1. INTRODUCTION

- The U.S. Food and Drug Administration (FDA) define bioavailability as "the rate and extent to which the active drug ingredient or therapeutic moiety is absorbed from a drug product and becomes available at the site of drug action". Because in practice it is rare that drug concentrations can be determined at the site of action (e.g., at a receptor site), bioavailability is more commonly defined as "the rate and extent that the active drug is absorbed from a dosage form and becomes available in the systemic circulation."

- Usually bioavailability refers to the absorption of a drug from the gastrointestinal tract following oral administration of a dosage form. The dosage form may be any type of product, including a solution, suspension, tablet, capsule, powder, or elixir. Bioavailability can also refer to other types of dosage form, such as intramuscular injections, ointments and other topical preparations, transdermal patches, and implants, which also require an absorption step prior to reaching the systemic circulation. The only route of drug administration that should always result in a bioavailability of 100% is an intravenous injection, in which the amount of drug reaching the systemic circulation is equal to the total administered dose.

- The term ‘relative bioavailability’ refers to a comparison of two or more dosage forms in terms of their relative rate and extent of absorption. If an intravenous injection is employed as the reference dose, one can determine the absolute bioavailability of the test dosage form. Two dosage forms that do not differ significantly in their rate and extent of absorption are termed ‘bioequivalent.’" Bioequivalence determinations may be made for ‘pharmaceutical alternatives,’ defined as ‘drug products that contain the identical therapeutic moiety, or its precursor, but not necessarily in the same amount or dosage form or as the same salt or ester.

- Each drug product individually meets either the identical or its own respective compendial or other applicable standard of identity, strength, quality, and purity, including potency and, where applicable, content uniformity, disintegration times, and/or dissolution rates." In some instance, two pharmaceutical alternatives exhibit markedly different bioavailability, for example, a rapidly absorbed elixir vs. a more slowly absorbed capsule. In other cases, two different dosage forms (e.g., a tablet and a capsule) may or may not exhibit very similar bioavailability. While the mechanisms
by which a formulation affects bioavailability and bioequivalence have been extensively studied in drugs, formulation factors that influence bioavailability and bioequivalence in nutritional supplements are largely unknown. As a result, in nutritional sciences, relative bioavailability or bioequivalence is the most common measure of bioavailability, comparing the bioavailability of one formulation of the same dietary ingredient to another.

- The focus of these regulations was on BA and pharmacokinetic information needed for submission in a New Drug Application (NDA) and to some extent on evidence of BE (relative BA). With passage of the 1984 Drug Price Competition and Patent Term Restoration amendments to the Food, Drug and Cosmetic Act, BE took on added importance for generic drugs. As defined in implementing regulations, an applicant submitting an Abbreviated New Drug Application (ANDA) under Section 505(j) of the Act (excepting Suitability Petitions submitted under 505(j)(2)(c) of the Act) must demonstrate both pharmaceutical equivalence (PE) and BE between the generic product and listed innovator reference drug product. With acceptance of this documentation by FDA, along with other information, the generic product is deemed bio-equivalent, therapeutically equivalent, and interchangeable with the listed reference drug product.

- **Description:**
  Gabapentin (brand name Neurontin) is a medication originally developed for the treatment of epilepsy. Presently, Gabapentin is widely used to relieve pain, especially neuropathic pain. Gabapentin is well tolerated in most patients, has a relatively mild side-effect profile, and passes through the body unmetabolized.

- **Pharmacology:**
  **Mechanism of Action:**
  Gabapentin is an antiepileptic drug structurally related to the neurotransmitter Gamma Amino Butyric Acid (GABA). Gabapentin is indicated as adjunctive therapy in the treatment of partial seizures with and without secondary generalization in adults with epilepsy and for the management of postherpetic neuralgia. Gabapentin can be actively transported across the brain–blood barrier and the gut via the L-system amino acid transporter, which recognizes L-isoleucine, L-leucine, L-phenylalanine and L-valine. The exact mode of action of GB has not yet been clearly defined.