Lilly Calls into Question the Validity of Published Insulin Concentration Results

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On December 21, 2017, an article titled "Insulin Concentration in Vials Randomly Purchased in Pharmacies in the United States: Considerable Loss in the Cold Supply Chain" was published in this journal.[1]

The authors acquired 18 vials of human insulin made by two manufacturers from US pharmacies to test for intact insulin concentrations in the drug products using mass spectrometry. Based on their testing, they reported significantly lower concentrations than the minimum US Pharmacopeia (USP) standard of 95 U/mL and concluded that the results imply the cold supply chain impacts insulin concentrations to a larger extent than anticipated.

We believe the conclusions are flawed due to the testing methods used. As the article may raise questions around the quality of insulins in general, we offer information that may help prescribers and people who use insulin put this article into perspective. The testing methods used in the report were not developed or validated for measurement of insulin concentration in the drug product, but were developed for measuring insulin in human plasma. The accepted FDA reference methods for determining insulin concentration in drug product are publicly available and published in the USP. The USP methods have been specifically developed and validated per International Council for Harmonization (ICH) for the accurate and precise measurement of insulin concentration in insulin drug product formulations.

The method referenced in the article subjected the well-characterized insulin formulations to unnecessary and complex manipulations, which significantly and negatively affect the solubility of insulin in the original formulations. It is not surprising that the recovery of insulin from the original formulation is poor and varied under this sample preparation method, casting considerable doubt as to the accuracy and validity of the published results and conclusions.

As a manufacturer of insulin, Lilly uses robust quality management systems and product control strategies to meet or exceed the high standards required by global regulatory agencies and expected by those who prescribe and use our products. We are extremely confident in the quality of our insulins. Lilly has controls and specifications throughout the manufacturing process, including validated testing of every batch that is distributed to the market. These controls ensure the solubility and stability of insulin over the shelf life of the product when stored under the stated label and in-use conditions.

Wholesalers and pharmacies that distribute insulin must hold a pharmaceutical distribution license issued by local government agencies in the United States, which requires appropriate cold chain storage and distribution practices. Additionally, regulatory agency surveillance programs are conducted periodically and we are not aware of any concerns arising from testing.[2,3]

If studies are pursued to further clarify this issue, every effort should be made to ensure the validity of the analytical results before drawing conclusions related to the postmanufacturing cold supply chain. This can be ensured by using a certified laboratory that has successfully demonstrated proficiency in executing the standard and accepted FDA reference methods (USP) for determining insulin concentration in drug product prior to analyzing any investigational samples.

Abbreviations

FDA, US Food and Drug Administration; ICH, International Council for Harmonization; USP, US Pharmacopeia.

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