Successful Analyst Assay Training and Assay Transfers- Basics and recommendations to achieve these goals

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Overview

1. Method Transfer: Definition and Guidelines
2. Different strategies for method transfer
3. Recommendations for method transfer
4. Analyst training
5. Summary

Introduction: Definition Method Transfer

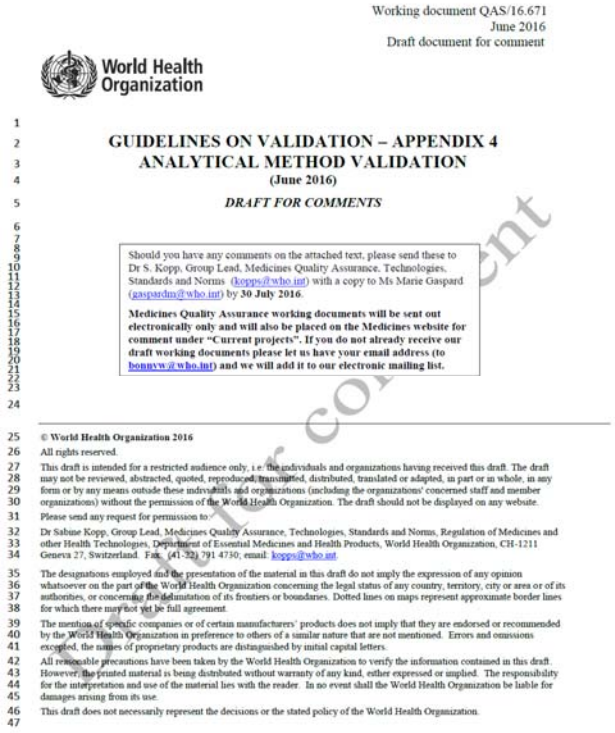
Definition USP <1224> TRANSFER OF ANALYTICAL PROCEDURES

The transfer of analytical procedures (TAP), also referred to as method transfer, is the documented process that qualifies a laboratory (the receiving unit) to use an analytical test procedure that originated in another laboratory (the transferring unit), thus ensuring that the receiving unit has the procedural knowledge and ability to perform the transferred analytical procedure as intended.

Introduction: Guidelines method transfer

Guidelines:

- **USP <1224>**
- **WHO draft guideline ‘GUIDELINES ON VALIDATION – APPENDIX 4 – ANALYTICAL METHOD VALIDATION**



Working document QAS/16.671
June 2016
Draft document for comment

World Health Organization

GUIDELINES ON VALIDATION – APPENDIX 4
ANALYTICAL METHOD VALIDATION
(June 2016)

DRAFT FOR COMMENTS

Should you have any comments on the attached text, please send these to Dr S. Kopp, Group Lead, Medicines Quality Assurance, Technologies, Standards and Norms (koppsi@who.int) with a copy to Ms Marie Gaspard (gasparcim@who.int) by **30 July 2016**.

Medicines Quality Assurance working documents will be sent out electronically only and will also be placed on the Medicines website for comment under "Current projects". If you do not already receive our draft working documents please let us have your email address (to bonnyw@who.int) and we will add it to our electronic mailing list.

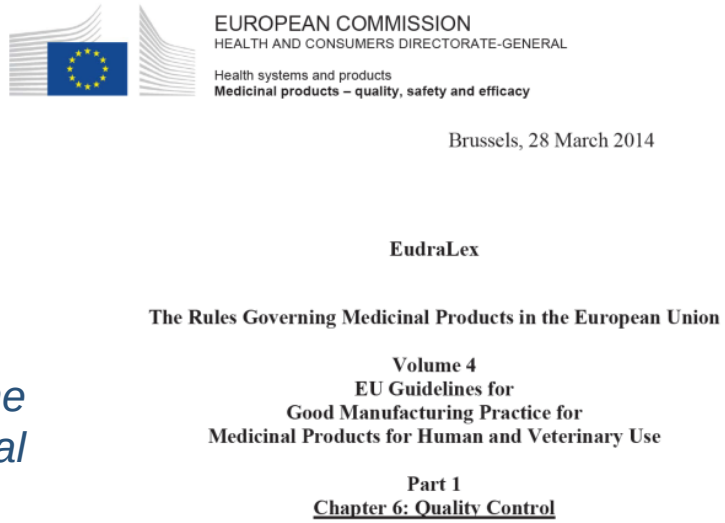
⟨1224⟩ TRANSFER OF ANALYTICAL PROCEDURES

INTRODUCTION

Introduction: Guidelines method transfer

Guidelines:

- **EU GMP Guide Volume 4 Chapter 6 Quality Control**



EUROPEAN COMMISSION
HEALTH AND CONSUMERS DIRECTORATE-GENERAL

Health systems and products
Medicinal products – quality, safety and efficacy

Brussels, 28 March 2014

EudraLex

The Rules Governing Medicinal Products in the European Union

Volume 4
EU Guidelines for
Good Manufacturing Practice for
Medicinal Products for Human and Veterinary Use

Part 1
Chapter 6: Quality Control

*Prior to transferring a test method, the **transferring site** should verify that the test method(s) comply with those as described in the Marketing Authorisation or the relevant technical dossier.*

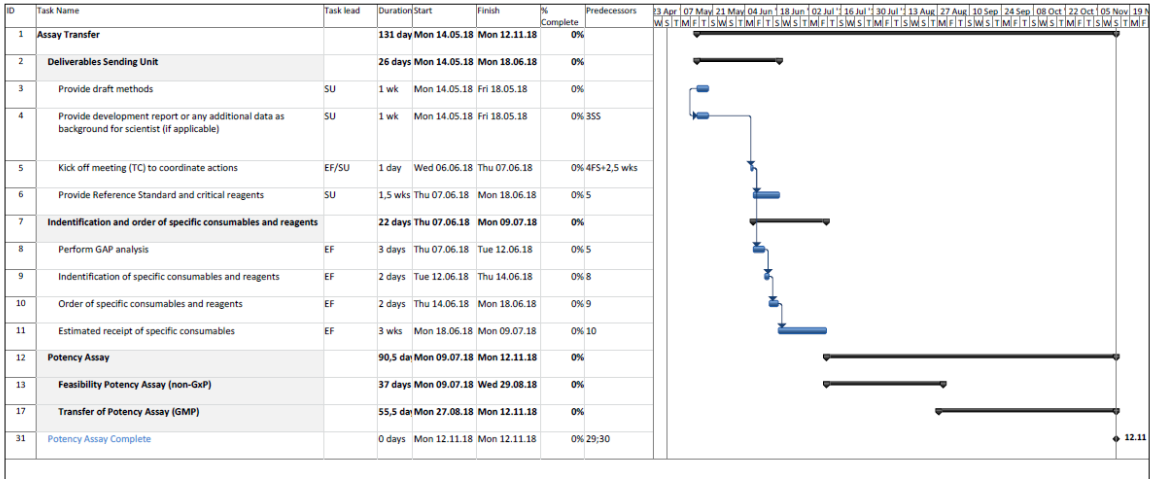
*The **original validation** of the test method(s) should be reviewed to ensure compliance with current ICH/VICH requirements.*

*A **gap analysis** should be performed and documented to identify any supplementary validation that should be performed, prior to commencing the technical transfer process.*

Activities during method transfer

1. Kick off meeting
2. Gap analysis
3. Purchase of reagents
4. *Training**
5. Feasibility
6. *Analyst Qualification**
7. Method Transfer activity (GMP)

* optional steps



ID	Task Name	Task lead	Duration	Start	Finish	% Complete	Predecessors
1	**Assay Transfer**		**131 day**	**Mon 14.05.18**	**Mon 12.11.18**	**0%**	
2	**Deliverables Sending Unit**		**26 days**	**Mon 14.05.18**	**Mon 18.06.18**	**0%**	
3	Provide draft methods	SU	1 wk	Mon 14.05.18	Fri 18.05.18	0%	
4	Provide development report or any additional data as background for scientist (if applicable)	SU	1 wk	Mon 14.05.18	Fri 18.05.18	0%	3SS
5	Kick off meeting (TC) to coordinate actions	EF/SU	1 day	Wed 06.06.18	Thu 07.06.18	0%	4FS+2,5 wks
6	Provide Reference Standard and critical reagents	SU	1,5 wks	Thu 07.06.18	Mon 18.06.18	0%	5
7	**Indentification and order of specific consumables and reagents**		**22 days**	**Thu 07.06.18**	**Mon 09.07.18**	**0%**	
8	Perform GAP analysis	EF	3 days	Thu 07.06.18	Tue 12.06.18	0%	5
9	Indentification of specific consumables and reagents	EF	2 days	Tue 12.06.18	Thu 14.06.18	0%	8
10	Order of specific consumables and reagents	EF	2 days	Thu 14.06.18	Mon 18.06.18	0%	9
11	Estimated receipt of specific consumables	EF	3 wks	Mon 18.06.18	Mon 09.07.18	0%	10
12	**Potency Assay**		**90,5 da**	**Mon 09.07.18**	**Mon 12.11.18**	**0%**	
13	**Feasibility Potency Assay (non-GxP)**		**37 days**	**Mon 09.07.18**	**Wed 29.08.18**	**0%**	
17	**Transfer of Potency Assay (GMP)**		**55,5 da**	**Mon 27.08.18**	**Mon 12.11.18**	**0%**	
31	Potency Assay Complete		0 days	Mon 12.11.18	Mon 12.11.18	0%	29;30

Different method transfer strategies

a. Method training by phone

b. Sending Unit SME trains Receiving Unit analysts at Sending Unit site

c. Sending Unit SME trains Receiving Unit analysts at Receiving Unit site

d. Assay co-validation performed by both Sending Unit and Receiving Unit

Different strategies – pros and cons

	Strategy	Pro	Con
A	Method training by phone	Possibility to save time in case RU is an experienced lab which can the assay set up without F2F training Prerequisite is that SU mentions EVERYTHING (important and not considered important) during the call	Saved time maybe equalized afterwards in case feasibility reveals that RU is not able to perform method in a similar way as the SU

SU: Sending Unit

RU: Receiving Unit

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B	Sending Unit SME trains Receiving Unit analysts at Sending Unit site	SU: No travel time, less stressful due to familiar environment RU: Procedure can be followed and learned in original environment which facilitates feasibility at RU	No guarantee that assay will work at RU site even when RU analysts perform assay successfully at SU site

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C	Sending Unit SME trains Receiving Unit analysts at Receiving Unit site	Depending on outcome of SU SME performing the assay at the RU lab either it is clear that assay works in new environment or troubleshooting can be done right away on site	SU: Travel time, can be stressful for SME as the assay has to be performed in unfamiliar environment with unknown equipment

SU: Sending Unit

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D	Assay co-validation performed by both Sending Unit and Receiving Unit	Saves time and efforts as only one 'validation/transfer' activity is to be carried out	Statistics may be more complicated Only applicable if both transferring and receiving unit can perform co-validation at about the same time & at the same pace

Different strategies- preferred ones from a CRO's point of view

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Recommendations for Sending Unit

- Make a journey through time back and beam you to the start of assay establishment
  - Put yourself in place of the Receiving Unit: What you would need to know about this specific method
  - Provide history of method (we did this and this because of …and this and that did not work)- this helps the scientist at the RU to understand better and helps in potential troubleshooting
- Consider clarifying all not clearly defined parts in the method SOP (e.g. way of pipetting (blow out /no blow out, tip changes, etc)- try to identify local lab understanding and ‘translate‘ it for the RU
- Providing a ‘starter package‘ (consisting of reagents which ave to be procured) to the RU may accelerate the project

Recommendations for Receiving Unit

- Ask ask ask – do not take things for granted as your interpretation of the method SOP may be wrong
- Take supply chain into consideration when ordering reagents and plasic ware (local vs overseas)
- Discuss any modification with the Sending Unit SME prior to implementation
- Plan ahead and keep the Sending Unit up to date all the time
- Use a project manager to support the transfer team in terms of communication and keeping track of project status

‘Transfer‘ of methods from R&D to an external QC lab

Recommendations:

- **Make a journey through time…..**
- **Define critical reagents**
- **Provide draft method document**
- **Provide pictures or videos if helpful for better understanding**
- **Method performance of second analyst prior to ‘transfer‘ (robustness check)**

Analyst training at Eurofins Munich

Each new analyst has to perform the following training modules:

- **General module**
- **Pipetting module**
- **Cell culture module**
- **Assay/method training module**

Analyst Training

General module

- Lab procedures
- Good Documentation Practices
- cGMP

Pipetting module

- Training with different multi channel pipettes: Practice serial dilutions in a mock scenario using cell culture medium including FBS
- Perform ‘pipette calibration‘ with already calibrated pipettes for practice purposes using gravimetric ISO pipette calibration method -> check accuracy and precison of pipetting

Analyst Training

Cell culture module

- General training how to perform cell culture (watch- under supervison-solo runs)
- Cultivation of two training cell lines (1 suspension+ 1 adherent cell line) for a period of ~ 2 weeks
- Training für assay specifc cell culture according to method SOP

Analyst Training

Assay/method training module:

- **First cell based assay: Performance of an Eurofins Munich internal potency assay prior to initiation of training of any client assay**
- **3 tiered model: Watch- under supervision- solo runs (several runs until analyst and supervisor feel comfortable); discussion of results after each run**
- **Analyst qualification under protocol followed by report**
- **Release for testing according to GMP by publishing new version of overview document (e.g. responsibility matrix)**

Summary

- Choose assay transfer scenario which fits best to the current situation (and given timeline)
- Sending Unit: Put yourself in the position of the ‘other‘ side and provide all relevant information
- Receiving Unit: Do not take things for granted as your interpretation of the method SOP may be wrong- ask!
- Direct and open-minded communication is a key factor for success of assay transfers
- Thorough training of analysts is the basis for robust assay performance

Acknowledgements

Thank you to all members of Eurofins Munich Bioassay team !