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31 Dec 2020

Cathie Vielle
European Directorate on the Quality of Medicines
7 allée Kastner
67000 Strasbourg
France

Re: Proposed Chapter 5.26 *Implementation of Pharmacopoeial Procedures* (Ref: PA/PH/Exp. MG/T (18) 9 ANP)

Dear Ms. Vielle,

PDA appreciates the opportunity to provide input into Ph. Eur.'s Consultation on Chapter 5.26 *Implementation of Pharmacopeial Procedures*. We provide detailed responses to your specific consultation questions in the attached document.

PDA views the Chapter proposal as a commendable and timely effort to provide additional guidance for the successful implementation of compendial analytical procedures as they apply to stakeholders' product-specific quality control context.

We encourage EDQM and Ph.Eur. to discuss this topic within the harmonization efforts of the Pharmacopeial Discussion Group, as the approach that the Ph.Eur. is taking goes beyond the current recommendations of USP General Chapter <1226> *Verification of Compendial Procedures*. A discussion about potentially harmonized approaches to the verification of compendial methods is also timely because it links to and is impacted by current work on ICH Q14 Analytical Procedure Development and to efforts by the USP Validation and Verification Expert Panel on General Chapter <1220> on analytical lifecycle approaches. The direction these discussions are taking will ultimately shape how users think about the lifecycle management of a given compendial method in their own laboratory, including what that means for verification.

Past efforts to modernize approaches to fundamental techniques, including the transition from HPLC to uHPLC, highlight the need for a broad yet structured and disciplined scientific dialog. Increased international exchange in recent years has led to the inclusion of modern scientific concepts, as well as updated metrology principles, in the compendia. PDA is hopeful that the current proposal can generate further progress in this space.

PDA is a non-profit international professional association of more than 10,000 individual member scientists having an interest in the fields of pharmaceutical, biological, and device manufacturing and quality. Our comments have been prepared by PDA members with expertise in pharmaceutical, biopharmaceutical, and combination products manufacturing and compendial topics on behalf of PDA's Regulatory Affairs and Quality Advisory Board and Board of Directors.

If you have any questions, please do not hesitate to contact me via email at johnson@pda.org.

Sincerely,

Richard Johnson
President and CEO

cc: Glenn Wright, PDA; Ruth Miller, PDA

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General Comments

General Comments	Rationale
The concepts laid out in the Pharmacopeial Procedure Implementation Assessment are reasonable; however, the pharmacopoeial procedures do not list the acceptable performance criteria for analytical procedure performance characteristics (APPCs) such as accuracy and precision that the test procedure was validated to meet.	Without the performance criteria, the user cannot know if upon evaluation or experimentation that they can meet the validated state of the test procedure, and therefore could not determine suitability.

Specific Comments to the Text

Line No.	Current Text	Proposed Change	Rationale
Pg. 1, lines 11-14	Ultimately, the implementation process runs under the user's responsibility and its successful outcome needs to be demonstrated to the satisfaction of the competent authority.	None	This is the key language to the document. User will need to justify any approach taken to verify a compendial procedure.
Pg. 1, lines 32-33	The purpose of the verification is to demonstrate that the implementation is feasible, i.e. **that the procedure is suitable for examination of the article under test,** under the actual conditions of use.	The purpose of verification is to confirm appropriate execution of the procedure under specific laboratory's actual conditions of use for the articles under test.	Demonstration of the suitability of the procedures is done at validation. The verification may be simple confirmation of the test execution. If the nature of the testing is similar to methods already employed within a laboratory with staff trained to perform the testing, verification may not be needed.
Pg. 2, lines 39-40	Signifies that the characteristic should be experimentally verified.	Signifies that this characteristic should be considered as an element to be verified, if experimental verification is deemed necessary.	As written, the language suggests that experimental verification is necessary for all impurities limit tests, impurities quantitative tests, assays, and other quantitative tests (specificity, sensitivity, and repeatability).

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Line No.	Current Text	Proposed Change	Rationale
Pg. 2, line 47	Robustness may be assessed on a case-by-case basis.	A DOE robustness study can be used to determine accuracy and precision as well to verify suitability of the compendial method in the implementation assessment.	Compendial methods are typically considered robust. However, robustness may actually be a key APPC for the purpose of verification under routine conditions as this is the one place where suitability over routine operation will be captured. A simple, well-designed DOE could determine the critical accuracy and precision assessment as well over the allowed operating conditions defined in the test procedure.