prescribers conduct a pre-audit of any potential vendor prior to considering a site visit. The primary purpose of this phase is to determine a better understanding of the potential vendor's company profile, demographics, and capabilities, as well as any previous violations or adverse events the vendor may have been involved in. During this phase, the vendor should be asked to complete or provide a copy of:

- USP 797 Compliance Gap Analysis tool results Critical Point Compliance Audit tool http://www.ijpc.com/USP/IJPC%20USP%20797%20GAP%20Analysis.pdf
- Request for Information (RFI) survey tool which will provide basic demographic information about the company
- ASHP Outsourcing Sterile Products Preparation Contractor Assessment Tool http://www.ashpfoundation.org/MainMenuCategories/PracticeTools/SterileProductsTool/SterileProductsAssessmentTool.aspx

The ASHP Outsourcing Sterile Products Preparation Contractor Assessment Tool has a number of advantages, in that it gives a very good overview of vendor capabilities and processes, provides a method for summary scoring across a number of dimensions, and contains a detailed scoring guide that can be helpful in vendor selection. It may not be ideal for use with smaller compounding pharmacies, however, and it does not validate the responses a given manufacturer, large or small, provides. The surveys and tools listed above can also not take the place of a thorough on-site audit and record review.

ON-SITE AUDIT

Once a health care organization or prescriber is satisfied with the pre-audit materials, an on-site inspection and review of the facility can be scheduled. This on-site visit should last about 6-8 hours and must include a complete tour of the facility, interviews with key members of the facility leadership team and front line staff, and an extensive record review. Ideally, the audits should

be conducted by the Chief Pharmacy Officer or a senior pharmacy leadership member. The audit team should also include an individual with expertise in USP chapters 797, 795, 71 and cGMP requirements as well.

The examiners on-site inspection should also be guided with a reliable and valid audit tool, such as the one provided by the ASHP. While the level of detail provided by such instruments is beyond the scope of this newsletter, many of the items that should be subject to inspection are overviewed below.

Throughout their tour, auditors should also be vigilant that compounding pharmacy staff are adhering to sterilization and clean room protocols through such practices as gowning, hand washing, use of aseptic technique, cleaning and compliance with established SOPs.

A check of the vendor's on-site records and paperwork should include reviews of:

- License and certifications for the facility and staff
- Standard operating Procedures (SOP)
  - USP 797 compliance
  - Dates, revisions, approvals
- Quality Control Measures: stability, sterility, and pyrogenicity testing procedures
  - beyond use dating
  - product concentrations
- Personnel training and competency
- Tracer Methodology record of a specific CSP prepared
- Environmental monitoring records
- Customer complaints
- Drug recalls

A physical tour of the compounding facility itself should include inspecting:

- Clean rooms and hoods for
  - Certification dates, testing results, equipment sterilization
- Inventory, distribution and quarantine areas to look for:
  - Areas that are clearly designated, temperature controls, refrigeration and freezer monitoring, security and controlled drugs

Auditors should also ask to observe the actual compounding process in action from start to finish, and if possible, it should be a product they would purchase. During this phase, examiners should be watching for:

- Compliance with established SOPs
- System double checks
- Use of medication safety technology, robotics and other instruments, including their documentation and calibration
- The pharmacist's role in product preparation and validation
- Documentation processes
- Reliability of labeling and bar codes
- Validation of the quality assurance process

If a health care organization and/or physician finds that the results of the pre-audit and on-site audit are acceptable, then the vendor should be asked to agree to submit periodic written reports that will include key quality assurance performance data on products that are being purchased. At a minimum, this report should include:

- Sterility test results and product potency certifications
- Competency assessments of staff
- Environmental monitoring outcomes
- FDA or State action notifications
- Equipment validation and testing reports
- Drug recalls

In conjunction with these written reports, any potential vendor should also be willing to agree to follow-up audits on an annual or bi-annual basis.

The Pharmacy Environment Today: Protecting Your Pharmacy

For those organizations that choose to facilitate their own compounding pharmacy, multiple new technologies are available that are changing the standard of practice. In addition, a number of changes have been made, and more are being considered, to the manufacturing and handling codes for compounding pharmacies at the local,

state, and federal levels. AMC PSO member Pharmacists and their staff need to be aware of how to incorporate both the new technologies available to them and changes in regulations into their process because of their impact on such issues as medication availability, costs or changes in formulations, patient safety and care, and liability.

Many of the new technologies being offered are specifically designed to improve medication safety technology and decrease the risk of compounding errors. These include advances in bar-code verification, optical scanning, workflow assist software, and robotic technology. Utilizing the quality and safety features of IV robotic devices, for example, can help insure that all products are made with the highest degree of accuracy, sterility, and safety.

Many of these tools minimize human interaction with drug preparation and as such also have the effect of shifting the roles of Pharmacy Technicians to include more responsibility for drug preparation and dispensing. The roles of the Pharmacist will also evolve with these technologies and be more patient-care-focused and less product-focused as these manufacturing improvements allow for medications to be custom-prescribed and produced for individual patients.

ADVANTAGES OF ROBOTIC TECHNOLOGY IN COMPOUNDING PHARMACIES

- Bar code verification
- Specific gravity and gravimetric verification
- Optical scanning
- Central data storage
- High degree of accuracy and precision
- Efficient work flow
- Workload prioritization and tracking
- Interfaces
- Limits human involvement in the compounding process

Note: HUMANS are the primary source of drug contamination

QUALITY ASSURANCE TESTING

Robots should be maintained and tested similar to IV hoods and maintenance and service should be contracted with an outside testing vendor every 6 months. Optimally, the following steps would also be incorporated into your pharmacies best practices:

- Funding a full time, on-site Quality Assurance Coordinator who is a Microbiologist by degree and background
- Staff testing conducted on-site with media fills and is supplemented by independent 3rd party testing
- Follow USP requirements for batch testing and longer term batch testing is also done to assure continued sterility and potency
- Send robot and human prepared products to an outside lab for end product testing
- Use of Simplify Product documentation of results.

Each of these steps, combined with the use of the latest medication safety technology, can greatly reduce the probability of compounding errors, increasing patient safety and lowering the risk of liability.

PITFALLS

While these advances in technology are changing the landscape of compounding pharmacies, it must be mentioned that many of these developments are relatively new and we are in the early phases of adopting them. As such, much of this technology is not proven as yet with evidenced -based studies. Additionally, the potential exists for new kinds of errors to occur due to the introduction of the new technology, processes and roles for staff. Clearly, Pharmacists and Technicians will need additional training to adapt to their new roles working with robotic technology and must be careful not to over-rely on the technology.

Conclusions

When selecting a vendor(s) to provide your practice or organization with compounded medications:

- Choosing an outsourcing company to prepare compounded sterile products should not be taken lightly.
- Due diligence in assessing the capabilities of the vendor are key steps that must be verified before contracting with any vendor.
- Part of due diligence includes on-site evaluation, record reviews, and the use of standard assessment tools.
- Assessment of these potential vendor partners must be done by individuals with enhanced knowledge of cGMP and USP regulations as well as experience in hospital based sterile products compounding.

When running a compounding pharmacy in-house:

- Volumetric preparation and visual checking should be retired.
- Innovative technology is now available that will allow for precise and accurate IV admixture preparation.
- Pharmacy leaders need to embrace the change and lead their departments into the future.

REFERENCES

Alicia Gallegos. Physicians entangled in tainted drugs lawsuits. American Medical News. Accessed on 05 July, 2013: http://www.amednews.com/article/20130211/profession/130219977/2/

O'Brien B. (1999) Anatomy of a Crisis: One Perspective on the Silicone Implant Story. Clinics Plastic Surg: 26(1)