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# An Analysis of the Mixing Efficiency of Neutral Protamine Hagedorn Cartridges

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## Abstract

In this issue of *Journal of Diabetes Science and Technology*, Kaiser and colleagues conducted an investigation to identify variations in the delivered dose of several different isophane insulin (neutral protamine Hagedorn, NPH) brands that use glass and metal bodies ("bullets") to facilitate mixing. Using a strategy where multiple pens from each of five different NPH insulin products (Insuman Basal, sanofi-aventis, three metal bullets; Humulin N, Lilly, one glass bullet; Berlinsulin H Basal, Berlin-Chemie, one glass bullet; Insulin B. Braun Basal, two glass bullets; and Protaphane Penfill, NovoNordisk, one glass bullet) were compared at multiple sampling points and over a range of mixing procedures (3, 6, 10, and 20 times), the authors identified deviations in the delivered dose of insulin at initial use and with repeated dosing. At the initial dose, adhering with manufacturer recommendations to conduct the mixing procedure 10–20 times was found to demonstrate minimal deviation and there was no pronounced difference among the products. Decreasing the number of mixing procedures from 10–20 to 3–6 times, a more profound deviation was noted, with the Insuman Basal product demonstrating less variability in comparison to all other products evaluated. A repeated dose study (1, 2, 6, and 10) with only six mixing procedures revealed that the insulin concentration of each dose increased for all products except Insuman Basal. Clinically, numerous factors may contribute to variability observed with subcutaneous administration of isophane insulin. While data presented by Kaiser and colleagues demonstrated that the issue of proper mixing is not trivial, the modest differences observed between and within products both at the initial dose and with repeated dosing may indicate that the clinical relevance of these findings is most applicable to those requiring large doses or, alternatively, those who have otherwise unexplained hypoglycemic episodes.

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**Abbreviations:** (IU) international units, (NPH) neutral protamine Hagedorn, isophane insulin

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