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Draft Guidance on Ferric Pyrophosphate Citrate

November 2023

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Active Ingredient:	Ferric pyrophosphate citrate
Dosage Form:	Solution
Route:	Intravenous
Strengths:	27.2 mg iron/5 mL (5.44 mg iron/mL), 272 mg iron/50 mL (5.44 mg iron/mL)
Recommended Studies:	Comparative characterization studies to support active pharmaceutical ingredient (API) sameness and request for waiver of in vivo bioequivalence study requirements

Recommendations to support API sameness:

The applicant is advised to perform side-by-side comparative studies using the test API and the API from the reference listed drug (RLD) product. A minimum of three batches of the test API and reference API should be characterized to assess API sameness. API sameness can be established by evaluating the equivalence of the physicochemical properties that include, but are not limited to the following:

1. Oxidation state of the iron in the API
2. Stoichiometric ratio of ferric iron to pyrophosphate and citrate
3. X-ray absorption near edge structure (XANES) and extended X-ray absorption fine structure spectroscopy (EXAFS)

Waiver of in vivo bioequivalence study requirements:

To qualify for a waiver of in vivo bioequivalence studies on the basis that bioequivalence is self-evident under 21 CFR 320.22(b), a generic ferric pyrophosphate citrate solution product,

including its phosphate, sulfate and sodium content, should be qualitatively (Q1)¹ and quantitatively (Q2)² the same as the RLD.

An applicant may seek approval of a drug product intended for parenteral use that differs from the RLD in preservative, buffer, or antioxidant provided that 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

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

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

³ 21 CFR 314.94(a)(9)(iii).