Transforming to a culture of safety in the Philippines.

KENNETH HARTIGAN-GO MD
TABLE OF CONTENTS

Foreword by............................................................................................................................. Rene I. Juaneza, MD

Chapter 1: ADR Reporting Systems for the Philippines ......................................................... pg. 1
Internist and how it fits into our Public health systems

Chapter 2: Types of ADR/Pharmacovigilance Mechanisms ............................................... pg. 5

Chapter 3: Drug Interactions, the dangerous ones ............................................................... pg. 10

Chapter 4: Finding Ways to Prevent Medication Errors ....................................................... pg. 13

Chapter 5: Vaccine-Related Injury ..................................................................................... pg. 22
Dr. Lyndon Llamado & KHG

Chapter 6: Assessing Causality ......................................................................................... pg. 25

Chapter 7: Participating in Drug Trials – Do’s and Don’ts ................................................... pg. 29
Dr. Anthony Leachon

Chapter 8: Erice Declaration .............................................................................................. pg. 33

Chapter 9: Detecting Substandard and counterfeit pharmaceutical products ..................... pg. 35

Chapter 10: If patients get sicker with medicines, ................................................................. pg. 39
consider adverse drug reactions as a differential diagnosis (medico-legal concerns)

Last words of advice
The PCP, at the start of my term and with new Board of Regents, has created a number of innovative advocacy programs, one of which is the Pharmacovigilance on Adverse Drug Reactions (ADR), with the intention of serving the best interests of our members and patients. In our country, we have observed that the culture of safety is often overlooked and disasters are recurrent. The PCP wanted to provide some practical tools for our members on the areas of medication use. This handbook is envisioned to serve as a continuing educational tool for our members and residents in training.

There are occasions that despite due care, the use of medicines can lead to inadvertent adverse drug reactions through no fault of the doctor. The doctor must know how to recognize these events, how to stop the medications, how to manage the reactions, how to report these and how to communicate the unforeseen, unwanted event to the patient. Information such as these must also be shared with the drug industry as part of due diligence and product stewardship. All these with the intention of protecting the doctor, preventing similar future adverse events, and providing continuing care at the highest possible level to our main stakeholders, the patient themselves.

Sometimes, the issue is not about a medicinal product but an adverse event might be due to how the drug was used. These can result due to some breakdown in communications, prescribing and dispensing errors. In this handbook, we share with you some practical tips on how to put in place sensible guidelines to avoid costly errors that could be detrimental to patients receiving the drugs.

Counterfeit and sub-quality medicines hounding the Philippine health sector is a common knowledge. It is imperative to make doctors aware that the drugs they use must come from legitimate and credible sources that are applying standards that are much higher than current local regulatory requirements. It is also within this context that the PCP Board of Regents is trying to find ways of improving our methods of giving quality care to patients and in consonance to what is within ethical norms and standards.

Lastly, the Board of Regents would like to acknowledge and thank the working committees, headed by Dr. Kenneth Hartigan-Go, the authors and the staff for taking time to make this worthy endeavor a reality in our time.
Pharmacovigilance is defined as the Science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other possible drug-related problems.

There is no such thing as a safe drug, but there are ways to make the drug safer whether it is the medicinal product itself or the manner by which such drug is used.

There is an international program within the World Health Organization that undertakes drug safety monitoring. This program relies on the member countries of United Nations reports of their country experience in adverse drug reactions. Each country experience utilizes the reports detected by health professionals and institutions. The results of the scientific evaluation by WHO are their shared to the different stewards for drug safety, like the medicine regulatory authorities, drug companies, and academic and medical bodies for action. Ultimately, this provides that critical intelligence for us to exercise due diligence when prescribing and using medicines.

This is the essence of public health, the translation of the lessons learned in clinical cases for the public good. It is therefore an imperative for us to educate PCP doctors that they need to exercise their public health duty to report cases that they suspect to be drug reactions to the government regulatory agency (the Bureau of Food and Drugs) for databasing and submission to the WHO for evaluation.

An internist-specialist is in a unique position in the areas of adverse drug reaction. An internist prescribes medicine to patient for a specific condition, patient develops adverse drug reaction in another part of the body, patient seeks another specialist for that part of the body inadvertently affected by the medicines. The internist who prescribed the first drug might be put in an embarrassing position if the second doctor, who does not know how to communicate the correct views on medicines and erroneously explained that it was the fault of the first prescriber. Doctors and patients alike must understand that adverse drug reactions are unforeseen, untoward and unwanted effects of taking medicines that can occur at some points for taking medicines. Taking medicines is an informed choice and that the doctor and patient jointly undertake some basic risk-benefit evaluation. Simply put, one is willing to use a medicine with some known adverse effects because not using it will be more harmful to the patient with a disease condition.

Hence it is critical that an internist understand that he has a public duty:

- To keep learning about ADRs and to share this with colleagues
- To explain the potential adverse effects and side-effects before the drug is given or when the reaction has already occurred.
- To manage the ADR or to refer if needed
- To report the suspected or observed ADR to a body for analysis and feedback.
It is only when doctors agree to share detected ADR cases that public health is served, and that is to improve the overall patient care and their safety. The same principle applies when a doctor observes ADR, these can be reported to their hospital where they practice so that drug supply management can be improved and ultimately benefits the practicing internist and patients.

In many cases, a public health program will also use medicines for mass treatment. When a community is given medicines either to prevent an endemic disease, or to treat medical conditions, invariably, some persons may experience ADRs. They then seek consult with you. We then have a duty to share such experience with the perspective that it will ultimately help the public health programs (in terms of sourcing better quality drugs, in terms of avoiding certain subgroups of susceptible patients, in terms of drug interactions, in terms of modifying usage and indications, etc.)

One detected ADR may mean an insignificant report, but when there are many other places with just one report of similar ADR, collectively, they can be group as a potential Signal.

Basically the report will have the following facts: details of the patient, details of the drugs used, details of the reaction, and details of the reporter. To protect confidentiality, the details of patient and reporter are anonymized.

The BFAD ADR confidential report form is included in the next page and can be downloaded from: http://www.bfad.gov.ph/NADRAC/downloads/Report%20form.doc

Adverse events can be opportunities for improvement. A recent commentary in PJIM (Evangelista 2006) outlined the importance of having a critical, honest, blame free system to encourage reporting and for us to learn from these lessons particularly because a doctor manages a patient through a health care system and sometimes unintentional error can occur.

Reference:

Confidential Report on Adverse Drug Experience

Note: Submission of this report does not constitute an admission that the drug caused the adverse reaction. Identities of the reporter, institution and patient will remain confidential. Please mark all appropriate items.

<table>
<thead>
<tr>
<th>Patient’s initials</th>
<th>age</th>
<th>sex</th>
<th>male</th>
<th>female</th>
<th>wt. (Kg)</th>
<th>ethnic group</th>
<th>Filipino</th>
<th>Chinese</th>
<th>others</th>
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Describe the reactions:

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<tr>
<th>Onset of reaction:</th>
<th>time</th>
<th>am</th>
<th>pm</th>
<th>mon</th>
<th>day</th>
<th>year</th>
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Drugs used prior to ADE (brand names) Pls. check the suspect drug/s.
Pls. indicate manuf. if generic names are used. Pls. indicate batch & lot number if applicable.

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<tr>
<th>Route</th>
<th>Dose</th>
<th>Dosing time</th>
<th>Date/time started</th>
<th>Date/time stopped</th>
<th>Indication/s</th>
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Treatment of reactions:

Outcome:

- [ ] Recovered Date ___/___/1999
- [ ] Not yet recovered
- [ ] Unknown
- [ ] Died Date ___/___/1999

Resulted in prolonged hospitalization? [ ] No [ ] Yes
Sequelae? [ ] No [ ] Yes Please describe

Comments:

- [ ] allergies
- [ ] previous exposure/reaction to suspect drug/s
- [ ] pregnancy with LMP
- [ ] relevant history
- [ ] others

Name of reporter签名

Date reported ___/___/1999

Address of reporter

Tel no.

[ ] MD [ ] Nurse [ ] Pharmacist [ ] Patient [ ] Others
Table: A Stakeholder’s Responsibility in the proper Communication of Pharmacovigilance Information

1. **Government**
   - Provide information (drug bulletins, national formulary, drug poison/information centre)
   - Legislation

2. **Health professionals**
   - To produce independent information for publication
   - Have a critical mind

3. **Patient/Consumer**
   - Consumer organization to inform patients about rational use of drugs
   - Target information to specific patient groups

4. **Pharmaceutical Company**
   - Adhere to legislation on advertising and promotion
   - No disguised promotion
   - Clinical trials informative not promotional
   - Provide up to date information to professionals and public

5. **Medical Schools**
   - To include in curriculum:
     - interpretation of clinical trials
     - benefit-risk assessment
     - rational use of drugs
     - communication with patients
     - training of clinical pharmacologists and pharmacists

6. **Media**
   - Have regard to consequence of stories
   - Check validity of story before publication
   - Adhere to code of practice
   - To refrain from acting as spokesperson in a promotional campaign
Types of ADR/Pharmacovigilance Mechanisms.
Kenneth Hartigan-Go MD

Definition

Medicines confer some health promotive, preventive and therapeutic benefits to patients. However, some risks and harm can also be observed as a result of taking drugs. Ultimately therefore, taking medicines means one has decided that the benefits of the disease management outweigh the known or potential harm they may cause.

Adverse drug reaction (ADR) is the response to a drug that is noxious and unintended and which occurs at doses normally used in man for the prophylaxis, diagnosis, or the therapy of disease, or for the modification of physiological function.

ADR is different from adverse drug event (ADE), which is, an untoward and unexpected experience by a patient following the use of a medicinal product but does not necessarily have a causal relationship with the treatment.

ADE does not confer a definitive causality relationship between the drug and the event but just a mere suspicion. ADR on the other hand, defines a more certain or probable relationship, the mechanisms of which might be explained by some pharmacological actions or in some cases, cannot yet be conventionally explained.

There is also a significant difficulty in the diagnosis of ADR because it often masquerades as other diseases. It is important to look at ADR as drug induced illness. Drug effects are the consequence of complex interactions between the drugs, the patient and the illness and external factors can also modify drug response.

In the United States, it is estimated that 3-5% of hospitalizations are due to ADRs while 30% hospitalized patients may risk having some drug-induced ill effects.

It is to the credit of the doctor who suspected and reported an ADR because it is likely that he will take some actions to protect the patient and indirectly his professional reputation. A doctor who ignores a patient who has reported adverse drug experience will less likely explain risk benefit to his patients during consultations, or be aware of a developing adverse effect to intervene in time.

Manifestations

There are various classifications of ADRs:

<table>
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<tr>
<th>Augmented</th>
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<tr>
<td>Bizarre</td>
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<tr>
<td>Continuous</td>
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Delayed Ending of use Failure of treatment

Augmented – an effect that is higher in intensity or magnitude than the expected pharmacological effect. It can occur either as an extension effect or part of the therapeutic effect or can occur as not part of the intended therapeutic effect (as a side-effect). It has usually a dose-dependent mechanism.

- Augmented extension effect – For instance a hypertensive patient is on a beta-blocker. Since the management of hypertension includes the lowering of cardiac output, and the resultant blood pressure, beta-blocker is ideal. Heart rate also plays a role in the pathophysiology of hypertension, and hence as part of therapeutic management beta-blocker can be useful because it has in part, the expected pharmacological action of slowing the heart rate. However, let’s say that the bradycardia seen in this hypertensive patient was less than 60 and the patient feels some discomfort, then this is a form of beta-blocker augmented extension effect. It is expected, and can be managed with dose reduction or shifting to another class of hypertensive agent.

- Augmented side effect – on the other hand, let us say that the same patient experienced bronchospasm as a result of beta-blocker use, this is a form of an augmented Side-effect. We know that this can happen as part of beta-blocker actions but bronchospasm is not an intended effect of treating hypertension unlike the earlier example, where lowering of the heart rate with beta-blocker can confer some lowering of cardiac output and blood pressure. The management in this ADR case will have to be shifting to another class of hypertensive agent. On the other hand, phenothiazines or haloperidols used to treat psychiatric conditions may induce extra-pyramidal side reactions that can be managed with small doses of benztropine or diphenhydramine. Anti-cancer drugs that induce nausea and vomiting can be given anti-emetic agents.

Bizarre – this effect can be likened to a hypersensitivity or idiosyncratic reactions. It is often unpredictable. There are no conventional tests to demonstrate which patients might experience this ADR in order to theoretically prevent its occurrence. It is not dose dependent to the medicine used. Some can occur immediately such as penicillin hypersensitivity and acute anaphylactic reactions. But some can occur at a much later time, even months later, such as Steven-Johnson Syndrome following use of phenytoin, carbamazepine, Phenobarbital or sulfa-containing drugs. Not all cases can be explained by known pharmacological actions of the suspected drug.

Continuous – This ADR happens after a prolonged use of a drug even at normal dosage. It affects organ systems. An example is phenacetin causing renal papillary necrosis. Another is Cushing’s syndrome from long-term use of steroids. Hypokalemia and dehydration can happen from long furosemide use. Because of the accumulation of the epileptogenic metabolites of meperidine following prolonged use, seizures can occur. Even large dose & long term use of pyridoxine can lead to neuropathy.
Delayed - this is seen when a drug used at some earlier time has some adverse effects are observed much later on, such as affecting the next generation. Diethylstilbestrol taken by women can cause vaginal and other reproductive organ damage in female offspring. In the 1960's thalidomide used by pregnant women invariably leads to the development of congenital malformations.

Ending of use – this is when a drug that was used on long term is suddenly stopped, the patient suffers a form of withdrawal reaction. These drugs exhibit tolerance phenomenon or have some dependency potential. Examples are: rebound hypertension following sudden cessation of clonidine, adrenal insufficiency after stopping prolonged steroid use, seizures from acutely ceasing anticonvulsants, and uncomfortable withdrawal syndromes from benzodiazepines and narcotics.

Failure of treatment - this is a new form of ADR recently recognized as a public health threat. ADR monitoring systems can pick up unusual and unexpected drug inefficacy and can detect possible fake, or substandard quality medicines. But the doctor has to be astute and keep an open, objective and critical mind to even suspect these. But once they do, they can be useful to the drug regulators, concerned industry and to the institutions that use these drugs. Patients' lives and the public health is the ultimate beneficiary.

ADR symptoms can be described as mild, moderate, severe. These are descriptive terms of the intensity of a particular sign or symptom. Serious, on the other hand defines the urgency and the impending critical threat to the life of the patient or to an organ-system.

An example to elucidate this concept might be: Drug X has cause severe headaches but is in fact not a serious life-threatening event. But on the other hand, a mild drug induced headache can be serious life-threatening event in the background of a cerebral aneurysm.

To understand manifestations of ADRs, the doctor should also understand important terms that describe their probability of occurring, expressed commonly as risks.

Terms and definition

Absolute Risk – probability of an event that affects members of a particular population (e.g. 1 in 1000).

Attributable Risk – the difference in the probability of an event happening, directly attributable to a drug or other variables.

Relative risk – a comparison of the probability of an event happening for the exposed and non-exposed population (the reference risk), expressed as a ratio.

To illustrate this, let’s presume that the background rate of people with skin disease developing skin rash when not taking any drug is 13 in 1000 people. If there are 13 experiencing skin
rash in a study group of 1000 people or patients, then it is unlikely due to the drug because the skin reactions can be explained by the background rate. However, if there are 22 rashes in the study group, then there is increased attributable risk (9 in 1000).

When doctors explain drug risks to patients, he will use lay terms. So how common is common? Common or Frequent is somewhere between 1 in 100 (1%) and 1 in 10 (10%). Uncommon or infrequent: between 1 in 1,000 (0.1%) and 1 in 100 (1%) and rare is between 1 in 10,000 (0.01%) and 1 in 1,000 (0.1%)

**Intervention**

If and when a prescriber suspect an ADR, he is in a critical position to intervene. The possible interventions are as follows:

- Stop the drug or Stop all of the drugs (dechallenge)
- Change to another medication
- Maintain the use of the drug.
- Modify the dosages
- Use another medication to modify the ADR.
- Identify possible drug – drug interactions
- Advise the patient whether to stop or to continue the use of that medications depending on risk – benefit considerations.
- Report the incident (the collection point for ADE is the Bureau of Food and Drugs).
- Do research.
- Establish causality through a system of analysis and assessment.
- Re-instituting the stopped medications should not be done just to re-affirm a suspicion of ADR as this might be dangerous (re-challenge).

The most important thing to remember is always monitor the patient for the expectant good effects of the medicines but also look for the possible or potential negative effects.

**Reporting**

While it is not mandatory for health professionals to report observed ADR cases, in the interest of public health, it is suggested that all doctors, nurses and pharmacists report suspected and serious, life-threatening ADRs. These can be the known and the unexpected, to the Bureau of Food and Drugs of the Department of Health using a standard form.

While the incidence may be rare in your perspective, if there are similar cases that arose in other areas and are similarly reported, a trend may be established for further investigations or for signaling. An early warning can save lives.

**Conclusion and the way forward.**

Adverse drug reactions are often suspected. Health professionals cannot always be certain
that an adverse event is entirely due to a recent drug given to a patient. But when there is reasonable suspicion, it is to the best interest of the health professional and also to the patient that the drug is stopped or dosage reduced, and the effects explained to the patient in a reasonable manner.

Addressing ADRs mean keeping the clinical eye open and an objective mind. Some wrong attitudes of health professionals should be reexamined. These include opinions of doctors and some eminent experts such as 'I have not seen it in my long medical practice or I have given this medicine to many patients, & I have not seen any bad reactions or I have not read anything in the textbook or medical literature and hence, it cannot be a drug induced event'.

Keep in mind that a rare serious event can occur one in 10,000 patients exposed, and no one single doctor can see that many patient on one drug and claim that ADR cannot occur.

Some simple rules to guide the prescriber:

Medicines are double-edged sword. It can heal but it can also harm. There is no such thing as a "pill for every ill." Use the lowest dose possible and titrate dose accordingly (individualized management). Don’t be afraid to use a medicine when it is really indicated just because of the known risk. Use as few medicines as possible, because the incidence of ADRs increases with the number of drugs. Following the decision to use medicines, educate your patient on what to expect and what to do in case of some untoward events. The prescriber should monitor both the expected good and the unexpected bad effects. Even the over-the-counter medicines that do not require a prescription may cause adverse reactions. Be cautious of drug-drug interactions or drugs that exhibit wide variability in dose response. Some doctors are afraid to modify the prescription of their peers who are co-managing their patient. In the interest of patient safety, do not be afraid to consult your peers if you think that the drugs they prescribed are suspected to be cause of the ADRs. Medication errors can occur as like an ADR. But errors can be preventable, so exercise due diligence and prudence. Do validate industry claims on the quality, efficacy and safety of their products.

References


Hartigan-Go K. Pharmacovigilance and the pursuit of Rational Drug Use, the Philippine experience. Uppsala Reports 14, April 2001 Supplement. WHO The Uppsala Monitoring Center.

CHAPTER 3

Drug Interactions, the dangerous ones.
Kenneth Hartigan-Go MD

Not all drug interactions are harmful. Clinicians need to constantly study and learn from books, journals, and experience that clinically significant drug interactions may be harmful and need to be vigilant and find ways to minimize drug interactions. Not all polypharmacy is bad. As long as it is necessary to use many drugs, as in the critical care unit or elderly with multiple chronic diseases, it will be incumbent to the attending doctor to pay attention to potential side effects.

But the more drugs used, the higher the statistical opportunities for adverse drug drug interactions and the relationship more describe a curve and is not linear.

Some examples include using captopril and potassium supplements and this combination may lead to life-threatening hyperkalemia. Many information about drugs really come from clinical trials where monotherapy is given. While the BFAD approves that drug, it does not foresee the possibility of patient taking many drugs in real life.

Practical clinical considerations

- Ask the clinically relevant question: Is the combination life-threatening and harmful?
- Adverse reactions may be attributable to the disease and not the drug combinations.
- But listen to your patients and what the nurse and relatives of patients tell you.
- When in doubt, stop the drug, reduce the dosage or change to another.
- Do not forget that IV drug-drug incompatibility (in-vitro drug interactions) may occur.

There may be negative implications of unrecognized bad drug interactions in clinical practice. For instance, the clinician may be liable for malpractice. Hence, it is quite important to do a good history taking; also to disclose critical drug use information to a patient. Anticipate that a patient may stop medicines without consult. It is an obligation of the drug industry to constantly improve package information to assist the prescriber.

It is traditional to remind doctors that high risk patient groups do exist, such as the very young, the very old, patients with multiple diseases taking multiple drugs (particularly, those with narrow margin of safety: examples of which are digoxin, phenytoin, warfarin. Oftentimes, critically compromised patients: cancer, HIV-AIDS, psychiatric, septic are risk for drug drug interactions.

But there are also non drug factors that affect drug intake in the course of our daily lives. These are:

- Coffee/caffeine intake
- Alcohol intake
- Cigarette smoke and second hand smoke
- Hormones, pesticides and antibiotics in food
- Food intake: grapefruit (QT prolongation), broccoli, cabbage (coagulation)
• Herbal/alternative supplements
• OTC drugs self medication by patients

In theory, drug interaction can have a variety of effects
• Enhanced effects to toxicity
• Diminished effect to antagonism
• Alteration to absorption and distribution
• Alteration to metabolism
• Alteration to clearance
• Adverse effects may be slow or may be rapid, hence may not be detected at all.

In the management of diabetes, the effects of hypoglycemic drugs may be decreased with ethanol abuse, concomitant use of rifampicin, nifedipine or thyroid hormones. The opposite, enhanced hypoglycemic effects may be expected with acute abuse of alcohol (except when these are mixed sweetened cocktail drinks) or when skipping meals.

For the heart patients, as in the case of RHD & arrhythmias, the combination of penicillin & oral contraceptive might cause the latter to diminish its effects. On the other hand, estrogen can decrease the effects of oral anticoagulants. Anticoagulants can increase the effects of phenytoin.

In the case of hypertension, expect antagonism of effects when using beta-blockers & theophylline together. Two or more anti-hypertensive medicines can lead to additive/synergism of effects (hypotension). The combination of captopril & spironolactone may lead to dangerous hyperkalemia.

For the congestive heart failure patients, digitalis toxicity can occur in both background of extreme hyperkalemia or hypokalemia. Bradycardia may be seen with concomitant use of digitalis & beta-blockers. Breakfast oatmeal can decrease the oral absorption of digoxin.

For an asthmatic or COPD patient, the combination use of steroids & ASA may lead to GI bleeding. The combination use of beta-agonists leads to potential hypersympathetic effects. Norfloxacin can increase serum theophylline levels.

Goiter patients who use thyroid hormones in combination with any sympathomimetics may lead to increased cardiac toxicity.

Drinking alcohol and taking inadvertently cephalosphorin or metronidazole sometimes lead to disulfiram effect.

Lifestyle issues like shabu (ampethamines) abuse and gets into a serious accident needing surgery, the use of general anesthesia may enhanced cardiotoxicity. Increased sympathetic actions can occur as a result of taking appetite suppressants like phenylpropanolamine and MAO inhibitors. Expect enhanced sedation with anticholinergics/antihistamines with benzodiazepines.
Psychiatric conditions requiring phenothiazines & metoclopramide may increase the risk for extrapyramidal syndrome (EPS).

With TB conditions, the use of INH & Rifampicin & PZA can lead to liver transaminase elevation or hepatotoxicity. Rifampicin may decrease the effects of birth control pills like oral contraceptives.

Example of situations in infectious cases where drug interactions may happen are decreased effect of tetracycline because of increased binding by milk or antacids & iron.

Enhanced phenytoin effect because of reduced clearance is seen with concomitant intake of isoniazid as in the case of TB meningitis. But if rifampicin and phenytoin are used together, the latter drug level is decreased and seizure may ensue.

Increased neuromuscular blockade are to be expected if aminoglycoside and neuromuscular blockers are used together say in an operating room setting. Increased nephrotoxicity can occur if aminoglycoside and cephalosporin or furosemide are used together.

Herbals processed into pharmaceutical dosage form, most often will not have drug interaction data to begin with. Examples are Gingko Biloba and St. John’s Wort.

The phenomenon of QT prolongation can be observed with concomitant use of grapefruit juice/ketoconazole and astemizole/terfenadine; quinolone affects liver metabolism of CYP2D3 leading to drug induced QT prolongation.

In the ICU setting, there are many in-vitro drug interactions (incompatibilities). The mixing epinephrine/dopamine with NaHCO3 drips will cause the former drugs to deteriorate. Mixing calcium drip with NaHCO3 can lead to insoluble calcium carbonate precipitation. Phenytoin with D5 containing water can cause precipitation.

In conclusion:
• Not every polypharmacy is bad and not all drug interactions are created equal.
• The lack of recognition makes drug interactions dangerous to the patient
• You cannot remember all possible drug interactions...hence read, consult and be vigilant
• But the absence of published drug interactions does not mean that they do not exist.
• Drug can interact with disease, another drug or with food and the mechanisms are not all understood.
• When exposed to three or more drugs the interaction becomes unpredictable.
Finding Ways to Prevent Medication Errors.
Kenneth Hartigan-Go MD

Introduction

Pharmacovigilance is about making drug products, as well as their use, safer. While the set-up for ADR monitoring catches product problems, it may also be a good system to detect if such a product was not being properly used. Medication error is one such problem. Lessons from medication error detection may help prevent future errors and protect health professionals and ultimately, their patients.

Generally, there is difficulty in obtaining the correct statistics on medication errors. Many of these errors are neither recognized nor reported. A study was published in the Archives of Internal Medicine based on data collected since 1999. In the United States, more than 40 potentially harmful errors a day were found on average in hospitals. The most common mistake is giving medicines at the wrong time, completely omitting the dosage, and over-dosing. Errors occurred in one of five doses in a typical 300-bed hospital. This translates to an average of 2 errors per patient daily. Although not all of these errors are dangerous, 7% of the errors were considered potentially harmful.

Medication errors can lead to manslaughter charges. The topic of medication error will make pharmacovigilance instruction more relevant and interesting. It will help prevent malpractice litigation and promote public health safety and awareness. While it is the drug regulator’s role to help improve the quality of drug and drug use by providing standards, medication errors can be minimized, if not completely eradicated at the clinical side. Its occurrence reflects on the quality of health care.

Causes of Medication Errors and some examples:

Errors originating from the drug industry:
1. Mistakes can happen in the manufacture of medicines (e.g. using the wrong excipients)
2. Proper storage procedures are not observed, making the drugs useless. Using expired tetracycline has been known to cause Fanconi’s syndrome, for instance.
3. Failure to provide the correct prescribing information. For example 10 mg/kg 6 hourly could mean: 10 mg/kg per dose given every 6 hours, which is the wrong interpretation, or 10 mg/kg/day to be divided every 6 hours which is correct.
4. Failure to do Post-Marketing Surveillance by manufacturers. And, if done, not communicating these data.
5. Misleading health and treatment claims by the industry.

Errors arising from medical doctors’ prescriptions:
1. Prescribing the wrong drug
2. Writing illegibly
3. Confusing the name of one drug with that of another
4. Prescribing the wrong dose
5. Writing wrong dose
6. Wrong route of administration as listed in the prescription
7. Prescribing the wrong formulation (an example is using slow release drugs inadvertently when the doctor meant ordinary tablets)
8. Prescribing the duration of treatment incorrectly
9. Prescribing wrongly for a given individual
11. Failing to account for pre-existing disease
12. Failing to account for concurrent therapy
13. Prescribing with inadequate or incorrect instructions
14. Prescribing without informed consent of the patient
15. Off-label use of drugs

Errors arising from pharmacists’ dispensing
1. Dispensing errors – for example, giving 250 mg/5mL paracetamol instead of the prescribed 125 mg/5 mL preparation.
2. Misinterpreting doctor’s prescription and failure to confirm with the prescriber.
3. Failure to provide advice to patients at the outlet level. In poor resource countries, patients sometime purchase only a few tablets because they cannot afford a complete course of treatment. The pharmacist or store clerk sells the medicines by cutting the medicine strips. As a result, the expiry dates are sometimes no longer indicated on the purchased portion and product information leaflets are rarely provided in such instances.

Errors arising from nurses’ administration of drugs
1. Errors in drawing up and giving medicines
2. Wrong drug
3. Correct drug, wrong dose
4. Correct drug, wrong dilution
5. Correct drug, wrong formulation
6. Entraining air, particles or other contaminants with the drug
7. Errors in administration (interchanging IV, IM, intrathecal, oral, sublingual route)
8. Giving a drug outside or against currently accepted practice (off-label usage)
9. Wrong route, wrong site, wrong rate, wrong patient

Errors arising from patient’s drug intake:
1. Misunderstanding medication instructions.
2. Poor patient compliance, not completing dosage regimen.
3. Drug paroxysm. This is when a patient takes a medicine but later becomes confused whether he actually took the medicines and ends up taking a second dose erroneously. This is not restricted to geriatric patients.
To counteract these possible errors, good prescribing practice guidelines are advocated:

- If it is possible to write the dose as a whole number, then do so.
- If it is impossible or more confusing to write the dose as a whole number, then ensure that a zero precedes the decimal point. Place the decimal point properly; a shift can mean 10 times more the intended dose, or can mean receiving only 10 percent of the intended dose. Use Gm for gram and gr for grain when specifying quantity. The best is to carefully spell out the whole word and dot the i. If grams are given instead of grains, the patient will receive approximately 15 times the dose intended.
- Communicate clearly. New technology like mobile phones and short message sending (texting) can lead to errors. Hospital should set up clear policies on telephone orders to prevent mistakes. Among the doctors, nurses and pharmacists, when transmitting orders, clear pronunciation of medical terms and listening carefully can prevent mistakes of similar sounding drug names.
- Write a prescription clearly and give the instructions to patients or their responsible companions. There was a case of an obese diabetic patient who was being managed with oral hypoglycemic medicine and instructed to decrease weight in a vague manner. The patient decided to skip breakfast as a “diet control” measure but continued taking her medicine, leading to symptomatic hypoglycemia.
- Prescription should have all the essential information like dosage strength, the number of tablets, frequency of administration, route.
- Be conservative. Prescribe only when absolutely needed. Don’t satisfy the whims of patients who request antibiotics to treat common colds.
- Know your patient’s conditions well before prescribing any drugs.
- Prescribe a medicine which you are thoroughly familiar with (adverse effects, contraindications, warnings). Do not be tempted to prescribe new medicines which are being promoted aggressively by drug companies.
- If you want to prescribe a generic drug, it is better to indicate the particular company source you trust, for two reasons: substitution of another company’s generic product can mean lower drug levels (for drugs with serious bio-availability variations) and, in some countries, there are substandard generic products in the market.
- Avoid overprescribing because this is costly and can lead to accidental overdose. Sometimes, an expired drug is unintentionally taken. Also, warn patients not to recommend an effective drug which they may have in excess at home to a member of the household or a neighbor without consulting a health professional.
- Avoid polypharmacy. Although not all polypharmacy is bad when these medicines are actually needed, be attentive to those with potential for harmful interactions. Be wary of drug-drug interactions.
- Spend time to educate a patient about the drug—when to take it, when to stop, what to expect (e.g., will it change the color of their urine?), how to recognize drug reactions and what to do, expiration dates, drug interactions and storage conditions. Patients should be made to understand that when they take medicines, they are essentially betting that the benefits derived from using the drug outweigh the harmful risks from the medicine and the consequence of the untreated disease condition. There are some medicines which, when started, should be continued for a long time (e.g. Anti-TB drugs and prevention of resistance).
There are some drugs which, when taken for a long time, should not be stopped abruptly (e.g. Anticonvulsants, steroids, sedative hypnotics).

There are also some drugs which, when taken long term, may lead to drug dependence and abuse.

Pay serious attention to the patient's history, such as records of hypersensitivity, allergies, idiosyncrasies to medicines, or medical conditions that are considered contraindications to drugs. Note these in patient's records and review them when necessary before prescribing. Take note of the patient's occupation and possible risky interactions with his medicines.

Drug safety and rational drug use

Due care must be exercised when handling drugs and treating patients. Negligence may lead to fatality, and commonly, a health professional may be charged with acts or omissions such as:

a. Not using available, objective and updated drug information and relying solely on drug industry detail person for this information.

b. Miscommunications on drug orders like poor penmanship, confusion between drug names, misuse of zeros and decimal points, wrong dosing units, and incorrect abbreviations.

c. Failure to obtain consent from a patient for the use of a drug in a manner not officially approved (off-label)

d. Treatment of a condition with a drug not suitable for the condition

e. Failure to note a history of drug hypersensitivity, concurrent medications, contraindicated medical conditions.

f. Failure to test patient for sensitivity to drugs like penicillin

g. Improper injection techniques

h. Failure to stop a medicine suspected to cause a reaction

i. Failure to provide adequate intervention to counteract an adverse reaction

j. Failure to communicate with patients.

k. Lack of correct labeling when drugs are repacked into smaller units

It is by recognizing possible errors that we can find suitable ways to prevent them.

Examples from the Philippines: Actual cases

Introduction: The Philippine Generic Drug Law of 1988 mandates that the labeling, prescription of drugs be done in generic or scientific nomenclature, with intention towards promotion of more affordable drugs and rational drug use.

The use of generic terms in prescription lessen chances of medication errors. Pharmacists validating prescriptions and checking important patient and drug details help prevent errors. Some case examples are presented here.
Mesulid vs Mellaril. The doctor prescribed Mesulid, without indicating nimesulide (the generic name), the pharmacist gave Mellaril (thioridazine) instead. Patient had to be hospitalized.

Ceporex vs Leponex. A doctor prescribed Ceporex, a trade name of an antimicrobial but the drugstore gave Leponex instead, a psychotropic medicine. Again, the patient had to be hospitalized.

Thiamine vs Thorazine. Even when using generic drug names, errors can still occur. Thiamine was prescribed to a 2-year-old boy; instead, thorazine was given by the drugstore clerk. The dispensing individual did not see the importance of checking why thorazine should be given to a 2-year-old boy. Patient was hospitalized.

Terbulin vs Theodur. A young asthmatic patient was given Theodur (a trade name product containing theophylline) by a doctor. On top of this, the doctor gave Terbulin, (a fixed dosed combination product trade name) mistakenly thinking that this is terbutaline alone but in fact contained theophylline as well. Patient went into theophylline toxicity, was hospitalized.

EMB vs EMBR. Tuberculosis patient was prescribed quadruple anti-Koch medications. The doctor abbreviated ethambutol as EMB but the patient was given instead the brand EMB a combination INH and ethambutol. Liver transaminases became elevated as the isoniazid dosage was more than necessary.

Unclear expiry dates. A patient had died due to a serious illness. Being attributed was the hospital staff using alleged expired medicine. The hospital misinterpreted the marked expiry date as month-day-year where in fact, should have been read as day-month-year. The national drug regulatory agency failed to note and standardize labeling as manufacturing and expiry dates presentation may vary from country to country.

Mislabelling of IV fluids. A patient kept on NPO became hypoglycemic because the intravenous fluid (0.9 saline) was mistakenly labeled by the nurse as D5+0.9 saline for a number of shifts until the doctor found the source of the problem by opening the IVF cover.

Misreading poor penmanship. A case of arterial occlusion in the leg, the doctor ordered Resume Heparin, the nurses misread it as remove heparin. Outcome: patient’s leg had to be amputated.
Some practical tips.

Dangerous abbreviations that can occur in the pharmaceutical laboratory, pharmacies, hospital and clinical practice are presented here.

- **D/C** - as used in the hospitals can mean discharge, discontinue or dilatation and curettage
- **Allo vs OU** - because of spelling errors, can confuse both ears with both eyes.
- **DPT vs dPT** - A cocktail drug preparations used in hospitals known as Demerol, phenergan and thorazine can be confused with pediatric vaccines called diphtheria, pertussis, and tetanus.
- **HCl vs KCl** - again, H and K can be misread and instead of hydrochloric acid, potassium chloride is used.
- **MgSO4 vs morphine** - Morphine sulfate might erroneously be substituted for Magnesium sulfate used in obstetrics for pre-eclampsia and eclampsia.

A story of medication error in the hospital.

An oncologist wrote instructions on the hospital chart for the IV administration of the oncolytic drug mesna (brand name Uromitexan), but the nurse mistook it for the respiratory solution also called mesna (brand name Mistabron). The respiratory solution meant for nebulization was injected intravenously for a total of 8 doses over a period of 3 days until the error was discovered.

Patient was never told of the error by the attending physician and was, in fact, sent home on the same night. Some tests were ordered but these were never carried out. Drug industry help was sought on pharmaceutical physico-chemical information but they could not be contacted over the weekend.

The Philippine FDA was informed of the incident on Monday and they were surprised how they managed to register two drugs sharing the same name.

The doctor, in following the Philippine Generics Act of 1988 mandating that the doctor should write the generic name of a prescribed drug, was unclear about his responsibility to indicate the specific product trade name.

The nurses (three shifts over three days) did not read the ampoule information prior to administration. The hospital pharmacist sent the ampoules to the floor without an accompanying box or product information leaflet.

Patient could not be followed up.
• OD vs right eye – Once a day and the right eye can be confusing.
• Per os vs left eye – os is sometimes used in hospital charts to mean opening, by mouth or by tube and can also mean the left eye.
• QD vs QID – once a day may be confused with four times a day.
• QN vs every hour qh – as letter N and H can be misread, every night is mistaken as every hour.
• QOD vs daily – this is particularly confusing when doctors make abbreviations misinterpreting every other day, or once every day.
• Sub q (subcutaneous) misread as every so hours.
• SC vs SL – because of possible pensmanship error, C for cutaneous can be mistaken as 1. for sublingual.
• IU vs IV – international units as opposed to intravenous, for instance, insulin expressed in units to be given subcutaneously may be erroneously given as intravenous bolus.
• X3d vs three doses – the confusion here may be due to misinterpretation that a drug is given for 3 days as opposed to just three doses or three times in a day.
• Inderal40 vs Inderal 40 mg (mistaken 140 mg) – it is not unusual to have a wide range of dosing for propranolol therapy as in the management of hyperthyroid states but when there is a penmanship mistake – in this case, the absence of a space between the last letter and the subsequent number – a mistake can happen.

Use of Cellphones for medical activities:

2 TXT D DOC or NOT 2 TXT?

Mobile phones have replaced pagers as the preferred communication tool of doctors. More and more medical doctors are using mobile phones to convey orders to nurses in the hospitals. Some are using the short messaging system (SMS) feature of mobile phones (i.e. test messaging) to transmit sensitive instructions. Nurses in hospitals nowadays are beginning to use the same to inform doctors of admissions and status of patients’ conditions. There are potential problems, however, such as errors in text message content, delay in receiving information and hence delayed response. Lives may be at stake. Sometimes senders do not identify themselves and what institutions they come from. Sometimes the senders do not get the benefit of a reply. There is also a problem with text-style writing- i.e., abbreviated words, incorrect grammar that might lead to gross misunderstanding of the messages. Who might be liable in case of errors or failed response?

The SMS feature of mobile phones could potentially be an efficient tool for health professionals-particularly doctors and nurses. Currently, however, protocols are non-existent. As a response to the absence of protocols with respect to the use of text messaging, The Zuellig Foundation, in consultation with health professionals from various hospitals within Metro Manila, is suggesting the following guidelines for the best use of this new technology in saving lives.

1. Given the emerging importance of new telecommunication technology in the country, hospitals and other health facilities should always be ready to adopt and regulate this to their advantage by developing sound policies as it applies in their own setting.
2. Given its various limitations, the use of text messaging in giving orders to nurses should be limited in extreme cases where the use of other means in relaying the message (e.g., telephone calls) are absent there is an urgency for doctors to do so. Remember that the patient's lives are at stake in these situations and there is a need to relay messages as fast and as accurately as possible. At any rate, in an emergency, it might be better just to call the hospital using phone rather than rely on text messaging.

3. Most hospitals have standing operational definition of what urgent cases are. If this standard definition does not exist, the hospitals' administration should develop and apply it to limit and appropriately regulate the use of text messaging to relay doctors' orders to nurses.

4. Hospitals and other health facilities should also consider investing in new telecommunication technology that can facilitate documentation/verification of doctors' orders via text messaging (e.g., a machine that can print out text messages, telephone equipped with long distance call features, mobile phones and other applicable telecom equipment).

5. If there's a need to use text messaging in giving orders, doctors should always consider sending it first to a fellow physician (e.g., residents or fellow consultants) who can then personally write/make the order himself. This can remedy the issue of legal liability or professional accountability for both nurses and the physician.

6. Doctors should never forget to include their name in the text message or if possible, a PIN or other forms of identification that nurses and other hospitals staff can officially recognize.

7. Doctors using text messaging in conveying their orders to nurses should be able to at least wait for one to two minutes for the nurses to acknowledge them or they must at least provide sufficient time for response; remember that one may not be able to return text messages or call immediately.

8. Nurses, on the other hand, should acknowledge doctors' orders as soon as possible by forwarding the original message and together with their name or identification and other relevant or appropriate responses.

9. Nurses should take note of the exact time when the message was sent by the doctor and the time they were able to respond. They should make sure that the doctors making the orders should be able to respond back to them within one or two minutes.

10. Doctors and nurses exchanging messages through text should be familiar and limit themselves with conventional abbreviations of drugs/medications' preparations and dose/dosage, among others. The use of uncommonly used or new abbreviations might be interpreted inaccurately and might have serious consequences in patient care.

11. Doctors should make it a point to personally acknowledge their orders by countersigning them later on in the patient's chart. Hospital administration should decide the time frame within which doctors should accomplish this.

12. Given the many limitations of text messaging in relaying vital information, a telephone call must always be considered as better alternative. However, hospital administration should also consider developing written policies as they apply for this purpose.
**Conclusion:**

Medication errors can happen unintentionally. Any health professional should be vigilant in finding ways to prevent and mitigate these errors. One way is to strengthen education and surveillance systems within the ADR reporting context. The role of pharmacovigilance centers or ADR National Centers can be expanded to address problems that occur in the clinical setting. Every health professional involved in the therapeutic chain should always question the decisions made by the ones before them (nurses and pharmacists question the prescriber on medications as prescribed etc.).

It would be serious to hear this from our patients: “Doctor, I prefer the disease to the side effects of the medicines you gave.”

**References:**


Bedell S et al. (2000). Discrepancies in the Use of Medicines. Archives of Internal Medicine, Vol. 160: 2129-2134


Zuellig Foundation’s think tank policy notes on the use of cellphone (text messaging or SMS) in hospitals 2002.
Vaccine-Related Injury.
LJQ Llamado, MD, FPCP, FPRA, CCD and Kenneth Hartigan-Go, MD

Vaccines are important part of our civilized life. In a way, they are like medicines but in some ways there are important differences. Program and field managers need to know these to be able to promote immunization properly.

Because vaccines are promoted to healthy persons generally as a preventive intervention, there is a perception that these products as well as the immunization process should not cause any problems. In reality, adverse events following immunization do occur. Modern vaccines although safe and effective can be associated with mild to even life-threatening adverse reactions. They may be real adverse reactions from the product itself, programmatic errors, coincidental events, or injection site reaction. Some examples will be shared.

In these situations, it is important for the clinician or the field health worker to be able to address and manage such adverse events. Because if this is not handled properly, there can be serious impact on the public health program, loss of confidence in the health workers, the government, the product or possible hostility by the community. The management will necessarily include rapid assessment of the condition, careful investigation, practical advice to the parents and patients, and communication to important stakeholders such as the community leaders and the media. Some clinicians who eventually see AEFI sometimes do not give the correct interpretation of the events and often misinform the patients.

There are many ways to prevent AEFI. The program managers and health workers should come to terms on how to educate the community targeted for the immunization, and will need to include social preparation, and also how to prevent common programmatic errors. These will be discussed.

The important groups of people who should ensure vaccine safety include the drug industry, the drug regulators, the program managers of the EPI, the field health workers and the clinicians.

Types of Adverse Reactions:

1. Cutaneous:
   Acute and long-term skin complications arising within the site of vaccination may occur. This may happen with either the initial vaccination or revaccination. This include development of benign tumors which may be in the form of exaggerated scarring which is the most common benign tumor reported, dermatofibroma, and nevus sebaceous. For the exaggerated scarring, these lesions in particular the hypertrophic scars, usually remain confined to the wound site and improve after a small number of intralesional steroid injections and do not recur. The same is not expected for keloids which usually extend beyond the original wound site and may appear months to years after the first scar formation. The nevus sebaceous is usually excised because it has a significant risk of developing coincident basal cell tumor. Malignant tumors may also develop from
the vaccination site and these include basal cell carcinoma, malignant melanoma, squamous cell carcinoma fibrohistiocytic tumors and fibrosarcoma. These lesions have been observed both with the scars from the primary vaccination and revaccination. For small pox vaccination, basal cell carcinoma is the most commonly reported lesion. Skin dyspigmentation has also been reported and it is suggested that these lesions should be routinely monitored for changes in size, color and appearance as these changes may suggest a malignant transformation. Other vaccines associated with cutaneous scarring at the injection site include Bacillus Calmette-Guerin (BCG) and vaccinia. Clinicians and other health care providers should be aware of the various cutaneous lesions that may occur after vaccination and should inform the patients that skin lesions developing at the injection site other that smooth scar should be shown to health care providers.

2. Anaphylactic reactions
Considering that many different constituents of vaccines can result in immediate-type allergic reaction, vaccines in some instances may serve as an inciting allergen resulting to the development of anaphylactic reactions. Usually the symptoms of anaphylaxis develop within 5 to 30 minutes and less commonly up to 4 hours or even more. The symptoms can be divided based on the organ involved. For respiratory, dyspnea, bronchospasm, glossal/pharyngeal edema, hoarseness have been reported. Nose/eye symptoms include sneezing, red itchy watery eyes, rhinorrhea and nasal congestion. Hypotension, palpitations, light-headedness, loss of consciousness and tachycardia are the cardiovascular symptoms commonly described with pruritus, urticaria, angioedema and flushing for cutaneous complications.

Adverse events from only one organ system or even from more than one organ systems but developed four hours after the vaccine was given are less likely to be anaphylactic. However, every suspected adverse reaction should be approached in the same manner as far as evaluation and management is concerned.

3. Neurologic
Despite being reported in different literatures, there are still reports on the failure of the physicians or other health care providers to recognize the clinical manifestations of neurological complications associated with vaccination. This is definitely a concern since this complication may be associated with serious outcome. Adverse reactions involving the CNS may affect any and all parts of both the central and peripheral nervous system. These adverse events may come in different forms. An example of which is acute disseminated encephalomyelitis. Some of these vaccines reported to may have involvement of the nervous system are measles, varicella and rubella vaccines. In the case of live viruses like polio, an actual infection by the virus itself may happen. In cases of encephalitis, patients may present with fever, headache, vomiting, drowsiness, convulsions, meningeal signs or even coma.

A proposed mechanism behind the development of these adverse events include vasculopathy that can lead to vessel obstruction and ischemia and alteration of the blood-brain barrier that can lead to edema of the nervous system.
Even with the most advanced diagnostic tools we have right now there is no way of knowing who will have an adverse event after vaccination. Genetics background and previous immunological history however may be used to determine individual’s susceptibility. More often public health providers failed to ask about the history of vaccinations when they see patients presenting with signs and symptoms mentioned earlier because of the belief that adverse events do not happen with vaccinations.

Immunization is a successful and a cost effective way of preventing certain diseases. It can even be considered as one of the most important achievements of public health. However, clinicians and other public health care providers should always keep in mind that although modern vaccines are generally safe and effective it still can be associated with side effects which can range from mild to serious and life-threatening. Aside from this, we still do not have a vaccine that can be completely effective. Some persons who already received vaccinations may still develop the disease after exposure. Thus, the decision to use vaccines involves knowing the risk of the disease, the benefit of giving vaccination, cost effectiveness and the risk associated with its use. There is definitely a need to continuously re-evaluate vaccines indication and safety.

Things that need to be asked before vaccination include adverse event occurrence in the past to the same or any vaccines or its components. It is also worth asking for the history of allergy to food like eggs, chicken and gelatin which may be components of vaccines. If there was a history of allergic reaction to vaccine, clinicians and other health care providers should determine whether subsequent doses of the suspect vaccine or other vaccines with common components are still required. Checking for the antibody level may be helpful since if a patient has already mounted a sufficient antibody response, not giving further doses of the vaccines may be considered. It is important to know however, that persons with fewer than recommended doses may have a level of protective antibody which may not persist long. Lastly, it is important that clinicians and other health care providers should be aware and familiar with vaccines precautions and contraindications. Some of the common contraindications include severe hypersensitivity reaction to a previous dose of the same vaccine or to its components like anaphylaxis, and administration of live-virus vaccines like MMR, varicella and OPV in immunocompromised persons and pregnant women. General precaution is the presence of moderate or severe acute illness regardless of the presence or absence of fever. Knowledge of these things is definitely an important aspect of vaccination practice since application of these valid contraindications and precautions will definitely help minimize the occurrence of vaccine-related adverse reactions.

References:

Assessing Causality
Kenneth Hartigan-Go MD

Causality assessment provides the health professional some degree of certainty as to the adverse event being related to the drug product. It is not a perfect system.

An example of such a system is the Naranjo algorithm, which is easy to understand and basic to apply.

<table>
<thead>
<tr>
<th>Naranjo’s Algorithm: Determination of ADR Probability</th>
<th>YES</th>
<th>NO</th>
<th>DO NOT KNOW</th>
<th>SCORE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Are there any previous conclusive reports on this reaction?</td>
<td>+1</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>2. Did the adverse event appear after the suspected drug was administered?</td>
<td>+2</td>
<td>-1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>3. Did the adverse reaction improve when the drug was discontinued or a “specific” antagonist was administered?</td>
<td>+2</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>4. Did the adverse reaction reappear when the drug was re-administered?</td>
<td>+2</td>
<td>-1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>5. Are there alternative causes (other than the drug) that could, on their own, have caused the reaction?</td>
<td>-1</td>
<td>+2</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>6. Did the reaction reappear when a placebo was given?</td>
<td>-1</td>
<td>+1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>7. Was the drug detected in the blood (or other fluids) in concentrations known to be toxic?</td>
<td>+1</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>8. Was the reaction more severe when the dose was increased or less severe when the dose was decreased?</td>
<td>+1</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>9. Did the resident have a similar reaction to the same or similar drugs in any previous exposure?</td>
<td>+1</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>10. Was the adverse event confirmed by any objective evidence?</td>
<td>+1</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>TOTAL SCORE</th>
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<td>&gt; 9</td>
<td>Highly Probable</td>
</tr>
<tr>
<td>5 - 8</td>
<td>Probable</td>
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<tr>
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<tr>
<td>≤ 0</td>
<td>Doubtful</td>
</tr>
</tbody>
</table>

Reference:

Annex: Understanding the WHO system of causality assessment classification
The use of the WHO-UMC system for standardised case causality assessment

Why causality assessment?
An inherent problem in pharmacovigilance is that most case reports concern suspected adverse drug reactions. Adverse reactions are rarely specific for the drug, diagnostic tests are usually absent and a rechallenge is rarely ethically justified. In practice few adverse reactions are ‘certain’ or ‘unlikely’; most are somewhere in between these extremes, i.e. ‘possible’ or ‘probable’. In an attempt to solve this problem many systems have been developed for a structured and harmonised assessment of causality (1). None of these systems, however, have been shown to produce a precise and reliable quantitative estimation of relationship likelihood. Nevertheless, causality assessment has become a common routine procedure in pharmacovigilance. The advances and limitations of causality assessment are reviewed in Table 1 (2).

Table 1. Advances and limitations of standardised case causality assessment

**What causality assessment can do**
- Decrease disagreement between assessors
- Give accurate quantitative measurement of relationship likelihood
- Classify relationship likelihood
- Distinguish valid from invalid cases
- Mark individual case reports
- Prove the connection between drug and event
- Improvement of scientific evaluation;
- Educational
- Quantify the contribution of a drug to the development of an adverse event
- Change uncertainty into certainty

**What causality assessment cannot do**

The WHO-UMC causality assessment system

The WHO-UMC system has been developed in consultation with the National Centres participating in the Programme for International Drug Monitoring and is meant as a practical tool for the assessment of case reports. It is basically a combined assessment taking into account the clinical-pharmacological aspects of the case history and the quality of the documentation of the observation. Since pharmacovigilance is particularly concerned with the detection of unknown and unexpected adverse reactions, other criteria such as previous knowledge and statistical chance play a less prominent role in the system. It is recognised that the semantics of the definitions are critical and that individual judgements may therefore differ. There are other algorithms that are either very complex or too specific for general use. This method gives guidance to the general arguments which should be used to select one category over another. The various causality categories are listed in Table 2. The original descriptions and an explanation are presented under ‘Definitions’ (3). In Table 2 the assessment criteria of the various categories are shown in a point-wise way, as has been developed for practical training during the UMC Training Courses.
Table 2. WHO-UMC Causality Categories

Causality term Assessment criteria*

**Certain**
- Event or laboratory test abnormality, with plausible time relationship to drug intake
- Cannot be explained by disease or other drugs
- Response to withdrawal plausible (pharmacologically, pathologically)
- Event definitive pharmacologically or phenomenologically (i.e. an objective and specific medical disorder or a recognised pharmacological phenomenon)
- Rechallenge satisfactory, if necessary

**Probable /Likely**
- Event or laboratory test abnormality, with reasonable time relationship to drug intake
- Unlikely to be attributed to disease or other drugs
- Response to withdrawal clinically reasonable
- Rechallenge not required

**Possible**
- Event or laboratory test abnormality, with reasonable time relationship to drug intake
- Could also be explained by disease or other drugs
- Information on drug withdrawal may be lacking or unclear

**Unlikely**
- Event or laboratory test abnormality, with a time to drug intake that makes a relationship improbable (but not impossible)
- Disease or other drugs provide plausible explanations

**Conditional /Unclassified**
- Event or laboratory test abnormality
- More data for proper assessment needed, or
- Additional data under examination

**Unassessable/Unclassifiable**
- Report suggesting an adverse reaction
- Cannot be judged because information is insufficient or contradictory
- Data cannot be supplemented or verified

* All points should be reasonably complied with

The use of the WHO-UMC system

To illustrate how the system works, we suggest to first make a comparison of the criteria and wording of ‘Probable’ and ‘Certain’. First of all there is one more criterion in the category ‘Certain’, the fourth: ‘Event definitive pharmacologically or phenomenologically’, i.e. an objective and specific medical disorder or a recognised pharmacological phenomenon (for instance ‘grey baby syndrome’ and chloramphenicol, or anaphylaxis immediately after the administration of a drug that had been given previously). This means that any other event is automatically excluded and can never qualify for ‘Certain’ (even in the case of a positive rechallenge observation). For ‘Certain’, rechallenge information with a satisfactory outcome is requested (i.e. what has happened when the drug was first stopped and later on resumed), unless the evidence in the report is already convincing without a re-exposure. For ‘Probable’, on the other hand, a rechallenge is not required. To qualify as ‘Certain’ the interval between the start of the drug and the onset of the event must be ‘plausible’; this means that there is in sufficient detail...
a positive argument in support of the view that the drug is causally involved, pharmacologically or pathologically. For 'Probable' the time relationship should be 'reasonable'; this is a more neutral term covering everything that is not unreasonable. Also, with regard to the second criterion, 'alternative causes', the wording is different in 'Probable'. For 'Certain' the occurrence of the event cannot be explained by any disease the patient is known to have or any other drug taken. For 'Probable', on the other hand, the event is 'unlikely' to be attributable to another cause. Also the dechallenge situations (i.e. what happened after stopping) are different. In a 'Certain' case report, the course of events constitutes a positive argument in favour of holding the suspected drug responsible, in pharmacological or pathological respects, whereas in a 'Probable' case it is sufficient if it is 'clinically reasonable' (i.e. not unreasonable). The essential distinctions between 'Probable' and 'Possible' are that in the latter case there may be another equally likely explanation for the event and/or there is no information or uncertainty with regard to what has happened after stopping.

The criteria that may render the connection 'Unlikely' are firstly the time relationship is improbable (with the knowledge at the time), and/or another explanation is more likely. The term 'Unclassified / Conditional' is of a preliminary nature and is appropriate when, for a proper assessment, there is more data needed and such data are being sought, or are already under examination. Finally when the information in a report is incomplete or contradictory and cannot be complemented or verified, the verdict is 'Unclassifiable'.

Since by far the most frequent categories in case reports are 'Possible' and 'Probable', the usual approach to using the system is to choose one of these categories (depending on the impression of the assessor) and to test if the various criteria fit with the content of the case report. If the report seems stronger one can go one step 'higher' (e.g. from 'Possible' to 'Probable'), if the evidence seems weaker one should try a 'lower' category. To see if that category is the right one or if it does again not seem to fit, the next adjacent term is tried. For drug-drug interactions the WHO-UMC system can be used by assessing the actor drug, which influences the kinetics or dynamics of the other drug (which has usually been taken over a longer period), in the medical context of the patient.

How does it work?
How the WHO-UMC causality assessment system can be used will be illustrated with the aid of a few real-life case reports. These will be made available on the UMC website in the near future.

References:
Drug trials offer a chance to participate in the development of potentially effective therapies. Whether or not to participate in this is a complex decision. To be a Principal Investigator in a drug trial requires a substantial commitment of both time and effort. So it is most important to know the responsibilities and the appropriate regulatory requirements when performing drug trials. The scientific, practical and financial implications should be weighed. Nevertheless, there are usually clear rewards in doing clinical trials.

The Principal Investigator

The Principal Investigator (PI) is usually an academic clinician working at a reputable institution and an expert in the particular field of clinical medicine of interest. The PI must be appropriately educated, trained and experienced in conducting drug trials. He or she must have adequate time, access to patients, clinical, technical and other capabilities, space and other facilities. As the PI is almost always a busy person, there needs to be some incentive for him to allocate previous time to perform a study. Investigators have different reasons for participating in a drug trial: for the pure science of study, for clinical merit of the study, potentially useful data for future publication or for financial gain. Depending on the type of study, pharmaceutical companies may require a PI to sign an investigator’s agreement that states that trial data belong to the company or impose some restriction on the publication of data.

The PI should have support from a team of doctors, nurses and other research personnel. The PI responsibilities can be delegated to a sub-Investigator (SI), who may regularly make important trial-related decisions. An SI needs to be closely supervised, suitably educated and qualified and be familiar with Good Clinical Practice (GCP). But the ultimate clinical responsibility still rests with the PI who will be medico-legally responsible for all breaches in patient confidentiality and any incidents of medical negligence, etc.

Responsibilities of a Principal Investigator:

Based on GCP, the Investigator:

- Must be qualified by education, training and experience to assume responsibility for the proper conduct of the trial.
- Should be thoroughly familiar with the appropriate use of investigational drug in the current Investigator’s brochure or in the product information.
- Should be aware of, and should comply with GCP, and applicable regulatory requirements
- Should permit monitoring and auditing by the sponsor, and inspection by the appropriate regulatory authorities.
- Should maintain a list of appropriately qualified persons to whom the investigator has delegated significant trial-related duties.
- Should have adequate resources such as required subject population, sufficient time, and adequate staff and facilities.
• Should be responsible for the medical care of subject trials.
• Should have primary responsibility in communication with the Institutional Review Board/Independent Ethics Committee which includes obtaining written and dated approval/favorable opinion, providing all documents subject to review, submitting progress report and study termination or final study report.
• Should conduct the drug trial according to protocol and should not deviate from it.
• Should be responsible in obtaining informed consent from trial subjects.
• Should ensure accuracy, completeness, legibility, and timeliness of data reported.
• Should be report all adverse events and do so promptly if serious.

Standards in Conducting Drug Trials

There are certain standards and rules and regulations being followed in conducting drug trials. As discussed earlier, one of the responsibilities of a principal investigator is to be aware and comply with GCP and appropriate regulatory requirements.

Good Clinical Practice (GCP)

GCP is an international, ethical and scientific quality standard for designing, conducting, recording, and reporting trials that involve participation of human subjects.

The Do’s in drug trials based on GCP are the following:
• The rights, safety and well being of trial subjects should be protected
• Conduct of drug trials should be consistent with the principles that have their origin in the Declaration of Helsinki
• And, that the clinical trial data should be credible

In many countries, implementation of GCP in all phases of drug trials is a legal requirement. Although not yet implemented in the Philippines, most pharmaceutical companies adhere to GCP in the conduct of their trials.

In addition to the do’s mentioned above, clinical research personnel and investigators should have a good and thorough understanding of the principles of GCP, and fully appreciates the interpretation and practical application of these guidelines and regulations.

Bureau of Food and Drug (BFAD)

A.O. No. 22-A S. 1982 is about the research policies and guidelines by the Department of Health (DOH). This mentioned that while collaborative research endeavors are being encouraged and supported by the DOH, safeguards in the conduct of these research activities to ensure the safety and welfare of human subjects and the pubic are also imposed. So DO NOT do any research until such approval is obtained.
A. Registration of New Drug

Based on BFAD Operation Manual on Drug Evaluation and Control (1992), one of the requirements of BFAD for registration of new drug is data from drug trials. These data are the basis in designing the most appropriate treatment of future patients with a given medical condition.

B. Monitored Release Prior to Approval of General Use

Investigational New Drug (IND), New Drug (ND) and Newly Introduced Drug (NID) will be required to complete pharmacological studies and pass through a 3-year monitored release before becoming eligible for application and approval for general use. They are referred to as Post Marketing Surveillance (PMS) studies.

The model protocol for monitored release would include an uncontrolled clinical study reporting the therapeutic effects and adverse reaction for 1000 patients per year or 3000 patients over 3 years, provided however that if the drug product is for a very limited therapeutic indication the 1000/year patient requirement will be waived and only 10% of the total patients given the drug will be required to be monitored and reported to BFAD by the pharmaceutical company.

Pharmaceutical Healthcare Association of the Philippines (PHAP)

The Pharmaceutical and Healthcare Association of the Philippines (PHAP) is a business association representing the providers of most of the country’s medicines. Members include the country’s leading research-based companies of pharmaceuticals and medical services.

PHAP has given their share of voice by providing additional guidelines in the conduct of PMS studies to pharmaceutical companies who are PHAP members. These guidelines set the objectives pharmaceutical companies must DO:

- To protect the true scientific purpose of PMS studies
- To distinguish between true PMS and marketing-inspired activities being passed on as PMS
- To rationalize current practices as to patient recruitment and remuneration.

This guidelines clearly state that remuneration or compensation of physicians enrolled must be provided within a reasonable amount. Pharmaceutical companies should not do things that will induce doctors to prescribe a particular drug. So pharmaceutical companies should only conduct PMS to monitor efficacy and possible adverse drug reactions and not to influence prescription habits of physicians.

Making a Decision

Reviewing an offer to participate in a drug trial is an Investigator’s option. In order to make
an informed decision, the following questions regarding participation should be asked:

**Scientific Aspects**
1. What question does the trial address?
2. Is the study likely to achieve its objectives?
3. What population of patients will the trial enroll?
4. What impact will the trial have on patients?
5. What are the benefit and risks on my patients?
6. How will the data be collected and recorded?
7. What staff will be required to perform the trial?

**Financial Aspects**
1. What will the cost be?
2. Is the payment schedule optimal?

The goal of drug trials is to determine if a treatment both works and safe. Awareness and adherence to the standards of Good Clinical Practice, the local regulatory requirements of the Bureau of Food and Drug and the ethical guidelines set by PHAP is a must for everybody who will participate in such endeavor. One has to recognize the importance of doing drug trials since this will definitely provide access to new research treatment that will be of benefit for mankind.

**References**

Department of Health, Administrative Order No. 22-A S. 1982
Operation Manual on Drug Evaluation and Control, Bureau of Food and Drug, 1992
Karlber J, Tsang K, Introduction to Clinical Trials, The Clinical Trials Centre, University of Hong Kong, Hong Kong, China, 1998

Erice Declaration

On Communicating Drug Safety Information

The following declaration was drawn up at the International Conference on Developing Effective Communications in Pharmacovigilance, Erice, Sicily, 24-27 September 1997. It was attended by health professionals, researchers, academics, media writers, representatives of the pharmaceutical industry, drug regulators, patients, lawyers, consumers and international health organisations.

Monitoring, evaluating and communicating drug safety is a public health activity with profound implications that depend on the integrity and collective responsibility of all parties - consumers, health professionals, researchers, academia, media, pharmaceutical industry, drug regulators, governments and international organisations - working together. High scientific, ethical and professional standards and a moral code should govern this activity. The inherent uncertainty of the risks and benefits of drugs needs to be acknowledged and explained. Decisions and actions that are based on this uncertainty should be informed by scientific and clinical considerations and should take into account social realities and circumstances.

Flaws in drug safety communication at all levels of society can lead to mistrust, misinformation and misguided actions resulting in harm and the creation of a climate where drug safety data may be hidden, withheld, or ignored.

Fact should be distinguished from speculation and hypothesis, and actions taken should reflect the needs of those affected and the care they require. These actions call for systems and legislation, nationally and internationally, that ensure full and open exchange of information, and standards of evaluation. These standards will ensure that risks and benefits can be assessed, explained and acted upon openly and in a spirit that promotes general confidence and trust.

The following statements set forth the basic requirements for this to happen, and were agreed upon by all participants from 34 countries at Erice:

1. Drug safety information must serve the health of the public. Such information should be ethically and effectively communicated in terms of both content and method. Facts, hypotheses and conclusions should be distinguished, uncertainty acknowledged, and information provided in ways that meet both general and individual needs.

2. Education in the appropriate use of drugs, including interpretation of safety information, is essential for the public at large, as well as for patients and health-care providers. Such education requires special commitment and resources. Drug information directed to the public in whatever form should be balanced with respect to risks and benefits.

3. All the evidence needed to assess and understand risks and benefits must be openly available. Constraints, on communication parties, which hinder their ability to meet
this goal must be recognised and overcome.

4. Every country needs a system with independent expertise to ensure that safety information on all available drugs is adequately collected, impartially evaluated, and made accessible to all. Adequate nonpartisan financing must be available to support the system. Exchange of data and evaluations among countries must be encouraged and supported.

5. A strong basis for drug safety monitoring has been laid over a long period, although sometimes in response to disasters. Innovation in this field now needs to ensure that emergent problems are promptly recognised and efficiently dealt with, and that information and solutions are effectively communicated.

These ideals are achievable and the participants at the conference dedicate/commit themselves accordingly. Details of what might be done to give effect to this declaration have been considered at the conference and form the substance of the conference report.

Erice, September 27 1997
The Conference was organised by:
the Uppsala Monitoring Centre,
the Clinical Pharmacology Unit, Institute of Pharmacology of Verona University,
the Ettore Majorana Centre for Scientific Culture, International School of Pharmacology,
the World Health Organisation
and supported by EQUUS Communications, London

Reference:

Detecting Substandard and counterfeit pharmaceutical products.
Kenneth Hartigan-Go MD

The production of counterfeit or substandard anti-infective drugs is a widespread and under-recognized problem that contributes to morbidity, mortality, adverse drug reactions, drug resistance, enormous financial consequences for companies producing the genuine product and loss of confidence in the health care systems and the drug regulatory authorities. Counterfeit drugs particularly affect the most disadvantaged people in poor countries, like the Philippines. A wide array of different counterfeit types based on packaging, sophisticated fake holograms styles on blisterpacks and spurious tablets that contain no active drug have been found in Southeast Asia.

To counter such threats, simple field tests and advances on Forensic Analysis and Chemical Characterization of counterfeit and substandard anti-infectives can be done. Among of which are High Performance Liquid Chromatography (HPLC); Gas Chromatography coupled with optical, electrochemical or mass spectrometric detectors; Thin-Layer Chromatography (TLC); and Colourimetry.

There can be no simple solution to the problem of counterfeit drugs. A comprehensive, pragmatic plan of action, linking various organizations, health workers, industry, and civil society is essential. The increasing evidence that the trade in counterfeit drugs is linked to transnational organized crime presage the necessity to harmonize definitions and penalties between countries, apply strict police and customs action, intensify inspection and drug regulation, increase public awareness, and reinforce a strong political will and openness among countries.

But, vigilant doctors can help detect and report counterfeit medicines.

BFAD does not have specific guidelines on how to detect counterfeit drugs since these drugs are almost the same in appearance compared to the genuine ones. What they usually advice the consumers to do is to buy only from licensed drug stores. The problem is that some drug stores source their drug supply from unlicensed and suspicious traders and importers.

Republic Act No. 8203 also known as **Special Law on Counterfeit Drugs**, Section 3, states that:

"Counterfeit drug/medicine refers to medicinal products with the correct ingredients but not in the amounts as provided hereunder, wrong ingredients, without active ingredients, with sufficient quantity of active ingredient, which results in the reduction of the drug’s safety, efficacy, quality, strength or purity. It is a drug which is deliberately and fraudulently mislabeled with respect to identity and/or source or with fake packaging, and can apply to both branded and generic products. It shall also refer to:

1) the drug itself or the container or labeling thereof or any part of such drug, container or labeling bearing without authorization the trademark, trade name or other identification
mark or imprint or any likeness to that which is owned or registered in the Bureau of Patent, Trademark and Technology Transfer (BPTTT) in the name of another natural or juridical person;

2) a drug product refilled in containers by unauthorized persons if the legitimate labels or marks are used;

3) an unregistered imported drug product, except drugs brought in the country for personal use as confirmed and justified by accompanying medical records;

4) a drug which contains no amount of or a different active ingredient or less than eighty percent (80%) of the active ingredient it purports to possess as distinguished from an adulterated drug including reduction or loss or efficacy due to expiration.

Hence, a substandard quality medicine is a counterfeit medicine by definition.

For the internist, the following can be indicators for fake drugs:

- Patients are not getting well or getting sicker—therapeutic failures. We have observed quite a few cases of attempted suicides with benzodiazepines, taking as much as over 50 tablets without any toxic effects. These drugs were sourced from undisclosed drug stores or from the streets. Hence, no active ingredients, patient do not get well or deteriorates and there is delay in treatment.
- Patient may report unusual side effects that are not known in current literature. Ask the patients where they had sourced their medicines. If they hesitate or refuse, suspect that the source is not from a legal channel. Please remember that even legal channels (i.e. licensed drug stores sometimes source medicines from illegal channels). Counterfeit medicines may contain nothing of the original active principles but something else (e.g. branded antihypertensive drugs were used, patients developed bleeding, while the diagnosis might be hypertensive bleed, the differential may be coumarin chemicals). Hence, wrong active ingredients can kill.
- The packaging is not in its original package, they do not have the requisite BFAD registration numbers and expiry dates, printing is misaligned, labels easily destroyed or removed, discoloration of the package, no package inserts, tablets crumble, parenteral or bottle for reconstitution is tampered (i.e. needle holes seen in the rubber stopper) and the contents cannot be dissolved easily, evidence of contamination, foreign particles.

What the doctors must not do:

- With knowledge of substandard or fake drugs and of less than active ingredients, the doctor must not double the dose.
- Refusal to share information with other colleagues and hence missed out on patterns.
- Refusal to consider substandard drugs or counterfeit medicines as differentials to deterioration of patient conditions.
• Refusal to cooperate with the concerned drug industry in the investigation of counterfeit drugs.
• Buy drugs from questionable sources or abroad on their own and sell these in their clinics.

References:

FAKE MEDICINES CAN KILL YOU

POSSIBLE SIGNS OF FAKE MEDICINE:

BOX CARTON
- The brand name or company logo is not clearly printed
- No generic name, D.R. No. and address of local manufacturer or distributor
- Suspicious Lot No. or address of manufacturer
- Color is easily erased on box carton of medicine

MEDICINE
- Different color of tablet or capsule
- Content of injectible/vial is dirty or mixed with other item such as “floating particles”

FOR MORE INFORMATION, PLEASE CALL HOTLINE

Para sa Karagdagang Kaaaman, tumawag sa number
1-800-10-FAKEMED
325-3633
Medico-legal concerns
Kenneth Hartigan-Go MD

One of the most common barrier to reporting observed or suspected ADR is because doctors belief that if they did this, they will be litigated for medical negligence. This is not true.

In fact, there are cases of medical litigation but these were because the doctors did not recognized the drug induced conditions, failure to monitor the patients during drug treatment, did not stopped the suspect medications or instituted counter-therapy to palliate the adverse drug reactions. Another reason is failure to communicate with the patients or their family members what is happening. Remember, an adverse drug reaction is often due to a product problem and not because of the doctor. But a drug safety problem can arise because of medication errors.

Lastly, if patients get sicker with the medicines you prescribe, consider adverse drug reactions as a differential diagnosis.
Information about medicines can be obtained from various sources. If your only source of information about usage of medicines is from the drug industry representative or from industry sponsored programs, do find an alternative source of drug information like textbooks and medical journals.

When using medicines promoted by industry, and you are unsure of the source, try these guide questions:

- Is the company reputation good and what is the track record in terms of drug quality violations.
- Does the company have compliance to Good Manufacturing Practices (cGMP)
- Does the generic drug have bio-availability or bio-equivalence studies
- Can the drug industry representative provide you with medical literature or studies demonstrating efficacy and safety.
- Do the drug company representatives or materials only emphasize the good points about the medicines and gloss over the risk profile.

When a doctor informs the drug industry of an adverse drug event, the industry may not always accept that that is the case primarily because they will stick to the legal definition of ADR as any noxious, unintended, unexpected reaction to a drug when used in its normal way (normal dosage and administration). But we, as health professionals is after drug product and usage safety, and even if the reaction falls outside of the normal pattern of usage, adverse events may and can develop. The culture of safety for our patients and for our own professional protection occupies a higher moral ground because it is for public good and not a simplistic issue of legality.

It was highlighted recently in a WHO meeting (2007) that doctors and patients must disabuse their thinking that all medicines work (this is a myth). In the same meeting, a recent Uppsala Monitoring Center (WHO Collaborating Center for drug monitoring) report showed data from 2005 revealed that unexpected ineffective medicines were the 7th highest ranking adverse event and medication errors ranked 11th highest ranking adverse event reported.

In our view a drug that does not work as intended is an unsafe drug. Not all products licensed by BFAD is considered good quality and we need to raise the bar for quality standards ourselves within PCP.

A doctor needs to spend some time educating patients about usage of medicines and in particular, to source their drugs from drug outlets that are licensed by the government. This is of particular importance to us because of the maldistribution of doctors in the Philippines where the doctors to patients ratio makes it extremely difficult for us to spend much time educating our patients during each clinical consultation. However, we cannot be remised with our obligation to patients. Perhaps it is time to revisit PCP Covenant.
Incomplete knowledge about drugs and how to use these drugs during patient self-medication can also be a serious safety concern.

Lastly, because we work within a hospital system, human nature tells us that no health professional will willingly report medication errors if the hospital is perceived as punitive and not nurturing or protective. These hospitals might find it to their best interest to put in place patient safety protocols to study how best to improve systems and not pinpoint personal errors.

There are four myths in medicine that we must remember:

- All medicines work.
- Medicines in the market are 100% safe.
- There is a pill for every ill.
- People will use drug rationally as intended.
DR. KENNETH HARTIGAN-GO

Academic background
Dr. Kenneth Hartigan-Go graduated from the University of the Philippines (UP), with Bachelor of Science degree from the College of Arts and Sciences and Doctor of Medicine from the College of Medicine. He is the recipient of the Honor Sword, two Honor Star medals and the Leadership medal in the UP Reserve Officers Training Corp program. He trained as an internist and medical toxicologist at the Philippine General Hospital and has received various trainings and clinical research fellowships abroad. He obtained his postgraduate doctorate degree from the University of Newcastle-upon-Tyne, United Kingdom in 1998.

International work and partnership
Since 1989, he has worked in the capacity of short-term consultant and temporary adviser for the World Health Organization (WHO) on various occasions with issues relating to drug regulatory affairs, pharmacovigilance, and medical toxicology. In 1994, he established the Adverse Drug Reaction Monitoring Program for the Philippine Government in partnership with Australian Assistance for International Development. In 2003, he was invited by the WHO to sit for a 2-year term in the Global Advisory Committee on the Safety of Medicinal Products, an independent select panel of scientific and clinical experts that advises the Director General and in 2006, he was appointed member of the WHO Global Advisory Committee on Vaccine Safety. He is a resource expert on pharmaceutical regulatory science network in APEC meetings. In February 2005, The European Commission (EC) engaged him as one of the consultant for the Formulation Mission Health Sector Policy Support Programme. In July 2005, US Agency for International Development through Chemonics International’s Private Sector Mobilization for Family Planning (PRISM) engaged his services as a consultant. In October 2005, as an Executive Committee member of the International Society of Pharmacovigilance, he spearheaded and hosted the 5th Annual Meeting in the Philippines in partnership with the Philippine Society for Experimental and Clinical Pharmacology (PSECP) with the theme: Pharmacovigilance: East meets West.

Government Service
In 1999, he was appointed as the Deputy Director of BFAD, and the head of the National Drug Policy Programme of the Department of Health. From 1999 to mid-2001, he was involved with the Department of Health Health Sector Reform Agenda: strategic planning and reforms. He served with the Dangerous Drugs Board as a member of technical committee for some years and briefly served as Vice Chair of the Board in 2001. He currently serves as a member of the Health Technology Assessment (HTA) Committee of the government’s National Health Insurance Program within the Philippine Health Insurance Corporation (PHIC), evaluating health technology and products, and advocating evidenced-based sound policy in the areas of financing, drug and medical procedure reimbursement.
ABOUT THE AUTHOR

Academic work
In June 1, 2001 to December 2005, he served UP Manila College of Medicine as a professor at the Department of Pharmacology and Toxicology. Since 1990, he has served as a consultant physician of the National Poisons Control and Information Service. He has authored a number of peer-reviewed published papers in scientific journals including contribution to chapters in pharmacology textbooks. Likewise, in June 2004 to January 2006, he was the Chair of the UP Manila Committee on Institutional Development, a committee that works on strategic reforms to develop and sustain the University’s image and resource generation. Currently, he is engaged with Ateneo University School of Medicine and Public Health in developing their joint medical and masters of management curriculum.

Social/civic responsibilities
He is the Executive Director of the Zuellig Foundation, a non-profit, non-governmental organization, and a health think tank group finding solutions to health and governance problems and a sounding board for rational health policies. As Executive Director of the Zuellig Foundation, he initiated the Health Leadership and Management Program (HLMP). The main concept of HLMP is to invest on institutional management skills of the middle level managers of the public health sector. This Program is on its fourth year of implementation and is undertaken in collaboration with the Department of Health and the Local Government Units. He is the Chairman of the Corporate Network for Disaster Response, an association of private institutions where coordination on managing disasters and disaster preparedness is undertaken. Among the past positions held in various organizations include serving as Vice-President for Operations from August 2002-2004 of the League of Corporate Foundations, an umbrella organization advocating corporate social responsibility; Board Member of the Philippine Coalition against TB from August 2002-2004 and Member of the health core group for the private sector initiatives on the Millennium Development Goals Project of the Philippine Business for Social Progress and the United Nations Development Programme.

Professional affiliations
He is a fellow and member of many scientific professional organizations both internationally and locally. He is the recipient of the prestigious Drug Information Association Outstanding Service Award from the United States in 2001.

He practices medicine at the Manila Doctors Hospital, Cardinal Santos Medical Center and The New Medical City.