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Draft – Not for Implementation

Draft Guidance on Heparin Sodium; Taurolidine

August 2024

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In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

Active Ingredients:	Heparin sodium; Taurolidine
Dosage Form:	Solution
Route:	N/A
Strengths:	3,000 units/3 mL (1,000 units/mL); 40.5 mg/3 mL (13.5 mg/mL) 5,000 units/5 mL (1,000 units/mL); 67.5 mg/5 mL (13.5 mg/mL)
Recommended Studies:	Request for waiver of in vivo bioequivalence study requirements

To qualify for a waiver of in vivo bioequivalence study requirement on the basis that bioequivalence is self-evident under 21 CFR 320.22(b)(1), a generic heparin sodium and taurolidine solution should 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 if the applicant identifies and characterizes the differences and 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 this product. Therefore, heparin in the test product should be derived from porcine sources. An

[1] Q1 (Qualitative sameness) means that the test product uses the same inactive ingredient(s) as the RLD.
[2] Q2 (Quantitative sameness) means that concentrations of the inactive ingredient(s) used in the test product are within ±5% of those used in the RLD.
[3] 21CFR 314.94(a)(9)(iii)

applicant may follow the guidelines in the current USP monograph of heparin sodium for the additional criteria to demonstrate sameness of heparin in the test and RLD.

Additional information:

Device:
The RLD is a drug-device combination product presented as a catheter lock solution in a vial. The water in the catheter lock solution is the device constituent part.

User interface assessment:
Usually, an abbreviated new drug application (ANDA) for a drug-device combination product should include complete comparative analyses so FDA can determine whether any differences in design for the user interface of the proposed generic product, as compared to the RLD, are acceptable and whether the product can be expected to have the same clinical effect and safety profile as the RLD when administered to patients under the conditions specified in the labeling. Refer to the most recent version of the FDA guidance for industry on *Comparative Analyses and Related Comparative Use Human Factors Studies for a Drug-Device Combination Product Submitted in an ANDA*.[a]

- If the proposed generic referencing this RLD will be supplied in a vial without other device constituent parts, comparative analyses may not be needed to support generic substitutability in the ANDA.
- We encourage generic firms to use the pre-ANDA controlled correspondence and/or meeting request process to ask questions about device user interface assessment during product development.

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[a] For the most recent version of a guidance, check the FDA guidance website at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.