Contains Nonbinding Recommendations

Draft – Not for Implementation

Draft Guidance on Ferric Pyrophosphate Citrate

November 2023

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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.

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 Ingredient:	Ferric pyrophosphate citrate
Dosage Form:	Solution
Route:	Intravenous
Strength:	6.75 mg iron/4.5 mL (1.5 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]

Document History: Recommended November 2023

Unique Agency Identifier: PSG_212860

[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 ±5% of those used in the RLD product.
[3] 21 CFR 314.94(a)(9)(iii).