# Bioequivalence of Reference and Biosimilar Preparations of Premixed Biphasic Insulin Aspart: A Comparative Clamp Study

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## Abstract

Biphasic insulin aspart 30 is a premixed formulation containing a soluble fraction of insulin aspart (30%) and a protamine-crystallized fraction (70%) that was developed to combine the rapid-acting and prolonged advantages of commercially available insulins. The aim of this bioequivalence study was to compare the pharmacokinetics (PKs) of GP-bi-asp and Novo-bi-asp, and evaluate the pharmacodynamic (PD) properties as well as the safety of these drugs in the hyperinsulinemic euglycemic clamp (HEC) procedure. This was a phase 1, randomized, double-blind, 2-sequence, 2-period crossover study. Thirty-four male volunteers who met the inclusion criteria underwent the HEC procedure following a single subcutaneous injection of 0.4 IU/kg of either GP-bi-asp or Novo-bi-asp in the abdomen. After the treatment, the subjects' plasma glucose levels were monitored for 24 hours and the glucose infusion rate (GIR) was adjusted to maintain the target blood glucose level. The PD parameters were calculated using GIR values. Insulin aspart concentrations were measured in blood plasma using validated ELISA assays to evaluate the PK parameters of the investigated drugs. The 90% confidence intervals for the geometric mean ratios of PK ($C_{ins}$ and $AUC_{ins\text{-}T}$ ) parameters of Gp-bi-asp and Novo-bi-asp were close to 100% and within the 80%-125% limits for establishing bioequivalence. The safety profiles of both drugs were also comparable.

**Keywords:** biosimilar; biphasic insulin aspart 30; hyperinsulinemic euglycemic clamp; phase I study; premixed insulin analogs.

**Link to publication**