PHARMACY BULLETIN

VOLUME 13, ISSUE 8 2012

INNOVATOR VS GENERIC : SIMILAR YET DIFFERENT? BY YAH LIN YE

Scenario I : *"My drug isn't working anymore when you change to other brands. I want the original"*
Scenario II *: "I heard from my other colleague that this generic Blood Pressure Lowering drug works. And it's cheaper! Can doctor let me try it so I won't have to pay so much? '*

We often hear of the pros and cons of using a generic. How do we evaluate whether the claims are true? Are we compromising quality & efficacy of drugs when we switch patients from original brand to generic ones? With the abundance of generic drugs around us, issues pertaining innovator and generics drugs such as their efficacy, interchangeability and safety is of much concern to both healthcare practitioners and patients alike.

An innovator drug is authorized for marketing based on **quality, safety and efficacy**. This new drug is granted a patent that gives the company an exclusive right to sell the medication as long as it is in effect. When the patent expires, other manufacturers can apply for permission to make and sell the generic version of that drug. However, the question remains; are generics = Innovator drug?

At a glance, generics has the similar active pharmaceutical ingredient (API) as the original. However, as the original new drug is protected by the patent, generics are not allowed to emulate most of the innovator formulae. Generics may differ in excipient such as binders, diluents or fillers. Even the colour, shape and marking of the oral drugs must not be the same. These differences may cause different rate of adverse drug reactions.

WHO requires generic product needs to be proven to be bioequivalent to the pioneer drug before it is deemed therapeutically equivalent and, therefore, interchangeable. When a generic drug is said to be bioequivalent, it refers to the rate and extent of absorption that is not significantly different from Innovator when administered at the same dose under similar circumstances. Bioequivalence study usually involves 18-36 human volunteers. With a systemically absorbed drug, blood levels (even from the same product) may vary in different subjects. Therefore, in a typical study, each subject receives both the innovator and the test drug products in a randomized crossover design, and as a result, serves as his or her own control. Single doses of the test and reference drugs are administered, and blood or plasma levels of the drug are measured over time.

Requires Bioequivalent (BE) study :	Equivalence studies are not necessary for :
Oral immediate release drugs	Aqueous solution topical & parenteral generic drugs
Systemic drug delivery system eg as transdermal patches & suppositories	Oral use solution generic drugs
Modified release drugs that act systemically	Powder for reconstitution
Fixed combination product with systemic action, where at least one of the API needs in vivo study	Aqueous solution nasal sprays/ophthalmic products/ nebulizer products

Under the FDA requirement, the mean response of the generic drugs must fall within 80% to 125% of the comparator drugs, which is statistically shown to be equal to a confidence level of 90%. Practically, this means 9 out of 10, the mean response of an individual in a controlled circumstance, would fall within the same numerical limits of the original test. In reality however, it is not always so. The controversy to just look at the BE studies of the comparator lies at the fact that efficacy of a drug can also be influenced by other factors such as :

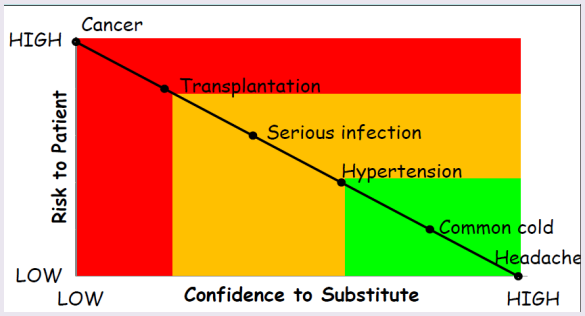
i. drug factor : The excipient used in generic drugs (fillers, binders, dyes etc) can affect the rate of dissolution and absorption by our body.

ii. patient factor : Concurrent diseases, differences in first-pass metabolism, interactions with concurrent medications, diet, the influence of fed versus fasted-state conditions, and gastrointestinal factors that affects bioavailability of the drug (e.g. gastric ph, blood flow & bacterial flora). Furthermore, patients' negative impression on the medication, thus exerting as negative symptom (placebo effect).

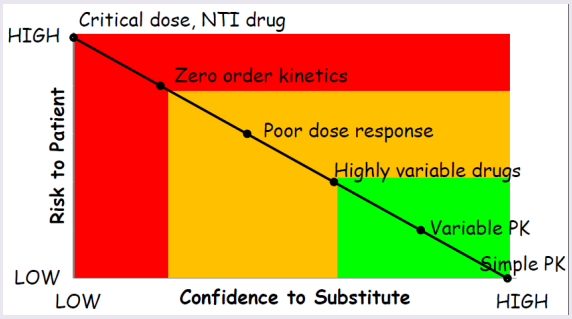
Various studies have been conducted to compare the safety, efficacy and adverse events of innovator compared to generic drugs which showed that the generics were not statistically different in efficacy and safety profiles (Rawdaree P *et al.* 2010*;* Ringe JD *et al.* 2009;) . With the new FDA registration of generic Plavix (Clopidogrel) , Montelukast (Singulair), Atorvastatin (Lipitor), Pioglitazone (Actos) patients will benefit enormously from the availability of the lower-cost generics. Insured patients will also be better off, as the insurance premium for generic drugs is much cheaper than that for branded drugs.

FACTS ABOUT GENERIC DRUGS

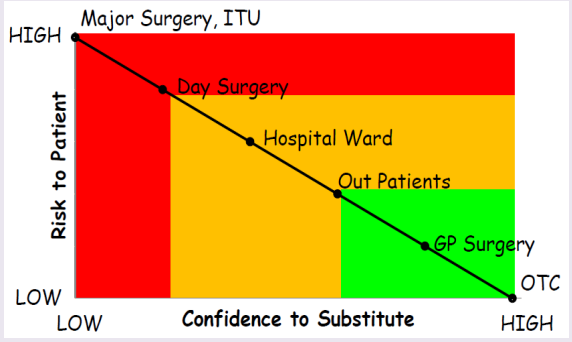
"*Quality is never an accident; it is always the result of intelligent effort*." John Ruskin 1819-1900



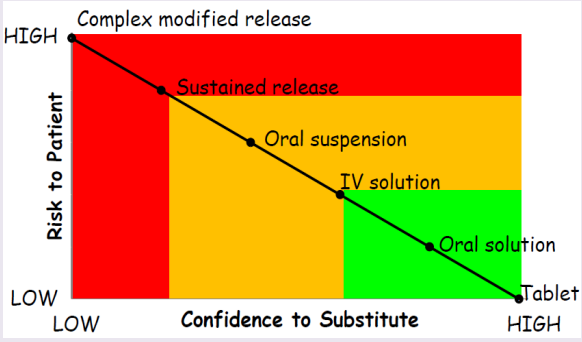
Risk related to Disease



Risk related to Pharmacology



Risk related to Clinical Setting



Risk related to formulation

(graphs adapted from Chris Stubbs, Aspel Pharmaceuticals)

In a nutshell, to decide whether or not we should use generics or innovator products, we should work together to agree on a consensus as to which type of drugs are suitable for generic substitution. (Please see "Confidence to substitute" graph above) In hospitals funded by government, generics help to save drug cost and these savings can be channelled to buy other drugs or allocate to more patients in need. Their safe and cost effective use requires constant supporting data for quality, safety and efficacy, continuous regulatory and medical monitoring. Hence close monitoring of safety, efficacy and toxicity should be advocated by the pharmacists and physicians alike to ensure optimum outcome for the benefit of the patients.

Please channel all product complaints to *portal.bpfk.gov.my —Healthcare Professionals — Reporting —Product Complain.*

Alternative you may obtain 'Borang Aduan Product Berdaftar' (Borang BPFK 418.4) from Drug Information Centre, Grd Flr .

Reference :

1. Ringe JD, Moller G. et al 2009 . *Differences in persistence, safety and efficacy of generic and original branded once weekly bisphosphonates in patients with postmenopausal osteoporosis: 1-year results of a retrospective patient chart review analysis*. Rheumatol Int 2009 Dec; 30(2):213-21.
2. Rawdaree P *et al. Efficacy and safety of generic and original pioglitazone in type 2 diabetes mellitus: a multicenter, a double-blinded, randomized-controlled study*.J Med Assoc Thai. 2010 Nov;93(11):1249-55.
3. Je´ roˆ me Vial, Me´ lanie Cohen, Patrick Sassiat, *Pharmaceutical quality of docetaxel generics versus originator drug product: a comparative analysis* CURRENT MEDICAL RESEARCH AND OPINION. VOL. 24, NO. 7, 2008, 2019–2033