

The Cost of QUALITY in Pharmacy

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*Webster's Seventh New Collegiate Dictionary*¹ provides the following definition of the word "error": "An act that through ignorance, deficiency, or accident departs from or fails to achieve what should be done." That may also be an appropriate definition for the pharmaceutical compounding errors discussed in this article.

Drugs are a tremendous resource in our society, and as compounding pharmacists we are extremely fortunate to have the responsibility of preparing formulations, dispensing them, and educating patients about their use. As drugs and drug products become more complex, it is inevitable that errors will occur in their preparation and distribution as well as in patient counseling. Errors in different aspects of health care occur each day: those made by the pharmaceutical industry, which are reflected in drug recalls; errors in diagnosis, prescribing, and surgery; dispensing errors; treatment errors made by nurses and/or caregivers; and those (made by laboratory staff) that lead to incorrect test results.

Many such errors are not serious, although some are publicized more than others. We all make mistakes, but we must do all we can to eliminate errors and minimize their effect.

When an error occurs, it is important to remember the following facts:

- **Mistakes** happen.
- **Punishing** and blaming are not productive ways of solving a problem.
- **Errors** are often minimized when a system of checks and balances is in place.
- **No one** should practice in any profession beyond the scope of his or her training, education, and expertise or without adequate facilities, equipment, and supplies.

The number of adverse drug events (ADEs) in the United States is alarming, and several stories about pharmacy compounding errors in the United States have been well publicized in the media. An incident in Kansas City, Missouri, involved a pharmacist who diluted antineoplastic agents so that prescriptions were dispensed in concentrations less than those ordered by prescribing physicians. That pharmacist confessed to Federal Bureau of Investigation (FBI) investigators that he had been underdosing patients since 1992. According to his testimony,² the approximate numbers of those potentially affected were:

- **Patients** in Kansas and Missouri = 4200
- **Physicians** in Kansas and Missouri = 400
- **Prescriptions** in Kansas and Missouri = 98,000

Recently, incidents also occurred in the following pharmacies: Doc's Pharmacy (Walnut Creek, California), Memorial Health Care (Memphis, Tennessee), and Med-Mart (Bakersfield, California; Atlanta, Georgia; Peoria, Illinois; and Leesburg, Virginia).³

The concept of quality in compounding pharmacy must be clearly defined. In this article, an explanation of the importance of that quality to patients served by compounding pharmacists and technicians and to the compounders themselves is presented.

Quality Defined

Joseph M. Juran, like W. Edwards Deming, George Box, Philip Crosby, and Kaoru Ishikawa, is one of the preeminent "founders" of the concept of quality. Those men made substantial contributions to quality management. Juran is best known for the following ideas: the involvement of top management; the Pareto principle; the need for widespread training in quality; the definition of quality as "fitness for use"; and the use of a project-by-project approach to quality improvement.

Developing and maintaining quality systems can be viewed as efforts that cost money or efforts that save money. Products and/or services that meet customers' needs, produce customer satisfaction, and are free of defects generate revenue. Various definitions of quality are presented in Table 1.⁴ Those definitions refer to quality from two different perspectives that address the same result: a product of higher quality. Pharmacy-prepared sterile products that are accurate (ie, accurately formulated) and free of contamination are quality products. Patients, physicians, nurses, and patients expect extemporaneously prepared products to be accurate and sterile.

Doc's Pharmacy, Walnut Creek, California

An incredibly sad but preventable error-related incident occurred at Doc's Pharmacy in Walnut Creek, California, in 2001. The basis for that incident was created when the pharmaceutical company Schering-Plough failed to comply with current good manufacturing practices (GMP) requirements, which resulted in the halt of the production of dozens of medications manufactured at that company's New Jersey and Puerto Rico facilities. This situation created a national backorder of one of the company's products, Celestone Soluspan (betamethasone acetate and betamethasone sodium phosphate).

Because of the shortage of Celestone, Doc's Pharmacy began to extemporaneously compound the medication in early 2001.³ According to the Contra Costa County Health Services, on May 17, 2001, a batch of betamethasone was prepared and

dispensed to the Sierra Surgery Center in Walnut Creek, California. That batch of medication was contaminated with bacteria of the genus *Serratia*. During the next 2 weeks, 38 people received spinal injections containing the contaminated betamethasone. Dozens of patients treated with the contaminated injections were hospitalized and treated with antibiotics. Meningitis developed in 5 patients, 3 of whom died as a result of the infection.⁵

The following information is a chronological list of events that affected Doc's Pharmacy as a result of the compounding and dispensing of the contaminated medication:

June 5, 2001. Contra Costa County health officials and California State Board of Pharmacy inspectors arrived at Doc's Pharmacy to conduct an inspection and investigation. During the inspection, several deviations from good compounding practices and standards of practice as recommended by the California Board of Pharmacy, the American Society of Health-System Pharmacists, and the United States Pharmacopeia were observed. Those deviations included:³

- Technicians who were wearing long-sleeved sweaters and jewelry while compounding
- Poor hand-washing techniques and the failure to wear gloves while compounding
- Improper segregation of the compounding area from other areas, open cans of cat food near the compounding area, and a tropical fish tank in the compounding area
- Failure to follow proper sterilization techniques

Several environmental microbial samples were taken, and *Serratia* bacteria were found throughout the area and on the compounding equipment. The county and state inspectors forced the recall of all injectable and ophthalmic medications that had been prepared at Doc's Pharmacy.

July 2001. The owner and co-owner of Doc's Pharmacy voluntarily agreed to stop compounding medications. An administrative law judge ordered Doc's Pharmacy not to mix medications. The US Food and Drug Administration (FDA) cited Doc's Pharmacy and its owners with significant vio-

lations of federal drug laws; those violations pertained to the failure to prepare sterile drugs of the proper purity or potency.

August 2001. The California attorney general filed charges of gross negligence against the pharmacists and the pharmacy technicians of Doc's Pharmacy and found many violations of pharmacy laws.

November 2001. The pharmacy owner surrendered his pharmacy license pending administrative hearings on the state charges, and Doc's Pharmacy was sold. Administrative law hearings began on state charges against the pharmacy's other employees.

January 2002. The pharmacy employees were heavily fined, suspended for 90 days, and sentenced to 5 years' probation by an administrative law judge.

March 2002. The California Board of Pharmacy adopted the administrative law judge's ruling and ordered the suspensions to commence on March 31, 2002. On the weekend of March 23, 2002, while his family members were visiting relatives, the 32-year-old co-owner of Doc's Pharmacy committed suicide by affixing six fentanyl transdermal patches to his neck and chest.

Professional and Personal Responsibility

It is essential that pharmacists and technicians clearly understand their professional and personal responsibility for the sterility and accuracy of pharmacy-prepared sterile products. They must be very knowledgeable about state-of-the-art compounding and the current standards of practice with which they must comply.

The *American Society of Health-System Pharmacists (ASHP) Guidelines on Quality Assurance for Pharmacy-Prepared Sterile Products* and the *United States Pharmacopeia (USP) Chapter <1206>* ("Sterile drug products for home use") are excellent resources that define state-of-the-art compounding and the current standards of practice. In those guidelines, a variety of parameters for the physical plant, the types of products used, and the length of product storage are described. The objective of the ASHP guidelines is to "help pharmacists and pharmacy technicians prepare sterile products of the

Table 1. Examples of the Effects of Quality in Compounded Preparations.⁴

Effects of High-Quality Products and/or Services That Meet Customers' Needs

(The major effect is on sales; higher quality costs more.)

1. They increase customer satisfaction.
2. They sell for premium prices.
3. They meet or exceed the quality of competitive products.
4. They increase the market share of the product sold.
5. They provide sales income.

Effects of High-Quality Products and/or Services That Are Free from Defects

(The major effect is on costs; higher quality costs less.)

1. They reduce error rates.
2. They reduce the need to rework the preparation.
3. They reduce the number of field failures, warranty claims, and waste.
4. They reduce customer dissatisfaction.
5. They reduce the number of inspections required and the need for product testing.
6. They increase product yield or output.
7. They enable greater operating capacity and efficiency.
8. They improve delivery performance.

highest quality."⁶ Those guidelines were developed for use in a variety of practice settings that include hospitals, community pharmacies, long-term care facilities, and home care organizations.

In USP Chapter <1206>, key requirements essential to the preparation of quality compounded preparations are defined. Several of those requirements are described below:⁷

1. Personnel must be capable of performing and qualified to perform their assigned duties.
2. Ingredients used in compounding must be of the expected identity, quality, and purity.
3. Critical processes must be validated to ensure that the procedure used consistently results in the expected quality of the finished preparation.
4. The production environment must be

suitable for its intended purposes with respect to environmental cleanliness, control, monitoring, and environmental microbial action limits.

5. Appropriate release checks or testing procedures must be performed to ensure that finished products have their expected potency, purity, quality, and characteristics at the time of release.

6. Appropriate stability evaluations must be performed to establish reliable beyond-use dates so that finished products have their expected potency, purity, quality, and characteristics, at least until the beyond-use date listed.

7. Processes must always be carried out as intended or specified and must be under control.

8. The procedures for preparing formulations must be designed to prevent mixups.

9. Effective procedures for investigating and correcting failures or problems in the preparation or testing of a product (or in the finished product itself) must be followed, and records of those incidents must be maintained.

10. Quality control functions and decisions must be adequately separated from those of production.

Noncompliance with Standards of Pharmacy Practice

The ASHP, while conducting two national surveys of quality assurance for pharmacy-prepared sterile products, found that few hospital pharmacies were equipped with adequately controlled compounding environments, which are essential in the preparation of a sterile product. The surveys also indicated that many pharmacists were not using environmental monitoring, end-product testing, and process validation to perform critical quality assurance checks.⁸ We continue to delude ourselves into thinking that proper hand washing, gowning and gloving procedures, and some recommended sterile product preparations are unnecessary.

The focus on developing, implementing, using, and maintaining quality systems during the preparation of pharmacy-prepared sterile products is essential to

ensuring the health and well-being of patients and the professional and personal enrichment of pharmacists and technicians. Some of us who practice pharmacy know what good compounding practices are but do little to comply with standards unless motivated by economics, regulations, or publicity. That inaction may be a result of the lack of effective management or proper supervision, the perceived cost of quality control and/or quality assurance programs, a lack of knowledge about effective quality control programs, or an apparent lack of increased profits.

The following list includes questions that pharmacists should consider as they review standards of practice and consider compliance with regulations or professional guidelines.

■ Should quality be considered *only* when poor quality results in patient injury or death, litigation, or less profit?

■ Does compounding high-quality preparations really cost more?

■ Why do some pharmacists believe that quality cannot be measured?

■ Do quality assurance programs cause pharmacists to spend money rather than to make money?

The errors and issues associated with sterile products prepared improperly in the pharmacy can be classified as clearly preventable ADEs or (more broadly) as medical errors. They include:

Morbidity. An Institute of Medicine (IOM) study⁹ indicated that almost 98,000 patients die annually from preventable medical errors.

■ Some nosocomial infections can be “seeded” from products prepared improperly in the pharmacy. An estimated 8% to 12% of hospitalizations are complicated by nosocomial infections that extend treatment from 4 to 7 days.¹⁰

■ As a result of infections or other treatment-related complications, patients may undergo rehospitalization if they are receiving therapy at home, or they may incur an extended stay if they are in the hospital when an infection develops.

Loss of income to the patient. The estimate of the total national cost of preventable adverse events (including lost income, lost

household production, disability, and the cost of health care) ranges from \$17 billion to \$29 billion annually.¹¹

Loss of quality of life. Blindness, organ loss, and other injuries have resulted from the use of sterile products prepared improperly in the pharmacy.

Secondary effect on families. Lost household production and other fiscal and emotional impact can be devastating.

Death. In addition to the deaths associated with the contaminated betamethasone from Doc’s Pharmacy, several patient deaths in the 1990s were associated with improper practices of preparing parenteral nutrition admixtures.¹² Those deaths could have been prevented if the proper use of compounding equipment and the physiochemical properties of parenteral nutrition components had been considered.

Increased liability. The cost of obtaining insurance and the ability to secure coverage are influenced by the degree to which the practice and control of high-risk, high-volume processes can be demonstrated.

Decreased market share. Nothing can harm an organization’s reputation in the community more rapidly than a news story about a patient injury caused by a preventable adverse event.

Increased risk for failure to comply with regulatory requirements. Local, state, federal, and/or accrediting bodies want evidence of process control and risk management. It is essential to have processes in place for producing pharmacy-prepared sterile products and to have supporting documentation of operational and procedural compliance.

The 85:15 Rule

W. Edwards Deming,¹³ one of the world’s foremost quality gurus, developed the “85:15 Rule,” which says that 85% of organizational problems are caused by system failures (ie, poor or nonexistent plans or procedures, a lack of measurable performance criteria, and work processes) and that 15% are caused by human factors. Deming and others established that the potential for eliminating errors in the workplace lies primarily in improving the systems used (not by blaming workers). Their obser-

vations have evolved into the following rule of thumb: At least 85% of work-related problems can be corrected by changing the work system, and fewer than 15% can be corrected by changing individual workers. Current research¹³ indicates that even more than 85% of work-related problems stem from system failure and that the ratio should probably be 95%:5% or 97%:3%. Dr. Deming proved through his famous Red Bead Experiment that the only way to improve a product or service is for management to improve the system that creates that product or service.¹³

Preventing the Next Walnut Creek Tragedy

The events that occurred at Doc's Pharmacy were preventable. Why weren't proper aseptic techniques or compounding and sterilization procedures followed? Was it because of a lack of training, time, or proper supervision? Many questions remain, and few have been answered.

The personal misery, emotional suffering, and financial effect on the patients who received the tainted betamethasone, the families of those patients, the physicians who administered the drug, the technicians who compounded the doses, and the owners of Doc's Pharmacy cannot be measured. It is time that pharmacists and pharmacy technicians embrace the following facts: that good compounding practices will yield quality products (accurate and sterile) and that compounders have a responsibility to meet or exceed state regulatory requirements for sterile preparations because their actions can determine the life or death of their patients.

References

- Gove PB, ed. *Webster's Seventh New Collegiate Dictionary*. Springfield, MA:G & C Merriam Company; 1963:282.
- List of drugs Courtney claims to have diluted [press release]. Kansas City, MO:Kansas City Division, US Department of Justice Federal Bureau of Investigation; April 22, 2002. Available at: <http://kansascity.fbi.gov/kcmstate042202.htm>. Accessed July 6, 2002.
- Hallissy E, Russell S. Who's mixing your drugs? Bad medicine: Pharmacy mix-ups a recipe for misery; some drugstores operate with very little oversight. *San Francisco Chronicle*. June 23, 2002:A-1.
- Juran JM, Godfrey AB. *Juran's Quality Handbook*. 5th ed. New York:McGraw-Hill; 1999:4.20-4.21.
- [No author listed.] Officials to shut pharmacy. [KTVU News Website]. July 6, 2001. Available at: <http://www.bayinsider.com/partners/ktvu/news/2001/07/06/meningitis.html>. Accessed July 6, 2002.
- ASHP guidelines on quality assurance of pharmacy-prepared sterile products. *Am J Health Syst Pharm* 2000;57:1150-1169.
- US Pharmacopeial Convention, Inc. *United States Pharmacopeia XXIV/National Formulary 19*. Rockville, MD:US Pharmacopeial Convention, Inc; 1999:2130-2143.
- Myers CE. Needed: Serious attention to sterile products. *Am J Health Syst Pharm* 1996; 53:2582.
- Kohn, LT, Corrigan JM, Donaldson MS. *To Err Is Human: Building a Safer Health System*. Washington, DC:Institute of Medicine/National Academy of Sciences; 2000:26.
- Stafylaraki A, Kalofissudis I. Nursing science in prevention and control of nosocomial infections. *ICUS and Nursing Web Journal*. ISSN 1108-7366. 2000;1. Available at: <http://www.nursing.gr/article1.htm>. Accessed July 3, 2001.
- Van Cott H. Human errors: Their causes and reduction. In: Bogner MS, ed. *Human Error in Medicine*. Hillsdale, NJ:Lawrence Erlbaum Associates, Inc; 1994:53-66.
- Buerger DK. Parenteral nutrition safe practices: A new roadmap for improved patient care [American Society of Consultant Pharmacists Website]. [No date listed.] Available at: <http://www.ascp.com/public/pubs/tcp/1998/nov/roadmap.shtml>. Accessed July 2, 2001.
- Barnes BJ, Van Wormer JM. Process thinking and the 85:15 rule applied to education [Baldrige in Education School Website]. [No date listed.] Available at: <http://www.grand-blanc.k12.mi.us/qip/ProcessThinking.htm>. Accessed July 6, 2002.

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