

Contains Nonbinding Recommendations

Draft – Not for Implementation

Draft Guidance on Heparin Sodium

February 2022

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the Office of Generic Drugs.

This guidance, which interprets the Agency’s regulations on bioequivalence at 21 CFR part 320, provides product-specific recommendations on, among other things, the design of bioequivalence studies to support abbreviated new drug applications (ANDAs) for the referenced drug product. FDA is publishing this guidance to further facilitate generic drug product availability and to assist the generic pharmaceutical industry with identifying the most appropriate methodology for developing drugs and generating evidence needed to support ANDA approval for generic versions of this product.

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This is a new draft product-specific guidance for industry on heparin sodium.

Active Ingredient:	Heparin sodium
Dosage Form; Route:	Injectable; injection
Recommended Study:	Request for waiver of in vivo bioequivalence study requirements

Waiver:

To qualify for a waiver of the in vivo bioequivalence (BE) study requirement on the basis that BE is self-evident under 21 CFR 320.22(b), a generic heparin sodium injection product must be qualitatively (Q1)¹ and quantitatively (Q2)² the same as the Reference Listed Drug (RLD).

An applicant may seek approval of a drug product that differs from the RLD in preservative, buffer, or antioxidant provided that the applicant identifies and characterizes the differences and

¹ Q1 (Qualitative sameness) means that the test product uses the same inactive ingredient(s) as the reference list drug product.

² Q2 (Quantitative sameness) means that concentrations of the inactive ingredient(s) used in the test product are within $\pm 5\%$ of those used in the reference listed drug product.

provides information demonstrating that the differences do not affect the safety or efficacy of the proposed drug product.³

In addition, the sources of heparin are expected to have significant impact on the efficacy of the heparin products. Therefore, test heparin should be derived from porcine sources. An applicant may follow the guidelines in the current USP monograph of heparin sodium for the additional criteria to demonstrate the active ingredient sameness of the test and reference products.

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³ 21 CFR 314.94(a)(9)(iii).