INTRODUCTION

In general, drugs that manufactured in Thailand are less expensive than the innovator preparations or original products imported from foreign countries. Nonetheless, to allow marketing of the generic products, it is important to approve their safety, efficacy and bioequivalence in comparison to the original one already shown to be safe and effective. Although the generic products are manufactured in the same molar dose and formulation, equality of drug content does not guarantee equality of efficacy. The different of excipients used to stabilized the drug, manufacturing process, handling and storage may result in different drug dissolution, absorption, disposition *in vivo* and hence bioequivalence. Bioequivalence refers to drug products in different formulations that contain the same chemical equivalence and that when administered to the same individual result in equivalent concentrations of drug in blood and tissues. Bioequivalence among drug products is important, especially for the formulations with extravascular modes of administration. Physicians and pharmacists are reluctant to switch from the innovator to generic products, unless bioequivalence testing to support their qualities have been demonstrated. If the two products are considered bioequivalent, they are likely to produce similar therapeutic or adverse effects. From these reasons, it is necessary to test bioequivalence of preparations of a drug intended to be switchable. Nevertheless, bioequivalence testing can be performed only when a patent on an innovator's drug expires and other manufactures intend to market the same formulation of the drug. This test is also performed during the course of new drug development, when a formulation is changed, or when the site or method of manufacture is altered.

Cefoxitin and ceftazidime are members of beta-lactam antibiotics which act by inhibiting bacterial cell wall synthesis in the manner similar to the penicillins.

They are bactericidal against both gram-positive and gram-negative bacteria, and are widely used to treat serious infections.

Cefoxitin is classified within the second-generation cephalosporin. It has *in vitro* activity against both aerobic and anaerobic bacteria including most strains of *Bacteroides fragilis* and other *Bacteroides* spp. Its clinical use is therefore emphasized on mixed infections such as pelvic inflammatory disease, lung abscess and intra-abdominal infections.

Ceftazidime is a third-generation cephalosporin with excellent antipseudomonal activity. It also has a broad spectrum of activity against enteric gram-negative bacteria and is especially useful for treating hospital-acquired infections caused by multidrug-resistant organisms.

At present, both drugs are marketed in several formulations for intravenous and intramuscular uses. Cefoxitin is available as Cefoxin® (Merck Sharp & Dohme, West Point, USA) and Cefxitin® (Siam Pharmaceutical, Bangkok, Thailand), while ceftazidime is distributed in Thailand as Fortum® (Glaxo, Greenford, UK), Kefadim® (Eli Lilly, Indianapolis, USA), and Cef-4® (Siam Pharmaceutical, Bangkok, Thailand). Each formulation composes of chemical equivalence of active ingredient; cefoxitin sodium or ceftazidime sodium. Nonetheless, as mention earlier, an individual formulation from different drug companies may have marked differences in manufacturing process as well as content and purity of inactive ingredients. These factors may affect drug bioavailability, including solubility, dissolution, the rate and extent of absorption. Major concern is the bioavailability differences of formulation for intramuscular administration. Bioequivalence testing between the generic and the innovator of intramuscular preparations of cefoxitin and ceftazidime are mandated to confirm

their therapeutic efficacy. The bioavailability studies of generic cefoxitin and ceftazidime have been never reported in Thailand.