

## First in Human 試験における初回用量設定方法の検討

## — 推定最小薬理作用量 (MABEL) 活用の試み —

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Starting Dose Setting in First in Human Study Using  
Minimum Anticipated Biological Effect Level (MABEL)

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## Summary

The European Medical Agency recommends that not only conventionally used NOAEL, but also Minimum Anticipated Biological Effect Level (MABEL) should be used to set initial doses to be investigated in First In Human (FIH) studies for highly innovative candidate drugs. However, there have been no reports on Japanese clinical studies for which MABEL was used to set initial doses. Therefore, for the drugs that were approved in Japan from 2001 to 2007, of which the submission packages are disclosed on the official website of the Pharmaceuticals and Medical Devices Agency, we defined the initial doses for FIH studies based on NOAEL and MABEL, and calculated the ratio of those doses to the initial doses that were actually tested in the FIH studies and the doses that have been used in medical practice after launch. Thus, we investigated the possibility that MABEL may be useful to set initial doses in FIH studies in the future. The results suggest that the conventionally adopted approach to set initial doses based on NOAEL (NOAEL approach) is applicable to many drugs, and it is considered to be still useful for FIH studies in the future. In the case of initial doses based on MABEL (MABEL approach), it was confirmed that if human equivalent doses to MABEL are set as initial doses, such doses are close to the initial doses set based on NOAEL, as well as to those that were actually tested in FIH study, regardless of the administration route, molecular weight and therapeutic classification. Accordingly, we believe it is possible to set scientifically based initial doses to be investigated in FIH studies by firstly choosing potential initial doses based on the NOAEL approach and then confirming the appropriateness of such potential doses based on the MABEL approach.

## Key words

First in human study, Starting dose, NOAEL, MABEL, Micro dose study