INTRODUCTION
Drugs are tested and clinical doses are invariably standardized in relatively healthy, fasted individuals. This situation does not reflect, however, the true clinical setting. Food can have marked influences on the absorption and metabolism of drugs that need to be considered in order to assure the collection of appropriate PK/PD data. The food effect on bioavailability of a drug is presently systematically investigated as soon as possible during the development phase (Godbillon J. et al., 1996, Williams L. et al., 1996).

Before one attributes a change in a patient’s response to a food-drug interaction, one must consider the possibility of other factors which may alter a patient’s response to a drug or diet. These include changes in pathologic state, differences in physiologic availability of the drug, genetically induced patterns of enzyme activity, dietary habits of general population and specific subgroups of population, patient’s age, attitude, life style, environment, and even the geographic location (Williams L. et al., 1996, Utermoulen V., 1999).

Infants, children and the elderly are at increased risk (Mason P., 1994, Thomas J.A., 1995). Both the young and the elderly have an inefficiency of drug metabolising enzymes, an often disturbed renal function and a narrow gap between drug’s therapeutic and toxic level (Mason P., 1994, Utermoulen V., 1999). In addition, the elderly often consume poor / restricted diets either by prescription or choice, and are frequently on long term polymedication (Mason P., 1994, Thomas J.A., 1995, Utermoulen V., 1999). Both obesity and undernutrition can alter the PK of drugs (Cerulli J. and Malone M., 1999). The latter may be associated with a loss of absorptive capacity of the intestine, a fall in plasma albumin and a reduced activity of the drug metabolising enzyme- all predisposing to food drug interactions (Chandler M.H. and Blouin R.A., 1992, Mason P., 1994, Thomas J.A., 1995). Concomitant disease states, such as renal/hepatic failure also influence pharmacokinetics (Cerulli J. and Malone M., 1999).

The risk of food-drug interaction is greater in patients who have increased or specific nutritional needs (e.g., burn/cancer patients), as well as in presence of certain chronic diseases which require various medications; e.g., hypertension, cardiac failure, diabetes mellitus (Thomas J. A., 1995).
Physiological states, such as pregnancy and lactation are of special concern because of possible repercussions in the offspring.

Over the last 10 years, the design, performance and evaluation of bioequivalence studies have received marked attention from various sources, including regulatory agencies, academia, and the pharmaceutical industry (Steinijans V. et al., 1992). One of the major controversies concerning the design of bioequivalence studies is the question of a fasting vs fed state and the time between drug administration and meal intake as well as the volume of fluid given after drug administration.

Unfortunately, it is only when an adverse drug reaction follows a food-drug interaction that the matter becomes of serious concern to the patient or to the clinician. Loss of therapeutic efficacy occurs when a food substance retards or impairs drug absorption, accelerates the rate of drug metabolism or elimination, or 'blocks' the drug effect through some pharmacodynamic interaction (Williams L. et al., 1996).

Although variable drug absorption due to the presence of food may be acceptable for most drugs, it may be critical for some agents. In general, any drug that has a narrow therapeutic index, well defined therapeutic serum levels, or may need to be titrated to a patient's condition is likely to have clinical consequences when absorption is altered (Welling P.G., 1977; 1989). The possible interaction between diet components and drugs with a narrow therapeutic index (e.g. anticoagulants) enhances the likelihood of their toxicity. Large doses of vitamin E (greater than 400 IU) can potentiate the effect of anticoagulants enhancing bleeding risk (Mason P., 1994). Fish oils contain omega 3 fatty acids, which many enhance anticoagulation (Mason P., 1994, Knapp H., 1996). On the contrary, dietary vitamin K tends to antagonize the anticoagulant effect of warfarins (Melnik R.G., 1990, Knapp H., 1996, Thomson C.A and Rollins C.J., 1997, Johnson D.R. and Nyffeler M.S., 1998).

In the USA the Joint Commission on Accreditation of Health Care Organization (JCAHO) has recommended monitoring of the possible drug and food interaction since 1985, and recommends that patient be informed of this (Cardona Pera D., 1999).
Furosemide, one of the most potent and widely prescribed loop diuretic is commonly used in the treatment of oedematous states associated with cardiac, renal and hepatic disease (Hammarlund-Udenaes M. and Benet L.Z., 1989, McCrindle J.L. et al., 1996). It exhibits absorption limited kinetics which means that absorption is limiting the rate of excretion of drug in urine (Alvan G. et al., 1992). There is also considerable intra- and inter-individual variability after oral administration in AUC, mean absorption time (MAT) and urinary excretion. This is a confounding factor in bioavailability studies of furosemide using limited number of subjects thus requiring the need of large sample sizes (Grahnen A. et al., 1984).

In healthy volunteers, food had variable/dramatic effects on furosemide's oral absorption i.e. in certain studies it had no statistically significant influence on extent of absorption and in others there was reported delayed absorption (Kelly M.R. et al., 1973, Hammarlund M.M. et al., 1984). In contrast certain studies exhibited around 30% reduction in the bioavailability of furosemide when given as tablet with food (Hammarlund M.M. et al., 1984, Beermann B. and Midskov C., 1986, Paintaud G. et al., 1995, McCrindle J.L. et al., 1996). In one study, this was associated with a reduction in diuretic response (Beermann B. and Midskov C., 1986) whereas diuresis in another study was almost unaffected (Paintaud G. et al., 1995). Overall, the pharmacokinetic evidence of a food-drug interaction with furosemide is not considered to be of major clinical importance, but it may explain why some individuals with apparent furosemide resistance may respond to bumetanide, as no food-drug interaction has been demonstrated with bumetanide (Beermann B. and Midskov C., 1986). The clinical relevance of these findings needs further investigation since these diuretics are often taken at breakfast time by patients in and out of hospital. Certain studies have suggested that food is a factor, which may influence the potency or pattern of response to diuretics within and between patients (Hammarlund-Udenaes M. and Benet L.Z., 1989).

The US: FDA guidelines prescribe the use of high fat non-vegetarian food for food-drug interaction studies (http://www.fda.gov/gov/cder/guidance/index.html 2001). Due to the wide variations in dietary practices and beliefs among populations throughout the world and due to the fact that nutrients, trace substances and non-nutrients present in the food are known to influence the bioavailability of drugs
(Barthe L. et al., 1999), there is a need for a complete evaluation of the influence of different kinds of food on the bioavailability of drug (Melander A. and Mc Lean A., 1983). India is a country largely inhabited by vegetarians & rice eaters and even most of the non-vegetarians usually consume/ cannot afford non-vegetarian diet more than 1-2 times a week. There is no information on the pharmacokinetics of furosemide in the Indian population or on the effect of Indian types of food on its absorption. It will therefore, be worthwhile to study the effect of isocaloric rice as well as vegetarian and non-vegetarian diets (each with low and high fat content) on the oral bioavailability of furosemide formulation in Indian subjects.