

ASEAN GUIDELINES FOR THE CONDUCT OF BIOAVAILABILITY AND BIOEQUIVALENCE STUDIES – QUESTIONS AND ANSWERS (Q & A)

(Version 2)

This has been agreed and adopted at the 16th ASEAN Consultative Committee for Standards and Quality (ACCSQ) Pharmaceutical Product Working Group (PPWG), 26th May 2009

Question 1

Q : Is BE Study Protocol required to be approved only by Ethics Committee or also by regulatory body?

A : Approvals from Ethics Committee on BE Study Protocol are required prior to the conduct of the BE study. However, in some countries, where applicable, the study protocol may also be approved by the Regulatory Authority especially when Clinical Trial Authorisation or Clinical Trial Import License is required.

Question 2

Q : How is the required number of subjects determined?

A : The number of subjects required is determined by :

- a) the intra-subject coefficient of variation of the drug to be studied either estimated from a pilot study, results of previous clinical studies or from published literature.
- b) the significance level desired ($\alpha=0.05$)
- c) the expected deviation from the reference product compatible with bioequivalence (delta, ie percentage difference from 100 % ie. $\pm 20\%$)
- d) the required power should be at least 80%

The clinical and analytical standards imposed may also influence the statistically determined number of subjects. However, generally the minimum number of subjects should not be smaller than 12.

Question 3

Q : Should genetic phenotyping of subjects be performed? And how?

A : Yes, phenotyping and genotyping of subjects should be considered if a drug is known to be subjected to major genetic polymorphism and when overdose will pose safety issues to the subject. Studies could be performed in panels of subjects of known phenotype or genotype for the polymorphism in question.

Question 4

Q : If *in vitro* dissolution of the drug in 3 pH conditions is similar, is it a guarantee that the test drug is bioequivalent to the reference product?

A : Please refer to Appendix II of ASEAN Guidelines for The Conduct of Bioavailability and Bioequivalence Studies which explains the purpose of dissolution studies.