

Draft Guidance on Amino Acids; Calcium Chloride; Dextrose; Magnesium Sulfate; Potassium Chloride; Sodium Acetate; Sodium Glycerophosphate; Soybean Oil

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

- Active Ingredient:** Amino acids; Calcium chloride; Dextrose; Magnesium sulfate; Potassium chloride; Sodium acetate; Sodium glycerophosphate; Soybean oil
- Dosage Form; Route:** Emulsion; intravenous
- Strengths:** 3.3%; 29mg/100mL; 9.8gm/100mL; 96mg/100mL; 174mg/100mL; 239mg/100mL; 147mg/100mL; 3.9gm/100mL and,
2.4%; 20mg/100mL; 6.8gm/100mL; 68mg/100mL; 124mg/100mL; 170mg/100mL; 105mg/100mL; 3.5gm/100mL
- Recommended Studies:** In vitro study

The in vitro study can only be used to demonstrate BE when each sub-component of the generic product is qualitatively (Q1)¹ and quantitatively (Q2)² the same as the corresponding sub-component of the Reference Listed Drug (RLD) product. Comparative studies should be performed on the Test product and Reference Standard (RS) immediately after activation (combining the three components). The comparative studies should be performed on at least three batches of the Test product and RS product.

Parameters to measure: Globule size distribution. Sponsors should also perform comparative physicochemical characterization including, but not limited to, zeta-potential, pH, osmolality and viscosity profile, on the activated Test product and RS product. Sponsors should compare the size parameter upon serial dilution (if applicable) of the combined activated Test product and RS product; and provide histograms of globule size distribution data of each diluted sample.

Bioequivalence based on (95% upper confidence bound): Population bioequivalence (PBE) based on D₅₀ and SPAN (alternatively harmonic intensity weighted average particle diameter and polydispersity index derived from cumulate analysis of the intensity size distribution) for the globule size distribution only (the other parameters do not require PBE)

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

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 reference listed drug.

analysis). The applicants should provide no less than 10 datasets from 3 batches each of the activated Test and the RS products to be used in the PBE analysis.