

Reducing Medication Errors and Increasing Patient Safety:  
Case Studies in Clinical Pharmacology

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## Abstract

Today, reducing medication errors and improving patient safety have become common topics of discussion for the President of the United States, federal and state legislators, the insurance industry, pharmaceutical companies, healthcare professionals and the patients we serve. But this is not news to clinical pharmacologists. Improving the judicious use of medications and minimizing adverse drug reactions have always been key areas of research and study for those working in clinical pharmacology. However, added to the older terms of adverse drug reactions and rational therapeutics, the now politically correct expression “medication error” has emerged. Focusing on the word error has drawn attention to “prevention” and what can be done to minimize mistakes and improve patient safety. Webster’s New Collegiate Dictionary has several definitions of “error”, but the one which seems to be most appropriate in the context of “medication errors” is, “an act that through ignorance, deficiency, or accident departs from or fails to achieve **what should be done**”. **What should be done** is generally known as “the five rights”: the Right drug, Right dose, Right route, Right time, and Right patient. One can make an error of omission (failure to act correctly) or an error of commission (acted incorrectly).

This paper now summarizes what is currently known about medication errors and translates the information into case studies illustrating common scenarios leading to medication errors. Each case is analyzed to provide insight into how the medication error could have been prevented. “System errors” are described and the application of Failure Mode Effect Analysis (FMEA) is presented to determine the part of the “safety net” that

failed. Examples of re-engineering the system to make it more “error proof” are presented.

If it was an error, then it can be prevented. However, the practice of medicine, pharmacy and nursing in the hospital setting is very complicated and so many steps occur from “pen to patient” that there is a lot to analyze. Implementing safer practices requires developing safer systems. Many errors occur as a result of poor oral or written communications. Enhanced communication skills and better interactions among members of the health care team and the patient are essential. The Informed Consent process should be used as a patient safety tool and the patient should be warned about material and foreseeable serious side effects and be told what signs and symptoms should be immediately reported to the physician before the patient is forced to go to the ED for urgent or emergency care.

Lastly, reducing medication errors is a process, an ongoing process of quality improvement. Faulty systems must be redesigned and seamless, computerized integrated medication delivery instituted by health care professionals adequately trained to utilize such technological advances. Sloppy hand-written prescriptions should be replaced by computerized physician order entry (CPOE), a very effective technique for reducing prescribing/ordering errors, but another far less expensive yet effective change would involve writing all drug orders in plain English, rather than continuing to use the elitists’ arcane Latin words and short-hand abbreviations that are subject to misinterpretation. After all, effective communication is best accomplished when it is clear and simple.

## **Introduction**

The modern age of quality improvement has come to medicine and therapeutics. Not only are accreditation agencies like the Joint Commission on Accreditation of Health Care Organization (JCAHO) requiring member hospitals to report severe and unexpected adverse drug experiences as Sentinel Events, but many states have enacted legislation to compel medication error reporting and require that hospitals and healthcare professionals develop risk management and patient safety plans (1). Integrated medication delivery (the entire process of prescribing, transcribing, dispensing and administering medications) is under the microscope. What started this increased awareness of medical and medication error, and why are health care professionals monitoring their own performance pulses? Arguably, the reason for this increased awareness of iatrogenic error stems from the 1999 publication *To Err is Human: Building a Safer Health System*, from the Institute of Medicine (IOM), (2).

Certainly one startling statistic that caught everyone off-guard was the IOM's report that between 44,000 and 98,000 people die in hospitals annually as a result of medical error (2). Since the publication of the IOM report, others have disputed the validity of the extrapolated numbers that were published (3) and at least one of its authors has defended the results (4). But one thing is for sure, the report got everyone's attention: health care practitioners, government, lawyers, insurance companies, and typical citizens at home listening to the nightly news.

However, despite the problem of medical and medication error, whatever its prevalence, the major reason patients sue their doctors is communication problems. In an interesting paper by Beckman et al, the authors analyzed 45 plaintiffs' depositions to determine the reason(s) patients sued their doctors. Their analysis indicated that problematic relationships and poor communication skills accounted for the reasons 71% of the plaintiffs sued their doctors (5). Moreover, the entire process of integrated medication (drug) delivery relies on the communication of the right drug, the right dose, the right route, and the right frequency of administration from one healthcare professional to another in order to obtain the desired therapeutic outcome in the right patient with a minimum of side effects. Miscommunications like illegible medication orders, look-alike drug names, confusion of brand and generic names all can and do lead to medication errors (6). One of the most common types of communication breakdowns occurs when patients or patient's family members tell healthcare providers, "I'm allergic to that drug." When a patient or family member says "allergic", frequently what they really are trying to tell you is that they tolerated the drug poorly. Side effects like nausea, diarrhea and sedation are frequently reported as allergies, when in fact there is no immunologic mechanism involved at all. For these reasons, it is important to query the patient about what symptoms actually appeared, rather than just writing drug allergy in the chart. There is certainly a big difference between developing diarrhea or a yeast infection from an antibiotic, as opposed to developing a rash, urticaria, or anaphylaxis. Centuries ago, Paracelsus admonished physicians, "Listen to your patient, for the patient will provide you with the diagnosis." Case 1 is an example of an actual wrongful death medical negligence case

that occurred because a physician did not listen to what the family member told him about the patient.

### Case 1

An 80 year old Italian-speaking man was brought into the ED by his son, after slipping and falling in the bathroom. The son told the admitting physician, “Don’t give my father Demerol<sup>®</sup> (meperidine), he’s allergic to it.” Later that evening, the patient is in pain and the physician prescribes meperidine 50 mg IM and Phenergan<sup>®</sup> 25 mg IM. In the morning, the patient is so obtunded that the admitting physician orders a CAT scan of the head. When they tried to position the patient for the scan, the patient became agitated. The radiologist ordered 10 mg diazepam IV push and the patient went into respiratory arrest. He was resuscitated but suffered hypoxic encephalopathy.

Thus, communications from the family or notations in the chart must have been disregarded in this case. The lessons to be learned from Case 1 are manifold. Remember the Beckman paper (5) and listen to what an informed member of the family tells you, bearing in mind that when a family member says “allergic” reaction, they may mean “didn’t tolerate” rather than a more precise immunologically-mediated reaction.

Communication of drug information to patients can also decrease the likelihood of serious adverse reactions from prescribed medications. In her outstanding presentation in this symposium entitled, “Informed Consent as a Patient Safety Tool in Clinical Pharmacology”, Fay Rozovsky, JD, MPH described the many ways communication of

drug information to the patient can lead to an increase in patient safety and a decrease in “therapeutic misadventures”. Because Ms. Rozovsky was unable to contribute a manuscript to this special issue of the Journal, it is appropriate to take a look at some of the pertinent issues she raised.

### **Origin of the Informed Consent Doctrine**

The Informed Consent Doctrine has its origin in the English common law (case law) dating back at least to 1767 (7). In the early 1900s in the US, case law began reporting “civil liability for unauthorized medical treatments” (8). In *Mohr v. Williams* (9), a patient was to have surgery on her right ear, and informed consent to this procedure had been obtained prior to taking the patient to the ER. While the patient was anesthetized, the physician decided the left ear was in greater need of surgery and performed the procedure on the left ear. Despite the fact that the procedure was “skillfully performed” and “was probably beneficial”, “...the court held that the left ear operation was not authorized and, therefore, constituted assault and battery on the patient.” (10) This case may have set the standard for the “wrong site” surgery cases reported by the news media over the past few years, as well as the inclusion of civil battery charges (unlawful touching) in legal complaints filed on behalf of women who were injured as a result of the implantation of an intrauterine device (IUD). Of further interest is the fact that had the patient been adequately informed about the risks of developing pelvic inflammatory disease (PID) and the possibility of subsequently developing sterility, and still consented to the implantation, there would have been no basis in law for claiming battery (11), (*i.e.*, the patient would have assumed the risk).

One of the most frequently cited legal cases on the informed consent doctrine stems from Justice Cardozo's 1914 opinion in *Schloendorff v. Society of NY Hospital* (12) where he proclaimed "every human being of adult years and sound mind has a right to determine what shall be done with his own body . . ." This doctrine of self-determinism has given rise to two differing perspectives of the same question. One standard states that a physician would be negligent for failing to inform a patient in situations where other physicians did inform. This standard assumed that there was a "discernible standard" within the medical community (10), which is not the case, since none has been set forth, established, or published within the medical community to this date. Since 1972, the courts have determined that the more appropriate standard is that the physician must provide the patient with the information a "reasonable man" would want to know in order to decide whether to accept or reject treatment. A more complete discussion of the problem and a review of the pertinent case law can be found in reference 10.

Physicians and other health care prescribers (*e.g.*, dentists, nurse practitioners, and physician assistants) almost always have a problem with understanding and complying with the duty to provide an informed consent to a patient. Comments like "How can I tell them everything in the PDR", "If I tell them about the possible side effects, they may not take the medicine", and "I just don't have time to sit and talk to every patient" are common, but just imagine how these statements would sound to a jury in a trial where a physician is being sued because a patient got injured or killed and the injury or death

could have been prevented by a prior warning. “What kind of a situation are you talking about?” one might ask. Here are a couple of examples.

Many medications can cause drowsiness, especially at the initiation of therapy, or following a dose increase, benzodiazepines, tricyclic antidepressants, and anti-seizure medications to name a few. Although the law differs from state to state, recent case law indicates that a physician can be held liable for injuries sustained by a patient who gets into a motor vehicle accident and injures either himself or another person (13). A brief admonition like: “Be careful driving or using dangerous machinery until you determine how this medication affects you. It could make you drowsy until you get used to it”, is all it takes. Medications like alpha blockers, tricyclic antidepressants, phenothiazines, butyrophenones, and ergot derivatives can cause postural hypotension, and failure to warn about fainting after rising suddenly from a seated or supine position has led to tragic consequences that could have been prevented by a proper instruction about rising slowly from bed (or reclining) and holding onto furniture or railings en route to the bathroom in the middle of the night (14). One particularly sad case involved a woman under treatment with a tricyclic antidepressant for post-partum depression who was awakened in the middle of the night by her crying baby and fell down a flight of stairs while rushing to care for her baby (14). Other patients under treatment with alpha blockers for hypertension or benign prostatic hyperplasia (BPH) have “blacked out” while driving due to cough paroxysms or deep inhalation of a cigarette, probably due to the combined effects of alpha blockade and a valsalva maneuver (15).

A 72 year old otherwise healthy white male has been having difficulty urinating. Laboratory examinations are negative for prostatic cancer, and a diagnosis of benign prostatic hyperplasia (BPH) is made based on digital rectal examination, history and symptoms. A decision is made to treat the patient with terazosin (Hytrin®) 1 mg at bedtime.

The patient has the prescription filled and takes his first dose about 11:00 pm before retiring. About 2:00 am the patient is awakened by the urge to urinate. He gets up out of bed and walks down the hall to the bathroom. With only a few steps to go, the patient becomes aware of a strange lightheadedness, faints, falls down a flight of stairs and sustains multiple injuries.

### Case 3

A 68 year old female in good health is seen by her family physician following the death of her husband. The patient reports feelings of loneliness, difficulty concentrating, sleep disturbances, decreased appetite and generalized feelings of depression. The physician decides to try the patient on a short course of tricyclic antidepressant medication and prescribes nortriptyline 75 mg at bedtime. The physician instructs the patient not to get out of bed too quickly in the morning and to sit on the side of the bed for a few minutes before attempting to stand up.

A few days later, the patient is lying on a chaise lounge by her swimming pool enjoying the sun. She decides to check her mailbox. After a few steps, she gets dizzy, and falls on the cement apron surrounding the pool breaking her hip.

Analysis: During the 1960s and 1970s, medical school students were taught to instruct their patients on alpha blockers “not to get out of bed too quickly in the morning and to sit on the side of the bed for a few minutes before attempting to standup.” Although this is good advice, it doesn’t convey to the patient that postural changes at any time during the day can trigger orthostatic hypotension, especially at initiation of treatment or following a recent dose increase. The injuries to the patients in cases 2 and 3 could have been prevented by an adequate instruction from the physician or the pharmacist.

However, the physician still maintains the “duty to warn” the patient, regardless of what the physician expects the pharmacist to do during an anticipated patient counseling session.

In thinking about the duty to warn a patient about potential adverse drug reactions, the key words to remember regarding informed consent are: **material** and **reasonably foreseeable**. Material means it is of consequence and reasonably foreseeable means that it is likely to occur as evidenced by its frequency of occurrence and presence in the package insert or in other respected medical or pharmacology textbooks. However, due to the sheer volume of information alone, it is still difficult for a physician to select those potential adverse drug effects from the lists in the labeling and the literature to convey to the patient. Using the “reasonable man” standard described above, try to provide the

patient with the information you would want to know if you were receiving the medication.

Moreover, there are certain uncommon but serious adverse reactions like Stevens-Johnson syndrome (SJS), Toxic Epidermal Necrolysis (TEN) and Acute Renal Failure that can occur with certain common drugs. Antibiotics and anti-seizure medications can cause SJS or TEN, and nonsteroidal anti-inflammatory drugs (NSAIDs) can cause SJS, TEN and acute renal failure in a small percentage of patients. Contrary to some practitioners' beliefs, these are not idiosyncratic reactions; they are rare but serious foreseeable reactions. Recent studies indicate that "Prompt withdrawal of causative drugs should be a priority when blisters or erosions appear in the course of a drug eruption." (16) "Clearly, given the effect of stopping a medication on outcome, the clinical challenge is to differentiate more and less serious reactions as early as possible in their evolution." (17)

### **Instruct Patients to Call When Anything Unusual or Unexpected Occurs**

In order to learn about the onset of a rash or other potentially serious drug reaction like acute renal failure, the informed consent briefing session presents the perfect opportunity to instruct your patients to call you at the first signs of a rash or dark urine. If you learn about the reaction at its first sign of onset and discontinue the possible causative agent(s), you may be able to stop a macular rash from blistering and developing into a full blown SJS or TEN which then may require hospitalization and lead to disfigurement and/or death. In addition, it is also a good practice to instruct patients to call you if anything

**unusual** or **unexpected** occurs. Also, with drugs capable of causing bone marrow depression, sore throat, excessive bruising and any type of bleeding should also be mentioned as a symptom that should be immediately reported to you. The thing you are trying to avoid is saying, “If only I had learned about that earlier!” If you didn’t hear about it from your patient, and you didn’t tell them to call you when it occurred, you could end up a very unhappy doctor.

### **What Information Should You Give to Patients?**

1. The nature of the proposed treatment or procedure.
2. A description of any reasonably foreseeable material risks or discomforts (including the incidence (likelihood) of occurrence, if known)
3. A description of the anticipated benefits.
4. A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous.
5. Any foreseeable risks should the patient be or become pregnant.
6. Special instructions regarding food, drink, lifestyles, taking the medication, or when to call, e.g., No Chianti with monoamine oxidase inhibitors (MAOIs), beware of postural hypotension with tricyclic antidepressants, and call if you develop a rash, sore throat, dark urine, or anything unexpected or unusual.
7. Ask the patient to repeat any special or critical instructions.
8. Ask the patient if he/she has any questions

According to one attorney author, defining material risks is a medical judgment that physicians must make (18).

As stated earlier, poor communication in the form of illegible medication orders, look-alike drug names, confusion of brand and generic names all can and do lead to medication errors (6). Case 4 illustrates one of the simplest prescription writing errors to correct.

#### Case 4

Mr. Smith is admitted to 4-West the day before surgery. A pre-operative medication order reads: Xanax<sup>®</sup> (alprazolam) 10 mg po hs. At 10 pm, the nurse attempting to administer the Xanax<sup>®</sup> discovers that she has only 10 0.25 mg single dose blister packs left on the floor and calls the pharmacy requesting another 7.5 mg of Xanax<sup>®</sup> be sent up in any dosage strength so she can comply with the doctor's order.

The pharmacy sends another 30 0.25 mg doses to the floor. The nurse asks two nursing assistants to help her open the 40 blister packs. As they are opening the blister packs and placing the tablets in a container, the patient's doctor comes in and asks: "What are you folks doing?" "Opening the single dose units so we can administer the 10 mg Xanax<sup>®</sup> dose you ordered", answered the nurse.

"Are you crazy?" asks the doctor, "I ordered 1 mg not 10 mg."

Analysis: The most likely explanations for this “near miss” medication error are that: (1) the doctor wrote the Xanax<sup>®</sup> (alprazolam) order in an ambiguous way, (2) the nurse misread the medication order, and (3) the healthcare team failed to communicate effectively. First of all, it is very upsetting to learn that a nurse would be willing to open 40 single-dose units in order to obtain what she thought was an appropriate dosage. Second, the nurse should have realized that 10 mg is NOT an acceptable single dose of alprazolam. Third, had the pharmacy been notified that a single 10 mg dose of alprazolam was ordered, the pharmacist should have recognized it as a (potential) medication error. And lastly, had the physician written the alprazolam order as “1 mg” instead of “1.0 mg”, the decimal point would not have been “missed” by the nurse, and the correct dosage would have been administered.

### **Regarding the use of Zeros in Written Prescriptions - Always Lead & Never Follow**

The lesson to be learned is that when writing a medication order or prescription for an integer or whole number dosage, NEVER use a trailing zero. Instead, write 1 mg, not 1.0 mg. On the other hand, when writing for a decimal amount, ALWAYS use a leading zero. The mnemonic to remember this easy risk management tool is, ALWAYS lead and NEVER follow.

### **Take Care to Write Prescriptions Legibly**

Poor physician handwriting can also lead to misfilled prescriptions. Figure 1 depicts a prescription which was the cover story in the American Medical News (19). Can you identify the first drug written on this prescription? If you said Plendil<sup>®</sup> (felodipine), you

are wrong. If you said Isordil<sup>®</sup> (isosorbide dinitrate), you are correct. One way of deciphering the prescription is by looking at the prescribed dosage. A quick review of the manufacturer's prescribing information (20) indicated that Plendil<sup>®</sup> was supplied only as 2.5 mg, 5 mg and 10 mg dosage strengths for once-a-day dosing, and that Isordil was available in a 20 mg dosage strength for administration 2-3 times per day. However, it shouldn't be that difficult, should it? According to the American Medical News (19), this is the "first negligence judgment against a doctor for illegible handwriting . . . ."

Moreover, both the pharmacist and the physician were found jointly liable, and each had to pay \$225,000 to comply with the Texas jury's award of \$450,000.

According to Max Wright, JD, the physician's malpractice lawyer, ". . . the misfilled prescription did not lead to the man's death. Other problems caused the man's death, but the jury latched on to the poorly written prescription and clearly indicated contempt for such sloppy work." (21) Attorney Wright indicated that "the case is much more than just a fluke" and sends "a clear warning . . . that juries will not tolerate sloppy handwriting that puts a patient's life in danger." (21) The citation for the case is Teresa Vasquez et al v. Ramachandra Kolluru, Ector County (TX) District Court. Case No. A-103,042.

In addition to poor handwriting, legibly written prescriptions can still be misinterpreted if the instructions are ambiguous. Several years ago, a prestigious Boston cancer treatment center made front page news when health reporter Betsy Lehman and a second patient both received fatal overdoses of cyclophosphamide, which had been prescribed as part of an experimental protocol to determine if cimetidine could augment the tumor-killing

effects of cyclophosphamide in the treatment of breast cancer. According to the IOM report which was cited in an ECRI publication (22), the cyclophosphamide order was written “4 g/sq m over four days.” Did this mean 4 g per day or 1 g per day for 4 days? Unfortunately, it meant 1 g per day for 4 days, but the full 4 grams were given in one day. Allegedly, the error was discovered by a Drug Utilization Review (DUR) clerk who noticed that the price charged to the patient’s bill was four times the cost of a single dose. In order to avoid confusion in prescription writing, one group of authors suggested that prescribers “Let Go of Latin!” (23) and use “plain English”. They also remind the prescribing community that “Using these shorthand terms does not consistently promote patient safety.” Discarding Latin abbreviations may help to foster a healthcare system more in keeping with *Primum non Nocere* (Above all, do no harm) than retaining an anachronistic, elitist practice that can easily lead to ambiguity and a deterioration of the quality of pharmacotherapy.

### **Studies Indicate up to Half of all Medication Errors Arise From Physician Orders**

Recent studies have indicated that when integrated medication delivery is subdivided into its integral parts, prescribing, transcribing, dispensing and administering medications, that a frequency pattern of errors has been identified. This pattern is shown in Table I.

The studies reported in Table I (24, 25) demonstrated that physician ordering is the most frequently observed stage of integrated medication delivery associated with errors. The reasons for these errors involved all of the factors discussed above. Nursing administration is second, followed by transcription errors and pharmacy dispensing

errors. Collectively, errors at any stage of the process lead to what has come to be called the Five Wrongs, which are summarized in Table II. The data from the PHICO closed claims project, which also appear in this issue of the Journal (26), are consistent with the data in Table I.

Reports of wrong drug, contraindicated drug, and incorrect dosage for the closed claim project for the years 1996-98 ranged from 42-50%, although these data do not permit an ordering error to be differentiated from an administration error, due to prescribing or legibility error. Data from the PHICO Event Reporting Trending System (PERTS) indicated a lower incidence of prescribing errors of 5% in each year studied. The data from the USP, which also appear in this issue of the Journal (27), detected an intermediate level of prescribing errors of 15%. The authors suggest that this lower incidence may be due to the fact that pharmacists are the principal reporters in the MedMARx program and that some prescribing errors may actually be reported in other systems as “clinical interventions” due to problems with workload or staffing.

However, studies have already been done to evaluate the effectiveness of alternative means of prescribing and administering medications. In one study (28), Computerized Physician Order Entry (CPOE) decreased serious medication errors by 55% and potential Adverse Drug Events (ADEs) declined 84% in the hospital setting. Electronic prescribing (e-prescribing) in the office or outpatient setting is also being explored with hand-held PDAs. According to a study conducted by Fulcrum Analytics and Deloitte Research, reported in the American Medical News (29), 6% of physicians prescribed

electronically in 2001, up from 4% the prior year. One of the major obstacles to physician “e-prescribing” reported in the study was that handheld PDAs did not transmit prescriptions directly to the patients’ pharmacies. However, newer systems can now incorporate such direct physician-to-pharmacy transmittals and it looks like just a matter of time till these systems are made available to office-based practitioners.

Administration errors were second in frequency in the studies of Leape and Bates. Neither the data from the PHICO Closed claim project cited above nor the PERTS data (26), permit an ordering error to be differentiated from an administration error, due to prescribing or legibility error. Therefore some administration errors are surely included in the 42-50% statistic cited above. The data from the USP, cited above (27), found administration errors to be the most frequent at 37%. These findings are similar to those reported by Leape and Bates (24, 25) show in Table I. Omission of dose and “wrong time” were quite common errors in this group and may reflect information readily available from the chart or Medication Administration Record (MAR). Also, many hospitals have a policy that states that a dose given more than 30 minutes late be recorded as wrong time. This may be misleading. Patients who may be off the floor receiving therapy or undergoing tests may not receive an intended dose at the proper time (or at all) and these circumstances would have been translated into an administration error.

However, the US Department of Veterans Affairs (VA) has devised a system utilizing “bar codes” to minimize drug administration errors. The VA Bar Code Administration Project (BCAP) has prevented an estimated 378,000 since its inception in August 1999.

Moreover, the American Pharmaceutical Association presented the VA Health Administration with its Pinnacle Award for its achievements in safe medication administration. According to Kenneth Kizer, MD, president and CEO of the National Quality Forum, who presented the award to Frances M. Murphy, MD, undersecretary for health at the VA, the BCAP “is a model for all health care systems to emulate everywhere.” (30)

Transcription errors of 11-12% (Table I) are the next most frequent medication error reported by Leape and Bates (24, 25). The PHICO closed claim project data did not record “transcription errors” as a separate category in its studies, but certainly some of the administration and dispensing errors that were captured reflect transcription errors. However, the PERTS data reported an incidence of 11% over the 1996-98 three-year period, and these data are quite consistent with the data of Leape and Bates (24, 25). The data from the USP collected from 1999-2001 and reported in this issue of the Journal detected an incidence of transcription errors of 10-15%, similar to other reported data.

Lastly, Leape and Bates (24, 25) reported pharmacy dispensing errors of 11-14% (Table I). The PHICO data reported only a 1-3% dispensing error rate in its closed claim project and a dispensing error rate of 5% in its PERTS. The USP data reflect a higher level of dispensing errors at 21%. Once again, these differences are most likely due to differences in classification of errors, reporter bias, and methodologic differences among studies.

Table II also includes inadequate monitoring as a class of medication errors. The PHICO closed claim project data reported 8-17% of reports involved “failure to monitor or prescribe”, while the PERTS did not capture these data. The USP data show that the incidence of medication errors due to inadequate monitoring is only 1%. Some discrepancy probably exists in the definition of the term “inadequate monitoring”.

Inadequate monitoring can mean many things. In its simplest form it could be synonymous with lack of proper follow up. One could interpret it in a “literal” meaning as in: failing to attach an EKG monitor or peripheral capillary oximeter, or a failure to have monitored vital signs (or other monitoring device) frequently enough to detect a significant sign of deterioration. These are the types of negligence claims that are brought against hospitals, physicians, nurses and other healthcare professionals when a wrongful death claim is made against a hospital. Case 5 is based on a real incident and provides all too realistic examples of both overmedication and inadequate monitoring.

#### Case 5

A healthy 32 year old female goes into the hospital to have her tonsils and adenoids removed. Her post-surgical analgesia is to be Patient Controlled Analgesia (PCA). Post-surgical medications are PCA, to be followed by the “pain team”, Phenergan<sup>®</sup> (promethazine) 25 mg IV q 4 hours prn pain, Compazine<sup>®</sup> (prochlorperazine) 10 mg po q 4 hrs prn nausea, Benadryl<sup>®</sup> (diphenhydramine) 50 mg PO q 4 hrs prn for itching, Halcion<sup>®</sup> (triazolam) 0.25 mg hs.

The patient is received on the floor at 11 am and PCA is initiated with a 5 mg morphine IV bolus plus Phenergan<sup>®</sup> 25 mg IV, morphine dose is set for 1 mg/activation, with a 6 minute lock-out time, and a basal rate of 1mg/hr. Vital signs are ordered: q 15 minutes for the 1<sup>st</sup> hr, q 30 minutes for the 2<sup>nd</sup> hr, hourly for the 3<sup>rd</sup> & 4<sup>th</sup> hours, q 2hrs for the next four hrs, then q 4 hrs thereafter. Reinforcing doses of IV Phenergan<sup>®</sup> 25 mg are given at 3 pm and 7 pm and Benadryl<sup>®</sup> 50 mg PO is given at 7 pm for itching. At 8 pm, the patient reports nausea and asks for Tums<sup>®</sup> or Rolaids<sup>®</sup>. The nurse tells the patient that those medications have not been ordered but she can call the doctor and inquire if one of them can be given. However, the nurse also tells the patient that another medication, Compazine<sup>®</sup>, has been ordered for nausea. “No, don’t bother the doctor,” says the patient, “Just give me what the doctor ordered.” Compazine<sup>®</sup> 10 mg PO is given at 8:30 pm. At 9 pm, Halcion 0.25 mg is given for sleep. At midnight, the patient is found cyanotic and unresponsive. A code is called but the patient could not be resuscitated.

Analysis: A healthy patient is not supposed to come into the hospital for a routine procedure and die from a medication overdose. Unfortunately, cases of respiratory depression and arrest are reasonably common occurrences. Morphine, other narcotics and Patient Controlled Analgesia (PCA) are among the medications listed by the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) in its initial report on “High-Alert Medications and Patient Safety” report in November 1999 (31) and shown in Table III.

### **Legal Implications of a Negligence Claim for Inadequate Monitoring**

Generally, the deceased's family will sue every party involved in the care of the deceased patient. This means suing the physician who prescribed the morphine/PCA dose, the nurse who monitored the PCA IV (and may or may not have "set up" the PCA), the hospital where the event occurred, and any other healthcare professionals who may have been involved (e.g., pain control service, anesthesiologist, residents, interns) . The family sues the hospital for negligence. Negligence is conduct below the standard of care for a "reasonable professional". The claim will state that the nurse failed to adequately monitor vital signs and that this was a deviation in the standard of care. Since the nurse was an employee of the hospital, the hospital would be vicariously liable for the actions of the nurse employee. This is the doctrine of *Respondeat Superior* or Let the Master Answer (32).

The prescribing physician will usually be sued for medical negligence. Other professionals and/or employees or apparent agents of the hospital could also be "joined" in the law suit. In order for a plaintiff to have a successful negligence case in court, four essential elements are required: (1) a doctor-patient or professional relationship has to exist between the patient and the healthcare professional (i.e., MD, RN, PharmD). This relationship ensures that the professional owes a duty of "reasonable care" to the patient, (2) the conduct of the professional had to be below the standard of care, (3) the patient was injured (damages), and (4) the action(s) (or inactions) that constituted the breach of duty was the "proximate cause" of the patient's injuries. According to the JCAHO (31), there have been "mix-ups" between the names of the drugs morphine and hydromorphone

as well as the concentrations, doses and infusion rates. There have also been errors in programming and pump settings. One way to minimize “programming errors” is to use only 1-2 types of pumps in each facility. Different pumps are programmed in different manners. People get confused. New employees, “floaters”, temporary help from agencies, and those who are covering for vacations or for employees who are out sick may not be familiar with the pumps on your floor and may program the pump incorrectly. In addition to opiates and PCA, the JCAHO also identified other medications as “High Alert” drugs, based on the frequency of reports submitted to their “Sentinel Events” program back in 1999. These drugs are summarized in Table III. According to the JCAHO website ([www.JCAHO.org](http://www.JCAHO.org)), the definition of a “Sentinel Event” is “an unexpected occurrence involving death or serious physical or psychological injury or risk thereof.” The terms serious and unexpected should ring a bell with pharmaceutical industry clinical researchers and principal investigators familiar with the post-marketing 15-day “Alert” reporting requirements described under 21 CFR 314.80 (c) (1). However, the additional caveat in the definition of a Sentinel Event, “or risk thereof” does require further explanation. According to JCAHO, the risk of a Sentinel Event signifies, “any process variation for which a recurrence would carry a significant chance of serious adverse outcome.” In this setting, the JCAHO is concerned with “System Errors” or flaws in integrated drug delivery that can and do lead to medication errors. For an in depth discussion of system errors, see Case 6 and the associated discussion.

The medications reported in November 1999 (31) have continued to appear in subsequent JCAHO reports; for example, Insulin and Heparin. Insulin and Heparin also share the

dubious distinction of being prescribed in “units” rather than milligrams. As a result, some prescribers have written orders for either of these drugs and failed to “spell out” units. Instead, they have written the dosage followed by “U”. This capital “U” has been misread for another zero, and the administered dose has been increased ten-fold.

A very recent publication (33) indicated that in a group of hospitals in Georgia and Colorado, the same spectrum of medication errors reported in the earlier literature, by USP, and in the PHICO data continue to be detected. Moreover, hospitals accredited by JCAHO did not have significantly lower error rates than non-accredited facilities. It appears that JCAHO audits and the dissemination of “Alerts” have failed to significantly reduce medication errors in the general hospital population. All institutions had medication error rates of nearly 1 error in every 5 doses.

### **“High Risk” Drugs Identified in Other Studies**

The Agency for Healthcare Research and Quality (AHRQ) has funded numerous studies around the country in order to determine which classes of drugs are most frequently associated with adverse reactions in patients. The results of these studies have been published (24, 34, 35, 36, 37, 38) and provide clear insight into medication-related morbidity and mortality.

AHRQ studies identified several classes of drugs involved in a significant number of adverse drug events. These classes of drugs are summarized in Table IV. A review of these data indicates that antibiotics top the list. Antibiotics were also one of the leading

causes of adverse reactions identified in the PHICO data. According to Robert F. Pendrak, MD, who was Medical Director at PHICO prior to PHICO going out of business, many of the reactions to antibiotics involved anaphylaxis, not simple rash or urticaria. It is important to remember that certain classes of antibiotics show some cross-sensitivity with members of another class, e.g., penicillins and cephalosporins. Up to 10% of the population may be allergic to penicillins (39) and as many as 20% of penicillin-allergic patients show immunologic evidence of cross-sensitivity to cephalosporins, although clinical studies indicate a much lower incidence of occurrence of 1% (40).

The term analgesics in Table IV is not broken down into narcotic and non-narcotic agents. However, the PHICO data do mention antirheumatics and antipyretics specifically to distinguish them from opiates. Nonsteroidal anti-inflammatory drugs (NSAIDs) could be listed due to their capacities to cause GI bleeding, acute renal failure, anaphylaxis in aspirin-sensitive individuals, and severe desquamating rashes like Stevens-Johnson syndrome and Toxic Epidermal Necrolysis (TEN), as described earlier. Opiates have been discussed in Case 5.

Third on the list of AHRQ-identified drugs is cardiovascular drugs. Certainly concentrated solutions of electrolytes, especially KCl, can cause cardiac arrest. In fact, KCl is the third drug used in “Lethal Injection”, after a fast-acting barbiturate like thiopental, and a paralyzer of respiratory function like succinylcholine. The PHICO data also list antihypertensives, adrenergics, anticholinergics, antiarrhythmics, cardiac

glycosides, fibrinolytics, and electrolytes. Concentrated electrolytes and anticoagulants are also listed, along with sedatives and antineoplastic agents. Overmedication with sedatives has already been discussed in Case 5 and the lethality of antineoplastic agents is established by its alternative name, cytotoxic agents, and the unfortunate incident involving Betsy Lehman described earlier. When the studies described in the literature, the PHICO data, and the USP experience are taken collectively, they all show great consistency in identifying the same classes of drugs and the same types of errors. It is apparent that those who misread history (or do not read the literature) are doomed to repeat the mistakes of the past.

### **Pharmacologic Criteria for Identifying “High Risk” Drugs**

It is not a coincidence that studies consistently report the same drugs involved in medication errors and adverse drug reactions. Pharmacologic criteria for identifying high risk drugs are presented in Table V. Perhaps the foremost underlying pharmacologic principle of rational therapeutics is the Therapeutic Index or TI of a drug. Although classically defined as the ratio of the  $LD_{50}/ED_{50}$ , modern advances in the correlation of pharmacokinetics and pharmacodynamics have established “therapeutic windows” for many medications where therapeutic drug monitoring is appropriate. However, without training in clinical pharmacology, some practitioners do not recognize the importance of the time interval between the last dose and the time of blood sampling and send patients for random blood samples rather than specifying “Take your medication and come to the office 2 hours later.” Although computerized dosing nomograms to optimize blood levels of low TI drugs like aminoglycoside antibiotics (41) are available, without training

in computer-based pharmacokinetics, practitioners continue to calculate dosage according to less reliable mg/kg criteria.

The significance of a low Therapeutic Index is shown in Case 6.

#### Case 6

BP was a woman who had been on Coumadin<sup>®</sup> 5 mg for years. During that time, her Prothrombin times (PT) had been within the desired therapeutic range. BP went to her local pharmacy to have her Coumadin<sup>®</sup> prescription refilled. The pharmacist mistakenly dispensed the 2.5 mg strength which was orange colored for the 5 mg dosing strength which was peach colored. BP took the lower dose for 12 days and suffered a thrombotic stroke which resulted in hemiparesis.

BP and her husband sued the pharmacist for negligence, and also sued the hospital where the PT was conducted, claiming the hospital failed to notify the patient in a timely manner of an abnormally low PT. The pharmacist filed a cross-claim against DuPont Pharmaceuticals, the manufacturer of Coumadin<sup>®</sup>, claiming that the similarity in colors of the two dosage forms contributed to the error. Despite evidence that DuPont had been receiving complaints about the similarity in colors for 10 years, the pharmacist's admission that he had been familiar with the similarity and confusion regarding the colors of the dosage strengths for 15 or 20 years paved the way for a \$722,500 jury award, less a 10% reduction for the patient's contributory negligence of not having noticed the dosage strength imprinted on the tablet. DuPont was also found negligent, but the negligence

was not determined to have been a proximate cause of BP's stroke and DuPont did not have to contribute any money to the award. Ultimately, the color of the 2.5 mg dosage strength was changed from orange to green, and BP and her husband received an award of \$900,000, which included post-suit interest. (42)

Inherent undesirable effect(s) are typified by steroids and chemotherapeutic agents. Certainly steroids affect more organ systems in the body than any other class of drugs in therapeutic use, and on a short-term basis, steroids can cause immunosuppression, impaired wound healing, salt and water retention, hyperglycemia, and mood changes. Over time, steroids can produce devastating effects like: cataracts, suppression of the hypothalamic-pituitary-adrenal axis, osteopenia, protein wasting and negative nitrogen balance, and aseptic necrosis of the femurs and humerii (43). Following discontinuation of steroids, suppression of the hypothalamic-pituitary-adrenal axis may take up to nine months to recover normal function (44). Of all the steroid-related side effects and secondary effects, there is none so disabling as osteonecrosis of the femurs and humerii, sometimes also called aseptic necrosis or avascular necrosis.

Unfortunately, this author's experience indicates that there is a perception among clinicians that short-term, even high dose glucocorticoid therapy, is devoid of long-term devastating effects. This is untrue. According to one author, (45) aseptic necrosis developed on a patient following a 16 day course of corticotropin. A second author's review of the literature indicated that osteonecrosis can develop in patients who received very short-term, high dose steroid therapy, long-term therapy, and even following

intraarticular steroid injection (46). This same author points out that even when steroids were correctly administered for life-threatening disorders, physicians were sued for failure to inform patients about the potential risk of developing osteonecrosis.

Part of the problem is that steroid-induced osteonecrosis takes at least six months to develop (46). Therefore, prescribers unfamiliar with the literature may fail to make the association between steroid administration and the cause of the aseptic necrosis six months later. Another reason is that prescribers do not wish to discuss the reality of the fact that steroids cause osteonecrosis is because steroids are so heavily relied upon for their therapeutic effects that to “slander” them for their undesirable properties is considered heresy! Unfortunately, this kind of “mural dyslexia” i.e., failing to see the handwriting on the wall, has led physicians into a scenario similar to the ostrich or the groundhog. You can hide your head in the sand or stay in your den until you see your shadow, but the process server will find you and you may be required to pay your dues in court. A better lesson from the animal kingdom would be to prescribe all medications in the same manner that porcupines reproduce, very carefully! The toxicity of chemotherapeutic agents has already been discussed.

Table V also include “classes of drugs which share toxicity”, and lists NSAIDs and angiotensin converting enzyme inhibitors (ACEIs) as examples. The fact that drugs in the same pharmacologic classes share similar therapeutic and toxic properties is a two-edged sword. Cross-sensitivity among class members has already been discussed. However, the fact that drugs in the same class also share toxic properties can be

interpreted as helpful from the perspective that drug side effects that occur most frequently are usually known to occur with that class of agents.

Several years ago, while teaching clinical pharmacology to a group of senior medical students, this author inquired of the class, “How do you know whether an adverse effect in one of your patients has been caused by a drug or the patient’s pathophysiological condition?” There was abject silence in the room. The sought after answer was that adverse drug reactions are usually excessive effects of known pharmacologic actions, i.e., secondary or side effects. If the prescriber is familiar with the known effects of a prescribed drug, then he/she should be on the lookout for reports of effects that are known to occur with that class of agents.

Newly-approved drugs most likely have been tested in only 2,500 to 5,000 “pristine patients”. In this setting, “pristine” means that patients have been excluded from study if they had other confounding medical conditions and/or were receiving other medications. Due to the small sample size and limited duration of study, pre-marketing trials often cannot detect serious, infrequent adverse drug effects (47, 48). With a patient population and denominator of 10,000 or less, the sensitivity limitation of detecting an adverse effect is 0.1%, or 1 in 1,000 (49). Moreover, the number of pristine patients that must be studied in order to detect an adverse reaction with an expected incidence of 1 in 1,000 is 3,000, not 1,000 (50). Temofloxacin (Omniflox<sup>®</sup>) is an example of a drug which only lasted 3 ½ months on the market. The first prescription was written on February 24, 1992

and the drug was voluntarily withdrawn from the market by the manufacturer on June 9, 1992.

According to the Summary Basis of Approval for Omniflox<sup>®</sup> (temofloxacin), approximately 4,261 patients were studied prior to marketing and an incidence of renal failure of <0.1% was detected. This translates into 4-5 cases. Since some patients ostensibly were treated for urinary tract infections and/or had pre-existing renal disease, 5 cases of renal failure were too few to determine if this was a normal background incidence in the population for acute renal failure, or if it was drug related. According to Freedom of Information Act data, after marketing, an estimated 300,000 patients received temofloxacin and 54 cases of renal failure were reported, an incidence of approximately 1 in 6,000 for renal failure. Moreover, 113 cases of hemolytic anemia were also reported for an incidence of approximately 1 in 3,000. These reports led to a very rapid withdrawal of temofloxacin from the market.

Off-Label use of medications is also listed as High Risk. This is because although there is nothing illegal about using an approved drug for an unapproved indication (51), the safety of the unapproved indication has not generally been studied in as organized a manner and in as large a patient population as it would have been during a complete Phase III clinical program. Take Fen-Phen for example. Phentermine had been on the market for years before it was combined with the newly-approved fenfluramine as a combined treatment for weight control. The valvular heart disease and primary pulmonary hypertension that developed in a significant proportion of the Fen-Phen-

treated population required at least 3 months of treatment to develop. Many of the original 250 patients (1/10 the number in a typical NDA) received shorter courses of the drugs. Moreover, physicians had no product information on the combined product to alert them to the possibility of these severe, infrequent drug-related effects.

Pharmacokinetic drug interactions leading to augmentation and inhibition of therapeutic activity by affecting the processes of absorption (52), distribution (53), metabolism (54) and excretion (55) have been known for decades. However, some drug-drug interactions may be difficult to predict like failure of an oral contraceptive due to impaired enterohepatic recirculation of estrogenic compounds as a result of antibiotic therapy which altered intestinal flora and hydrolysis of estrogen conjugates (56). Moreover, with the increased prescribing of selective serotonin reuptake inhibitors (SSRIs), even therapeutic doses cannot be ruled out in contributing to the death of one patient taking prescribed doses of clozapine (57) and other deaths where therapeutic blood levels of SSRIs were found in conjunction with elevated levels of other concomitantly-ingested illicit and prescription drugs, with and without ethanol (58).

Last on the list of high risk drugs are drugs promoted by direct-to-consumer ads. Direct-to-consumer ads induce patients to ask their physicians to change established regimens, substitute new drugs for older drugs, or add new medications to existing therapies. While in principle, some patients who are not receiving optimal therapy may benefit from a revision of their medications, some will deteriorate. Moreover, costs of newer drugs are greater than older ones, or generic equivalents. In addition to all of these concerns,

according to one author, “. . . unnecessary prescription ordering can be detrimental to the patient-physician relationship.” (59) Another problem faced by clinicians reviewing consumer ads is that the information has not been peer reviewed and may be more “advertorial” than informative and “places an additional burden on the prescriber to carefully read through and analyze all of the “slick” pharmaceutical advertisements . . . to make the best therapeutic decisions for his or her patients (51). Even pharmaceutical journal ads, which are regulated by the Food and Drug Administration (FDA), have been criticized for a lack of fair balance between efficacy and safety data claims that a certain drug was the “drug of choice” for a particular indication, or other expressed claims (60).

### **How Do We Cure the Sickness in the Healthcare System?**

Writing in an editorial in the Journal of the American Medical Association, Leape and his colleagues described modern health care as presenting “the most complex safety challenge of any activity on earth.” The authors diagnose healthcare’s problem as a failure to have designed “our systems for safety, relying instead on requiring individual error-free performance enforced by punishment . . .” and prescribe the following treatment “. . . to make health care safe we need to redesign our systems to make errors difficult to commit and . . . injury prevention is recognized as everyone’s responsibility.” (61) A simple “redesign” solution to a complex problem would involve changing the design of the fittings on the ends of tubing used for nasogastric (NG) tubes so they cannot be plugged into intravenous (IV) lines, making it virtually impossible for an NG tube to be connected to an IV line and minimizing the probability that nutritional products will not be given inadvertently by the IV route when they should be given by NG tube.

In 1995, Leape et al identified 13 system errors or “proximal causes” of medication errors in the hospital setting, (62) summarized in Table VI. Case 7 illustrates how many of the “system errors” listed in Table VI contributed to the unfortunate death of a patient.

#### Case 7

A 63 year old male had been receiving enalapril for one year for treatment of his hypertension. Last week, he experienced some difficulty swallowing and discomfort in the back of his throat. He called his doctor and was told to go to the emergency room at the local hospital. Upon arrival in the ED, the patient was experiencing some mild breathing difficulty and was treated with Benadryl<sup>®</sup> (diphenhydramine), 50 mg IM and oxygen by mask. Within 30 minutes, the patient was breathing more comfortably and was admitted to a general medical floor for observation.

The next morning, the patient’s wife arrived with a bag of the patient’s “other medications”, which she said she administered to her husband every day. The nurse called the admitting physician and received permission to administer the patient’s other medications, during the course of which, the nurse also administered another dose of enalapril.

The patient was discharged later that day. The day following discharge, the patient suffered an episode of acute angioneurotic edema with dysphagia, lip swelling and airway obstruction, and expired before the paramedics could respond.

Question: How many of the “system errors” listed in Table VI occurred in this case?

Analysis of Case 7. Of the 13 system errors listed in Table VI 1, 2, 3, 4, 7, 8, and 10 definitely occurred. System error 1, Lack of knowledge about the drug, occurred because the healthcare team did not recognize that enalapril, an ACE inhibitor, can cause acute angioneurotic edema and permitted a second dose to have been given. Error 2, Lack of information about the patient, occurred because somewhere in the chart, a healthcare professional should have written, “Rule out reaction to enalapril”. Error 3, Rule violations, probably occurred. Most hospitals require that ALL medications given to patients go through the hospital computer and come from the hospital pharmacy. To allow a well-meaning spouse to provide even one drug dose from a “brown bag” means that there is no way to check that drug for incompatibilities using the hospital’s multi-million dollar computer system. Error 4, Slips and memory lapses could have occurred on the part of both the admitting physician and the nurse. Error 7, Faulty interaction with other services, makes everyone wonder just what was said between the nurse and the doctor. Error 8, Dosing error, is self-evident. Error 10, Inadequate monitoring, or lack of proper follow-up may have occurred. A call to the discharged patient’s home the next day may have provided some information that could have altered the course of events. This case is based on an actual occurrence.

The phenomenon associated with angioneurotic edema is very interesting and may be poorly understood by pharmacologists and practitioners alike. The reaction appears to be anaphylactoid and biological in nature since it can occur in the absence of antibodies to

the precipitating agent, and without activation of the immune system. (63) Since angiotensin converting enzyme (ACE) is identical to kinninase II which inactivates bradykinin (64), inhibition of ACE also increases levels of bradykinin, which is known to cause lip swelling and tongue dysesthesia. (63) Moreover, angioneurotic edema may be more common than the 0.1% incidence generally reported because death in such patients is usually attributed to the patient's underlying hypertensive heart disease and/or congestive heart failure and referral to a coroner or medical examiner for autopsy is waived. In one series reported by the Franklin County Coroner's office in Columbus, Ohio, seven deaths from angioneurotic edema occurred in Afro-American men and women during the three year period of 1998-2000 (65) The reaction is more common at the initiation of therapy, but can occur at any time during therapy, and there is cross-reactivity among members of the ACE class (63, 65).

### **What Can be Done to Remedy Faulty System Errors?**

Certainly there are basic safety strategies that can be implemented. Using the criteria for identifying high risk drugs presented in Tables III, IV, and V, review your protocols for administering these drugs and take care to ensure that these drugs are being ordered, dispensed and administered according to the most recent practice guidelines. Where dosing issues are important, consider developing special ordering forms for these drugs which list the approved doses, intervals and contraindications (dose limit protocols). When possible, institute computer-based patient medical record systems and physician computerized order entry. Also, the use of clinical pharmacists to assist physicians in selecting and prescribing medications has proven to be very useful in reducing adverse

drug reactions 66% and was reported to have the potential to save one intensive care unit an estimated \$270,000 over the course of a year, based on an estimated cost of \$4,685 per preventable adverse drug event (66).

### **Failure Mode Effect Analysis (FMEA)**

Failure Mode Effect Analysis (FMEA) has been used for many years in other industries like aviation, to identify, anticipate, and remedy steps in a process that are likely to lead to failure. (67) FMEA has recently been adapted to problems encountered in healthcare by the Veterans Administration National Center for Patient Safety (VA NCPS) where it carries the acronym HFMEA, Healthcare Failure Mode Effect Analysis (68). The American Society for Healthcare Risk Management recently has developed a “White Paper” on FMEA (68) that is available free of charge to interested parties and can be downloaded from their website at [www.ASHRM.org](http://www.ASHRM.org).

Using FMEA as a risk assessment tool can be useful in identifying and redesigning faulty systems for integrated drug delivery which can and do lead to medication errors. The basic steps in FMEA are shown in Table VII. Applying the steps in Table VII to “Prescription Writing” provides an example of the application of FMEA to redesigning all the steps in integrated medication delivery, prescribing, transcription, dispensing and administering medication.

Select a process:	Integrated Medication Delivery
Select a sub-process:	Prescription Writing
Diagram the process:	Identify all Steps that Could go Wrong/Develop a Flow Chart

Identify steps that can fail: Wrong Patient Name, Wrong Drug Name, Wrong Dose,  
Wrong Route, Wrong Duration, Contraindication due to  
History of allergy, or interacting drug

Asses & Characterize risk: Wrong Drug Name or opinion of FMEA Team members

Select a high priority risk: Wrong Drug Name

Root Cause Analysis: Who – Prescriber

What – Confusion

Why - Illegible writing, no CPOE

When – Any time

How – Order misread by clerk, RN, Pharm.D

Redesign the process: Institute Computerized Physician Order Entry

Measure/track performance: Join MedMARx, Record/Benchmark Medication Errors

Obtain Legal Privilege: Report to USP or other Patient Safety Organization  
qualified to provide legal privilege

## **Conclusions**

A medication error is defined by the National Coordinating Council for Medication Error Reporting and Prevention (NCCMERP) as “any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the healthcare professional, patient, or consumer. Such events may be related to professional practice, healthcare products, procedures, and systems, including prescribing; order communication; product labeling, packaging, and nomenclature; compounding; dispensing; distribution; administration; education; monitoring; and use.”

(69) In this comprehensive description of a medication error, the most important word in the definition is “preventable”. The recognition that errors are preventable is the first step in reducing or eliminating them, enhancing the quality of pharmacotherapy and increasing patient safety. Although training and vigilance are important in reducing medication errors, they are not enough. In order to reduce medication errors, it is necessary to dissect and analyze the entire process of integrated medication delivery (from pen to patient), and replace older error-prone processes with newer, simplified systems that will not permit traditional errors to occur. Using computerized physician order entry, electronic patient medical records and bar coding patient identification bracelets and medications produce dramatic results. Identifying “look alike” drug names, and storing them in different areas of the pharmacy and drug cabinets on the floors and special care units reduces the risk of selecting the wrong one. In hospitals that cannot afford costly computerized systems, writing both the Brand and generic names on the medication order, followed by the condition to be treated, e.g., Lamictal<sup>®</sup> (lamotrigine) for seizures minimizes the likelihood of reported confusion with the look-alike anti-fungal, Lamisil<sup>®</sup> (terbinafine).

High risk drugs like Heparin, coumarin anticoagulants, and Insulin require close scrutiny when being prescribed, dispensed and administered, and proper follow up after administration. Updating protocols for these drugs and utilizing pre-printed prescribing forms can help reduce errors. Writing medication orders in the chart, dispensing medications, and administering medications are the wrong times to accept phone calls,

respond to pages, or make small-talk with colleagues; these are the right times to concentrate on what you are doing.

Most importantly, it is time to recognize that healthcare is a team activity. Although the physician is still the leader of the team, helpful input from clinical pharmacists, nurses and other healthcare professionals can provide invaluable assistance and improve the quality of care for the patient. Practicing medicine, nursing and pharmacy is too complicated for healthcare professionals to be able to carry all required information in their heads. Electronic and computerized systems can help, but first, all healthcare professionals must acknowledge that a problem exists. This means reporting errors, analyzing errors and redesigning faulty systems. The current philosophy is to develop a “blameless culture”, where making things right, not finding a scapegoat predominates.

If you think that instituting computerized physician order entry (CPOE) or hiring clinical pharmacists to make rounds with your physicians costs too much, remember that every preventable medication error costs almost \$5,000 in extended or re-hospitalization expenses. The data are clear (66), one Pharm.D. in one unit saved that hospital a projected \$270,000 that year. Preventing medication errors will pay for your computerized system or Pharm.D in no time. Moreover, fewer errors will be committed, you will provide a higher quality of care, patients will be safer and better served and less litigation will ensue. There is no question that quality improvement costs less than medication errors.

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Table I

Occurrence of Medication Errors  
in Studies of Hospitalized Patients

Physician ordering:	39-49%
Nursing administration:	26-38%
Transcription:	11-12%
Pharmacy dispensing:	11-14%

From: Bates, DW, Boyle, DL, Laird, N, et al. Incidence of Adverse Drug Events and Potential Adverse Drug Events, JAMA 1995;274(1):29-34.

Leape, LL, Bates, DW, Cullen, DJ, et al. Systems Analysis of Adverse Drug Events, JAMA 1995;274(1):35-43.

Table II  
The Five Wrongs\*

Wrong drug

Wrong dose

Wrong route

Wrong patient

Wrong time

\*Inadequate monitoring  
is also frequently included.

Table III  
High Alert Drugs Reported to  
JCAHO's Sentinel Event Alert\*

Insulin

Opiates/PCA

Concentrated solutions of

KCl & Potassium Phosphate

IV Anticoagulants (Heparin)

NaCl solutions above 0.9%

\*Issue 11, Nov. 19, 1999.

Table IV  
Classes of High Risk Drugs  
Identified in AHRQ Studies\*

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Antibiotics	19-30%
Analgesics	7-30%
Cardiovascular drugs	8-18%
Concentrated electrolytes	1-10%
Antineoplastic drugs	7-8%
Sedatives	4-8%
Anticoagulants	1.3-3%

\*References 24, 34, 35, 36, 37, 38

Table V  
Identifying High Risk Drugs

<u>Characteristic</u>	<u>Prototypes</u>
Low Therapeutic Index	digoxin, anti-coagulants
Inherent Undesirable Effect(s)	steroids, chemo
Class of Drugs Which Shares Toxicity	NSAIDs, ACEIs
Narcotics- PCA	morphine, all
Newly-Approved Drugs	temofloxacin
“Off-Label” Uses of Drugs	Fen-Phen
Pharmacokinetic Drug Interactions	SSRIs
Direct-to-Consumer Promoted	add-a-med

Table VI  
“Proximal Causes” of  
Medication Errors\*

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1. Lack of knowledge about the drug
2. Lack of information about the patient
3. Rule violations
4. Slips and memory lapses
5. Transcription errors
6. Faulty drug identification
7. Faulty interaction with other services
8. Dosing errors
9. Infusion pump/Parenteral delivery error
10. Inadequate monitoring
11. Drug stocking or delivery problem
12. Preparation error
13. Lack of standardization

\*Leape, LL, Bates, DW, Cullen, DJ et al  
System Analysis of Adverse Drug Events  
JAMA 1995; 274:35-43.

Table VII  
Steps in Conducting a FMEA Risk Assessment

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Select a process or sub-process to analyze

Assemble a multi-disciplinary team

Identify all the steps in the process that could fail

Diagram the process to be assessed

Assess the risk priority, likelihood and severity of failure

Select a high priority risk and conduct a root cause analysis (RCA) of the factors leading to failure. Ask: who, what, why, when, and how might this fail?

Redesign the process

Identify ways to measure and track performance under the redesigned system

Protect the process from being subpoenaed in a legal proceeding by involving legal counsel, Peer Review statutes and/or reports to Patient Safety Organizations as proposed by pending federal legislation, e.g., Patient Safety and Quality Improvement Act (S. 2590) and Patient Safety Improvement Act (H.R. 4889), whenever possible

Adapted from: Strategies and Tips of Maximizing Failure Mode Effect Analysis in Your Organization. American Society for Healthcare Risk Management, Chicago, IL, July 2002

Figure 1

In this symposium Dr. Bob Pendrak has shared data from PHICO's Closed Claim project on medication errors over the 1996-1998 period of time. In addition, Judy McMeekin, Pharm.D. and John Santell, MS, RPh. have presented their data from the last three years of USP's broad-based MedMARx Reporting system. Collectively, these data provide an excellent overview of the types of errors, where in the process the "system errors" occurred, and which drugs were involved most frequently. Another valuable source of data on "High Risk" drugs is the Joint Commission on Accreditation of Health Care Organization's (JCAHCO) Sentinel Event program.