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Perspective

# Therapeutic Equivalence Cornerstone for Ensuring Safe and Effective Generic Drug Substitution

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## DESCRIPTION

Therapeutic equivalence is a fundamental concept in pharmaceutical science, serving as the basis for substituting brand-name medications with their generic counterparts. As global healthcare systems continue to emphasize cost-effectiveness and accessibility, the assurance that generic formulations can deliver the same therapeutic outcomes as innovator drugs has become increasingly important. Therapeutic equivalence embodies not only the similarity in Active Pharmaceutical Ingredient (API) quality but also encompasses bioequivalence, pharmacokinetic behavior, clinical performance, and safety. By establishing rigorous scientific and regulatory requirements, therapeutic equivalence upholds public confidence in generic medicines and supports sustainable healthcare practices.

At the core of therapeutic equivalence lies the demonstration of bioequivalence, which ensures that the generic drug exhibits no significant difference in the rate and extent of absorption compared with the reference product. Parameters such as Cmax, Tmax, and AUC are measured using validated bioanalytical methods, typically relying on advanced techniques like LC-MS/MS. These pharmacokinetic indicators provide objective evidence that plasma drug exposure from the test formulation will mirror that of the innovator. When these metrics fall within predefined regulatory acceptance limits, usually 80% to 125%, a generic drug is considered bioequivalent. Since therapeutic action is closely related to systemic availability for most drugs, bioequivalence serves as a reliable surrogate for clinical equivalence.

Beyond pharmacokinetic matching, regulatory agencies such as the Food and Drug Administration and European Medicines Agency require that generic products maintain comparable quality attributes, including purity, stability, dissolution profile, and manufacturing consistency. Dissolution testing, in particular, plays a pivotal role by linking in vitro performance with *in vivo* bioavailability. Consistent dissolution behavior helps predict

absorption and supports the establishment of *in Vitro-In Vivo* Correlations (IVIVC), when feasible. This ensures that formulation differences do not translate into clinically meaningful variations. Excipient composition, though not required to be identical to the reference product, must not alter safety or efficacy. Any changes must be justified through thorough pharmaceutical development studies.

Therapeutic equivalence also extends to product performance in real-world clinical settings. Even when bioequivalence is demonstrated, certain drug classes demand additional scrutiny. Narrow Therapeutic Index (NTI) drugs, for example such as antiepileptics, anticoagulants, and thyroid hormones may require stricter bioequivalence limits or supplemental clinical evaluations. These drugs carry higher risk when plasma concentrations deviate slightly from the optimal range, making precise therapeutic substitution essential. Similarly, modified-release formulations must demonstrate that changes in formulation technology do not compromise pharmacokinetic profiles across the entire dosing interval.

In clinical practice, therapeutic equivalence has profound implications for healthcare economics and public health. The widespread use of generic drugs significantly reduces treatment costs, enabling broader patient access without sacrificing therapeutic quality. This is particularly important in low- and middle-income countries, where affordability remains a major barrier to treatment adherence. By enabling safe substitution, therapeutic equivalence supports cost-efficient prescribing while maintaining high standards of drug performance and safety.

Continuous advancements in analytical technologies, formulation science, and regulatory science continue to enhance the rigor and reliability of therapeutic equivalence assessments. As drug molecules become more complex and innovative delivery systems evolve, establishing equivalence will require increasingly sophisticated approaches. Nonetheless, the foundational principles remain consistent: a generic drug must deliver the same therapeutic outcome as its reference product.

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In conclusion, Therapeutic Equivalence: A Cornerstone for Ensuring Safe and Effective Generic Drug Substitution underscores the scientific, regulatory, and clinical significance of ensuring that generic medicines provide comparable efficacy and

safety to innovator drugs. This concept remains essential for promoting patient confidence, supporting healthcare sustainability, and advancing global access to high-quality medications.