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European Medicines Agency

Overview of comments received on " Implementation strategy of ICH Guideline M10 on bioanalytical method validation"(EMA/449486/20233)

Interested parties (organisations or individuals) that commented on the draft document as released for consultation.

Stakeholder no.	Name of organisation or individual
1	AstraZeneca
2	Eli Lilly and Company
3	Maria Cruz Caturia, Ph. D. Founder & President, Anapharm Bioanalytics, Barcelona, Spain.

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1. General comments – overview

Stakeholder no.	General comment (if any)	Outcome (if applicable)
1	The guidance is welcomed and viewed as a useful and pragmatic position from EMA. However, the dates related to activities requiring re-validation appear to be aligned with the effective dates of the previous EMA Bioanalytical Method Validation (BMV) guideline. It should be noted that dates may differ when submitting in another region where the last regional BMV guideline prior to ICH M10 was for example in 2014 or 2015 (MHLW) or 2018 (FDA). Global alignment with other agencies may be required to prevent re-validation requirements from being a regional requirement for several years.	Not accepted. It is not the case that " *re-validation appear to be aligned with the effective dates of the previous EMA Bioanalytical Method Validation (BMV) guideline*". The Implementation Strategy states: "*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*". Therefore, reference is being made to the implementation date of ICH M10 (21 January 2023) and not to that of the EMA 2012 guideline. The point on global alignment is noted. It is the case, however, that re-validation requirements are implemented at regional level and therefore the present implementation strategy applies only within the EU.
2	We have determined that we do not have any comments or questions on the proposed guideline at this time	
3	First and foremost, I would like to express gratitude for the attention and interest shown in addressing the challenges posed by the implementation of M10. The new document, given the various interpretations we have encountered, helps ensure that all agencies are requesting the same standards.	Accepted Methods validated according to the EMA 2012 guideline may be acceptable even if employed in studies conducted after the date of coming into effect on 21 January

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	Nevertheless, there are pending issues that require resolution: 1. In a Contract Research Organization (CRO), Project A involves the development of a method for quantifying A, followed by its validation in accordance with the relevant legislation at that time. If the method remains unchanged and is consistently used over time for different clients, the validation supporting that method remains valid. What is the rationale for re-demonstrating the validity of the method for quantifying A if the methodology has not been altered? 2. The EMA Guideline for the Validation of Bioanalytical Methods 2012 has been universally utilized for over 10 years with great success. Hundreds of thousands of methods have been developed, validated according to the EMA 2012 guideline, and used to approve thousands of medications on the market. What is the purpose of repeating the entire validation process simply because a new guideline has been published with the real objective of harmonizing the EMA guideline with that of the FDA? It is evident that any method valid according to the EMA 2012 will also be valid following the M10. 3. Furthermore, the pharmaceutical industry, which places great emphasis on SUSTAINABILITY, should strive to prevent unnecessary repetitions of validations that have already been properly conducted. For several months, CROs have been repeating validations arbitrarily—whether due to client requests, marketing strategies,	2023, since it is understood that deviations from the 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 equivalent to those described in ICH M10 are not expected to be acceptable. The strategy has been updated accordingly.

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	or to enhance their services and avoid issues with regulatory bodies, among other reasons. It is crucial that economic resources, professional efforts, and the consumption of materials, reagents, human plasma, etc., are used rationally to contribute meaningfully to humanity's benefit. In conclusion, I believe that any Bioanalytical Method developed after the publication of the M10 guideline should be validated according to the new guideline. However, methods developed, validated, and utilized prior to that date should continue to be accepted. It's like a package—the method and its validation.	