

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

(Version 4)

This has been agreed and adopted at the 18th ASEAN Consultative Committee for Standards and Quality (ACCSQ) Pharmaceutical Product Working Group (PPWG), June 2011

Question 1

Q : If a generic drug which has been registered and its bioequivalence compared to the innovator drug has been proven, does the BE study need to be repeated if there is a change in the API source?

A : Generally, a new BE study is not required for changes of API source. However, applicants should provide comparative dissolution data depending on the dosage form of the proposed product.

To substitute an API source, all of the following circumstances should be complied:

1. The previous API source is not being withdrawn due to deficiencies specifically relating to that API, such as:
 - Lack of adequate controls
 - Evidence of adulteration
 - Evidence of falsification of data in the application or identified in the preapproval inspection.
2. The previous batch used in BE studies and the BE studies were acceptable, except for the cGMP issues that were specific to the previous API.
3. The specifications of the API from new source are essentially the same as the API from previous source, such as the particle size, polymorphic form, no change in route of synthesis, impurities profile, etc.

The above condition is based on USFDA Guidance for Industry : Alternate Source of the Active Pharmaceutical Ingredients in Pending ANDA (December 2000)

Question 2

Q : If a generic drug which has been registered and its bioequivalence compared to the innovator product has been proven, does the BE study need to be repeated if there were changes in manufacturing sites (different location whether both company owned or contract manufacturing facilities) or building within a single production site?

A : Repeated BE study is not required for those changes which comply to requirements, such as same specification/manufacture of API, formulation, manufacturing process, equipment specifications, environmental conditions and controls, and personnel qualification to both manufacturing sites are used.

However, changes in manufacturing site should perform equivalence test (comparative dissolution profile in 3 media) of the drug product at the previous and proposed sites by conducting multi-point dissolution profile in compendial medium at 15, 30, 45, 60 and 120 minutes or until an asymptote is reached. If the dissolution requirements do not exist in the pharmacopoeia, the dissolution test should be performed using 3 pH media and the dissolution profiles of both drug products should be similar. For changes in buildings but still in one production site, the comparative dissolution test is not necessary, but dissolution test according to the pharmacopoeia is required.

Kindly refer to USFDA Guidance for Industry on 'Scale-Up and Post-approval Changes' (SUPAC) for more detail.