# PHASES OF CLINICAL TRIALS

Four phases of clinical trials and medicine development exist and are defined below. Each of these definitions is a functional one and the terms are not defined on a strict chronological basis. An investigational medicine is often evaluated in tow or more phases simultaneously in different clinical trials. Also, some clinical trials may overlap two different phases.

Phase I: Initial safety trials on a new medicine. An attempt is made to establish the dose range tolerated by volunteers for single and for multiple doses. Phase I trials are sometimes conducted in severely ill patients (e.g., in the field of cancer) or in less ill patients when pharmacokinetic issues are addressed (e.g. metabolism of a new antiepileptic medicine in stable epileptic patients whose microsomal liver enzymes have been induced by other antiepileptic medicines). Pharmacokinetic trials are usually considered Phase I trials regardless of when they are conducted during a medicine's development.

Phase IIa: Pilot clinical trials to evaluate efficacy ( and safety) in selected populations of patients with the disease or condition to be treated, diagnosed, or prevented. Objectives may focus on dose-response, type of patient, frequency of dosing, or numerous other characteristics of safety and efficacy.

Phase IIb: Well controlled trials to evaluate efficacy ( and safety) in patients with the disease or condition to be treated, diagnosed, or prevented. These clinical trials usually represent the most rigorous demonstration of a medicine's efficacy. Sometimes referred to as pivotal trials.

Phase IIIa: Trials conducted after efficacy of the medicine is demonstrated, but prior to regulatory submission of a New Drug Application (NDA) or other dossier. These clinical trials are conducted in patient populations for which the medicine is eventually intended. Phase IIIa clinical trials generate additional data on both safety and efficacy in relatively large numbers of patients in both controlled and uncontrolled trials. Clinical trials are also conducted in special groups of patients (e.g., renal failure patients) , or under special conditions dictated by the nature of the medicine and disease. These trials often provide much of the information needed for the package insert and labeling of the medicine.

Phase IIIb: Clinical trials conducted after regulatory submission of an NDA or other dossier, but prior to the medicine's approval and launch. These trials may supplement earlier trials, complete earlier trials, or may be directed toward new types of trials (e.g., quality of life, marketing) or Phase IV evaluations. This is the period between submission and approval of a regulatory dossier for marketing authorization.

Phase IV: Studies or trials conducted after a medicine is marketed to provide additional details about the medicine's efficacy or safety profile. Different formulations, dosages, durations of treatment, medicine interactions, and other medicine comparisons may be evaluated. New age groups, races, and other types of patients can be studied. Detection and definition of previously unknown or inadequately quantified adverse reactions and related risk factors are an important aspect of many Phase IV studies. If a marketed medicine is to be evaluated for another (i.e., new) indication, then those clinical trials are considered Phase II

clinical trials. The term post-marketing surveillance is frequently used to describe those clinical studies in Phase IV (i.e., the period following marketing) that are primarily observational or non-experimental in nature, to distinguish them from well controlled Phase IV clinical trials or marketing studies.

Spilker, Bert. Guide to Clinical Trials, Raven Press, 1984. Page XXii-Xxiii.