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——資　　料——

開発段階における経口固形製剤（通常製剤）の製剤変更時のバイオアベイラビリティ評価試験について*

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Consideration of Bioavailability/Bioequivalence in Drug Development Stage and Proposed Methods to Evaluate Bioavailability/Bioequivalence in Formulation Changes of Oral Solid Dosage Forms

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Summary

The concept of bioequivalence (BE) was devised to assure therapeutic equivalence of generic drug products to innovator's drug products for interchangeability of products in medical treatment, or to assure therapeutic equivalence of drug products changed in post approval to pivotal clinical trial batch or the drug product before change. Guidelines on BE study have been published by the WHO, EMEA, FDA, MHLW, etc. and these guidelines practically stand on the concept of BE, and mainly focus on scale-up and post approval changes including generic products.

In drug development, formulation changes are done with development of clinical study, and the quality of drug products is improved in these changes, and safety and efficacy of drug products are confirmed in Phase III. At the stage prior to Phase III study, the safety and efficacy of drug products are not fully established, and changes made during drug development do not necessarily have to meet the requirement of interchangeable use of formulations. Therefore, the concept of BE is not perfectly suitable to changes made during drug development. Nevertheless, pharmaceutical companies do consider consistency of BE between formulations before and after such changes and spend much time and money in demonstrating BE.

The concept of BE, in the original sense, should be applied to post approval changes or at most changes made during Phase III. Hence, new changeability concepts other than BE should be introduced to deal with changes during early drug development stage, especially before Phase III. A more flexible approach may facilitate not only formulation development, but also drug development itself.

The Committee of Pharmaceutical Sciences of the Japan Pharmaceutical Manufacturers, Association (JPMA) conducted a survey of current strategies of formulation development among representative Japanese pharmaceutical companies. Based on this survey, we publish here our considerations of bioavailability/bioequivalence in drug development stage and propose methods to evaluate bioavailability/bioequivalence in relation to formulation changes of oral solid dosage forms.

Key words

Drug development, Formulation designing, Formulation development, Formulation change, Bioavailability, Bioequivalence, Changeability, Oral solid dosage form