



Leaflet: Verification of Pharmacopeia Methods

Information for our customers

The verification of compendial methods as a pre-requisite to their application for release testing is described in the different pharmacopoeias. However, the given instructions in these general texts leave room for interpretation on the scope of a method verification. In addition, method verification is currently a topic in audits and within the focus of the regulatory authorities.

As a service provider, we attempt to provide here suitable suggestions, how to handle the requirements on method verification. The recommendations are based on our experience and intend to help you comply with the Good Manufacturing Practises for testing and minimise potential regulatory issues in the future. Of course, they are non-binding and reflect only our personal opinion.

Common questions on verifications are:

Why is there a need for method verification?

The verification process for test procedures is the assessment of whether the procedure can be used in a laboratory for its intended purpose, under the actual conditions of use for a specified drug substance, excipient and/or drug product matrix. The requirement for verification is given in various regulations and/or regulatory documents, e.g., Ph. Eur. 9.4; Chapter 1, USP 41-NF 36 Chapter <1226>. It is not required to validate or re-validate these procedures when first used, but documented evidence of suitability should be established under actual conditions of use.

In addition, verification should assess whether the analytical procedure is suitable for the drug substance, excipient and/or the drug product matrix, taking into account the synthetic route, the method of manufacture etc. It should also assess the effect of the matrix on the recovery of analytes as well as the suitability of chromatography conditions such as columns, mobile phases, and signal detectors. Drug substances from different suppliers may have different impurity profiles that are not covered by the compendial test procedure. Especially in chromatography procedures, we experienced several cases with unexpected impurities that were only detected during thorough method verification.



What are the requirements for a verification?

Our internal SOP reflects these general requirements. Generally speaking, we categorise the pharmacopoeial methods in 3 groups:

- a) Basic compendial methods, e.g., loss on drying, sulphated ash, pH (with some exceptions), conductivity, melting point.
Under normal circumstances, those methods are not subject to verifications.
- b) Simple compendial methods for assay and purity tests, e.g., assay by simple titration and water content by Karl Fischer.
These methods are usually subject to a short verification, usually repeatability/precision with n=3.
- c) Complex methods for assay and purity or methods that include a difficult sample preparation: e.g., HPLC/U(H)PLC, GC, ICP-MS.
These methods are usually subject to an extensive verification.

The details/extent of the verification is quoted according to this general categorisation. Some testing methods are mentioned in the Pharmacopoeias to be verified (e.g. AAS, ICP-OES or Microbiology); these will also be offered.

Your requirements/SOP for verification differs from our perspective: What now?

In case that you have your own SOP that describes your requirements for verifications, we can perform the verification accordingly (for details see below). This will be documented in the analytical report providing the analytical results. The assessment of the verification's key parameters and scope is then within your responsibility.

Can testing be performed without prior verification?

Yes. However, if you decide to analyse your materials/products without method verifications, this will be indicated as a comment on the analytical report (for details see below).

Your substance is very common and has probably been tested by UFAG before – why do you still need a verification?

On the one hand, UFAG performs verifications for different customers. As this data is generated on a customer-, and product-specific manner, this information is dedicated to the customer and is confidential. It must not be disclosed to any third party.

On the other hand, the synthetic route, the method of manufacture and/or the supplier are different. As described above, these matrix effects might have a significant influence on the suitability of a procedure and/or the detection of impurities.

How will different verification requirements be commented on the testing report?

Depending on what you order for verification, the following comments will appear on your testing reports:



Explanation	Comment on Testing Report (GER)	Comment on Testing Report (EN)
Testing according to GMP, following the UFAG recommendations for verifications or validations.	Die analytischen Prüfungen wurden in Übereinstimmung mit den GMP-Anforderungen durchgeführt. Alle angewendeten Methoden entsprechen den gesetzlichen bzw. regulatorischen GMP-Vorgaben.	The analytical testing was performed in compliance with the GMP requirements. All applied methods meet the legal resp. regulatory GMP guidelines.
Testing according to GMP, following the client's specification and scope for verification or validation.	Die analytischen Prüfungen wurden in Übereinstimmung mit den GMP-Anforderungen durchgeführt. Alle angewendeten Methoden entsprechen den gesetzlichen bzw. regulatorischen GMP-Vorgaben. Die Methodvalidierung / Methodenverifizierung oder der Methodentransfer wurde gemäss Kundenvorgaben durchgeführt.	The analytical testing was performed in compliance with the GMP requirements. All applied methods meet the legal resp. regulatory GMP guidelines. Method validation / method verification or method transfer was performed according to client specifications.
Testing in the GMP accredited area (pharmaceutical testing division). Verification, method transfer or validation is not ordered or is missing essential GMP requirements.	Die analytischen Prüfungen wurden im GMP-zertifizierten Bereich durchgeführt. Die finale Beurteilung der Konformität des untersuchten Produktes mit den GMP-Regularien (z. B. hinsichtlich der Validierung, der Verifizierung, des Methodentransfers) liegt in der Verantwortung des Auftraggebers.	The analytical testing was performed in a GMP certified area. The final evaluation of the compliance with legal resp. regulatory GMP guidelines that are relevant for the tested product (e.g. regarding matters as validation, verification, method transfer) is incumbent on the client.

How long does it take to perform a verification?

The time period for carrying out a verification depends on many different factors. Amongst them are the scope of the verification, the availability of reference standards and special chemicals. Usually, we provide a detailed timeline in our quotations. We start the preparations as soon as the order is given, and we will send a verification plan to you for approval. After the signed plan is returned, we carry out the verification work and sum up the results in a verification report. After the verification report is approved by your side, routine testing can be started.

Do you have further questions?

Contact us! Our team will be happy to advise you.

Thank you in advance for your order and for putting your confidence in us.

Kind Regards