Notes on the Design of Bioequivalence Study: Pyridoxine

Notes on the design of bioequivalence studies with products invited for submission to the WHO Prequalification Unit – Medicines Assessment Team (PQT/MED) are issued to aid manufacturers with the development of their product dossier. Deviations from the approach suggested below can be considered acceptable if justified by sound scientific evidence.

The current notes should be read and followed in line with the general guidelines of submission of documentation for WHO prequalification. In particular, please consult the "Multisource (generic) pharmaceutical products: guidelines on registration requirements to establish interchangeability" in: *Fifty-first report of the WHO Expert Committee on Specifications for Pharmaceutical Preparations,* Geneva, World Health Organization, 2017. WHO Technical Report Series, No. 992, Annex 6.

Below, additional specific guidance is provided on the invited immediate release products containing pyridoxine.

Pharmacokinetics of Pyridoxine

Pyridoxine peak absorption is observed after 1.3 h and its half-life is very short (0.75 h), which may be responsible for a large intra-subject variability.

Pyridoxine is considered a highly soluble and highly permeable drug substance.

Guidance for the demonstration of *in vitro* bioequivalence

Taking into account the pharmacokinetic properties of pyridoxine, a biowaiver approach (similar to a BCS-based biowaiver) is recommended.

The following requirements should be met:

a) Comparability between the WHO-accepted comparator product regarding the qualitative and quantitative composition of the formulations should be demonstrated.

b) Dissolution data should be submitted at pH 1.2, 4.5 and 6.8 at 50 rpm in the paddle apparatus or 100 rpm in the basket apparatus showing very rapid or rapid dissolution of the 10 and 50 mg tablets, similar to those of the corresponding WHO-Comparator product.