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Implementation strategy of ICH Guideline M10 on bioanalytical method validation

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Introduction

The purpose of this document is to address specific considerations to enable the practical implementation of ICH Guideline M10 on bioanalytical method validation and study sample analysis (EMA/CHMP/ICH/172948/2019) in the European Union. It is intended to provide guidance for Marketing Authorisation (MA) Applicants and MA Holders (MAH), Contract Research Organisations (CROs), as well as Regulators. In addition to new applications, it will apply to variations to existing authorised medicinal products.

Background

ICH Guideline M10 came into effect 21 January 2023, formally superseding the previously enforced EMA Guideline on bioanalytical method validation (EMEA/CHMP/EWP/192217/2009 Rev. 1 Corr. 2**), which had been in effect since 1 February 2012.

The responsibility for the scientific validity of data supporting marketing authorisation of medicinal products lies with MA Applicants and MAH. Bioanalytical methods used to generate data supporting MA should be robustly validated and updated following state-of-the-art science that is suitable for their intended purpose.

Implementation of ICH Guideline M10 on bioanalytical method validation

As of the date of coming into effect on 21 January 2023, ICH M10 should be used in **all** method validations without exception.

Therefore,

- If you are starting out your development after 21 January 2023, all validations should be based on ICH M10.

However,

- If you started your development shortly before 21 January 2023 (e.g., you are in early clinical phase development), you should consider segueing to M10.
- If you were late in development as of 21 January 2023 (e.g., in phase 3 trials with pharmacokinetic studies completed or, in the case of a generic submission, the validation of the bioanalytical method has already been conducted and the bioequivalence study is near to completion), studies may be completed if the EMA Guideline on bioanalytical method validation has been applied throughout.
- If you have completed the (non-)clinical development of your dossier before 21 January 2023 and will be submitting your application after this date, there is no need to change or revalidate the bioanalytical methodology in your application according to ICH M10. This applies if you have used the EMA Guideline on bioanalytical method validation and also applies to studies conducted prior to that guideline being in effect but considered as mostly in line with it. This also applies to completed bioequivalence studies that are sold to new Applicants.
- If the validation of the bioanalytical method has already been conducted before 21 January 2023, and the bioequivalence study is conducted later e.g., in 2024, then methods validated according to the EMA guideline may be acceptable. This is because it is understood that deviations from guidelines may be acceptable, if scientifically justified. In such cases, the

submission should identify the differences between the bioanalytical method validation conducted and the requirements defined in the ICH M10 guideline (e.g., the investigation of the matrix effect with an alternative methodology) and justify why those differences do not affect the reliability of the data. However, the absence of validation requirements that are equivalent to those described in ICH M10 are not expected to be acceptable.