**Validation plan / protocol**

***(Re-)* Validation of the identity method xxx (Title)**

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| --- |
| **Document Approval** |
|  | **Name (Function / Department) \*** | **Signature** | **Date** |
| Compiled | Xxx (Lab xxx) |  |  |
| Reviewed | Xxx (Head of Lab xxx) |  |  |
| Approved | Xxx (Head of QC) |  |  |
| Approved | Xxx (Head of QA) |  |  |

*\* These are just examples, to be adjusted according to your procedures. There should be an author, a reviewer and a QA.*

|  |
| --- |
| **Document History \*** |
| **Version** | **Description of change** |
| 1.0 | New version |

*\* Might be placed here or e.g. at the end of the document. Can also be added by other columns such as author and date, if no digital document management system is used.*

|  |
| --- |
| **Further applicable documents and references \*** |
| **Document Number** | **Document Title** | **Version** |
| SOP-xxx | Validation of analytical methods *(your internal SOP describing how to perform method validations)* | 1.0 |
| SOP-xxx | Performance of method xxx *(if a SOP describing the method which should be validated already exists e.g. in case of revalidation or a draft version of the new method, this SOP should be listed here)* | 1.0 |
| SOP-xxx | Deviation management *(your internal SOP dealing with deviation management)* | 1.0 |
| xxx | Risk assessment for method xxx *(your internal risk assessment document, if performed and applicable, see chapter 6.2 )* | 1.0 |
| ICH Q2(R1) „Validation of Analytical Procedures: Text and Methodology”, 2005 |
| *Further documents can be added* |

*\* This is not a must, but might be useful especially if an already existing method can be referenced. Otherwise the method can also be referenced in another section or fully described.*

**Table of contents**

[1. Aim of this validation 3](#_Toc30161766)

[2. Principle / Description of the method 3](#_Toc30161767)

[3. Schedule, roles and responsibilities 4](#_Toc30161768)

[4. Samples to be applied in this validation 4](#_Toc30161769)

[5. Abbreviations 4](#_Toc30161770)

[6. Execution of the validation and parameters to be evaluated 5](#_Toc30161771)

[6.1 Specificity 5](#_Toc30161772)

[6.2 Robustness 5](#_Toc30161773)

[6.3 System suitability 6](#_Toc30161774)

[7. Attachments 6](#_Toc30161775)

# Aim of this validation

This validation plan / protocol describes the procedure and the aspects to be evaluated during the validation the method xxx.

The method is intended to be used as identity test in xxx samples (according to SOP-xxx\*).

*\* if already applicable*

According to SOP-xxx *(your internal validation SOP)* /(and) the ICH guideline Q2(R1) for an identity test specificity and robustness \* will be evaluated. Details about the corresponding acceptance criteria to be met is provided in Table 1.

*\* if not yet already investigated during method development*

Table 1: Parameter overview and acceptance criteria

|  |  |  |
| --- | --- | --- |
| Parameter | Acceptance criteria # | Details in section ^ |
| *# these are just examples, to be adjusted to your method**^ The corresponding section describing the details should be referenced here.* |
| Specificity | No other peaks visible during RT x - y min / xxx | 6.1  |
| Robustness ° | Resultsmodified condition: meet batch release specification | 6.2  |
| *° Sample stability (if applicable) might be investigated during robustness or listed as separate point.* |

The performance of the method is outlined in SOP-xxx and will not be detailed in this plan / protocol, if not indicated differently in this plan / is described in the following chapter 2. [All equipment used is maintained and calibrated (see attachment 1). The staff involved in this validation is trained in the method and will be referenced in the report (see attachment 2)] \*

*\* optional*

[All attachments provided in this validation plan / protocol will be filled out during execution of the validation experiments and will be part of the report.] \* The results of these validation experiments will be summarized in a validation report; this includes the evaluation against the acceptance criteria defined in this plan / protocol. In case any deviations from the plan / protocol described here will occur, they will also be described in the report and/ corresponding actions will be initiated according to SOP-xxx *(your internal SOP dealing with deviation management)*.

*\* optional*

# Principle / Description of the method

*e.g.* To proof the identity of xxx, peptide mapping is applied. Therefore, the sample is tryptically digested into specific peptides which are then separated by RP-HPLC, resulting in a sample-specific peak profile. This profile is compared with the known profile of the reference standard.

*A short overview of the method’s principle is enough in case a method describing SOP is already in place. In case no method describing SOP exists yet (and cited in chapter 1), this chapter can be used to provide a detailed description on how to perform the method.*

# Schedule, roles and responsibilities \*

*\* optional, mostly applied in case a contract manufacturing or research organization (CMO / CRO) is performing the method validation or during method transfers in case of co-validation is used*

The activities to be performed for this validation, the timeline and the corresponding responsibilities are outlined in Table 2:

Table 2: Tasks, timeline and responsibilities

|  |  |  |
| --- | --- | --- |
| **Task** | **Due date** | **Responsibility** |
| Performance of all validation experiments \* | xx.xx.2020 | Lab x |
| Compilation of the validation report including presentation and evaluation of all results, as well as justification of potential deviations | xx.xx.2020 | Lab x |
| Review of the validation report and corresponding raw data | xx.xx.2020 | Client x |
| Approval of the validation report | xx.xx.2020 | Client x and Lab x |
| *\* in case of a co-validation during a method transfer it can be detailed here which lab is performing the evaluation of which validation parameter* |

In case changes to the specified procedure of the validation plan / protocol are necessary to be made during the experimental phase a written consent of client x is required and an amendment to the validation plan / protocol must be provided by lab x before further validation experiments will be executed.

# Samples to be applied in this validation

Table 3 shows which test substances are planned to be used as samples in this validation:

Table 3: Overview about the test substances to be used for validation

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Name and description** | **Lot** | **(Protein) / xxx content** | **Buffer** | **Storage conditions** |
| Y25a (Reference standard) | L3412 | 12 mg / mL | x M Phosphate buffer | 2-8°C |
| X23 (Intermediate product of step xxx) | Xxx(manufactured the xx.xx.2020) | 20 mg / mL | xxx | 2-8°C |
| H48(Drug product) | Xxx(manufactured the xx.xx.2020) | 12 mg / mL | x M Phosphate buffer | 2-8°C |
| Placebo solution (Formulation buffer) | - | - | x M Phosphate buffer | 2-8°C |

# Abbreviations

All abbreviations used in this validation plan / protocol are explained in Table 4.

Table 4: Abbreviations *(some examples, to be adjusted individually, in alphabetical order)*

|  |  |
| --- | --- |
| **Abbreviation** | **Definition** |
| AC | Acceptance criterion |
| RT | Retention time |
| … |  |

*\* CV and RSD express the same. Choose the wording you prefer.*

# Execution of the validation and parameters to be evaluated

As outlined in chapter 1 specificity and robustness will be assessed.

## Specificity

Specificity is defined as the ability to assess unequivocally the analyte in the presence of components which may be expected to be present. Typically, this might include the drug itself, impurities, degradants, buffer components etc.

For the demonstration of specificity, the sample, a solution of substance xxx (closely related to the sample), a placebo solution and the reference standard are analyzed individually according to the method and the electropherograms / chromatograms / western blots will be compared.

Acceptance criteria:

* The electropherograms / chromatograms / western blots of the placebo solution and the substance xxx solution don’t show any interfering peaks / bands in the corresponding pI / RT / molecular weight range.
* The electropherogram / chromatogram of the sample is identical to the reference standard with a pI of x ± y / a RT of the main peak of x ± y min. / The molecular weight of the sample has to be between x and y kDa and the band must be visible at the same height as the one of the reference standard.

## Robustness (to be evaluated in case not yet performed during method development)

The robustness is defined as a measure of a method’s capacity to remain unaffected by small, but deliberate variations in method parameters and provides an indication of its reliability during normal usage.

[According to a previously performed risk assessment (document no. xxx – *please cite your internal risk assessment document or the number thereof here*) / according to the following risk evaluation (*please add e.g. a small table (with e.g. risk factor, potential consequences, evaluation, activity for method validation if applicable) showing the risk evaluation of your method*), critical performance parameters of the method will be investigated during the robustness studies detailed hereafter.] \*

*\* optional*

*HPLC method as an example:*

For the assessment of robustness, the following method parameters will be modified:

* pH of mobile phase x: *e.g.* 5.8 and 6.2 *(e.g. original: 6.0)*
* Composition of mobile phase x: *e.g.* 0.25 M and 0.75 M *(e.g. original: 0.5 M)*
* Column temperature: *e.g.* 25 and 35°C *(e.g. original: 30°C)*
* Flow rate: *e.g.* 0.8 and 1.2 mL/min *(e.g. original: 1.0 mL/min)*
* Detection wavelength: ± 2 nm
* Sample stability: Analysis of the sample after x *(e.g. 48)* h of storage in the autosampler / 3 days at room temperature / 3 days at -20°C /… \*

*\* Sample stability might be part of the robustness study as shown here, but might also be listed as a separate point*

* Different column lots / suppliers
* …

All evaluations will be performed three times using reference standard and/or sample xxx at 100% target concentration. The results obtained when applying the modified conditions will be compared to three runs performed under original method conditions (at time 0).

Acceptance criteria:

* The RT of the reference standard and/or sample under modified condition must meet the actual batch release specification i.e. show a RT of not more than x ± y\* min *\*This value (y) is typically 2 or 3SD of the reference standard.*

In case an acceptance criterion will not be met by one (or more) modified conditions, a remark to pay special attention to that point will be incorporated into the method’s description.

## System suitability

The tentative system suitability parameters defined in the method (see chapter 2 *in case no SOP exists yet and the whole method is described in that chapter*) will verified after method validation. Therefore, all analyses performed with reference standard during this validation will be evaluated accordingly and final acceptance criteria will be set.

# Attachments

**Attachment 1: Overview of equipment used in this validation**

|  |  |  |
| --- | --- | --- |
| **Equipment Name** | **Serial # or internal equipment #** | **Date of last calibration** |
|  |  |  |
|  |  |  |
|  |  |  |
|  |  |  |

**Attachment 2: Overview of personnel involved in this validation**

|  |  |  |  |
| --- | --- | --- | --- |
| **Name of the operator** | **Involved in validation experiment(s)** | **Date of last training** | **Training reference document #** |
|  |  |  |  |
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|  |  |  |  |