Österreichische Agentur für Gesundheit und Ernährungssicherheit

www.ages.at

Challenges on the way to implementing new standards

Source: https://gd.epp.int

Helga Reisenzein, AGES, Austria

`You can't cross the sea merely by standing and staring at the water´

R. Tagore

ISO 17025:2017 `General requirements for the competence of testing and calibration laboratories`

The standard for which plant health labs must hold accreditation in order to perform official diagnostic activities

ISO 17025:2005 vs ISO 17025:2017

Comparision of the content/matrix

ISO/IEC 17025:2005		ISO/IEC 17025:2017	
1 Scope		1 Scope	
2 Normative references		2 Normative references	
3 Terms and definitions		3 Terms and definitions	
4 Management requirements	4.1 Organization	4.1 Impartiality	4 General requirements
		4.2 Confidentiality	
		5 Structural requirements	
5 Technical requirements	5.1 General	6.1 General	6 Resource requirements
	5.2 Personnel	6.2 Personnel	
	5.3 Accommodation and environmental condition	6.3 Facilities and environmental conditions	
	5.5 Equipment	6.4 Equipment	
	5.6 Measurement traceability	6.5 Metrological traceability	
4 Management requirements	4.5 Subcontracting of tests and calibrations	6.6 Externally provided products and services	
	4.6 Purchasing services and supplies		

https://pecb.com/whitepaper/isoiec-170252017---general-requirements-for-the-competence-of-testing-and-calibration-laboratories

ISO 17025:2005 vs ISO 17025:2017

Comparision of the content/matrix

ISO/IEC 17025:2005		ISO/IEC 17025:2017	
5 Technical requirements	5.4 Test and calibration methods and method validation	7.2 Selection, verification and validation of methods	
	5.7 Sampling	7.3 Sampling	
	5.8 Handling of test and calibration items	7.4 Handling of test or calibration items	
4 Management requirements	4.13.2 Technical records	7.5 Technical records	
5 Technical requirements	5.4.6 Estimation of uncertainty of measurement.	7.6 Evaluation of measurement uncertainty	7 Process requirements
	5.9 Assuring the quality of test and calibration results	7.7 Ensuring the validity of results	
	5.10 Reporting the results	7.8 Reporting of results	
4 Management requirements	4.8 Complaints	7.9 Complaints	
	4.9 Control of nonconforming testing and/or calibration work	7.10 Nonconforming work	
5 Technical requirements	5.4.7 Control of data	7.11 Control of data and information management	
	4.13 Control of records (4.13.1 General)		

https://pecb.com/whitepaper/isoiec-170252017---general-requirements-for-the-competence-of-testing-and-calibration-laboratories

Examples for implementation

Source: reporting-dms-metrics

Risk assessment for instruments, control charts, managing of corrective actions

Example: Risk assessment for instruments

Requirments of the new ISO 17025

- The laboratory shall establish and maintain metrological traceability of its measurement results by means of a documented unbroken chain of calibrations…
- The laboratory shall ensure that measurement results are traceable to the International System of Units (SI) through:
  1. a) calibration provided by a competent laboratory (fulling the requirements of ISO 17034)
  2. b) ……
- The laboratory shall ensure that only **suitable externally provided products and services** that affect laboratory activities are used…
  - Service can include **calibration service**, sampling service, testing service, facility and equipment service….

Example: Risk assessment for instruments

Risk assessment for pipettes based on the purpose of use

External calibration interval

*

1 Risk assessment

Provider	serial number	Nb. of pipette carousel	Room	Measurement range (µl)	Purpose of use	Standard calibration interval (years)	ISO 17025 calibration (every 5 years)
Eppendorf	2007756	1	D/1.72	20-200	Master mix	1	necessary
Eppendorf	250564Z	1	D/1.72	1-10	Master mix	1	necessary
Eppendorf	4607339	1	D/1.72	10-1000	Master mix	1	necessary
Eppendorf	3837353	1	D/1.72	2-20	Master mix	1	necessary
Eppendorf	1286579	2	D/1.72	20-200	Master mix	1	necessary
Eppendorf	2478819	2	D/1.72	10-100	Master mix	1	necessary
Eppendorf	4367619	3	D/1.80	2-20	Bacteriology	2	Not necessary
Eppendorf	309391	5	D/1.75	1-10	Extraction	2	Not necessary

*Explanation for this example: There is no technical difference between standard and ISO 17025 calibration. The column with ISO calibration only means that a calibration cerificate for a standard calibration has to be issued every 5 years.

Example: Risk assessment for instruments

Risk assessment for balances based on

a) the probability and extent of error

b) the contribution of the balance to the measurement uncertainty of the entire test

FORM

Balances: Tolerance and inspection interval

Valid for: LMS, LWT, PQO, STS, VET

Organization unit: ..... **Instrument labeling:** .....

Tolerance allowed : ≤ ± .....

Tolerance has to be defined for each balance:

Probability of error [1]		Extent of error[2]		Classification
rare	and	low	→	A
rare	and	noticeable	→	A
frequently	and	low	→	A
rare	and	significant	→	B
frequently	and	noticeable	→	B
frequently	and	significant	→	C

1 Rare = errors occur less than 1 once a year.
frequently = errors occur more than 1 once a year
Comment: Probability of occurrence of an error is depending on the frequency of use

2 Low = the error is immediately recognized internally; the correction causes hardly any additional effort.
Noticeable = the error is detected too late, but does not lead to a complaint
Significant = the error (wrong analysis result) is passed on to the customer

Contribution of the balance to the measurement uncertainty of the entire test procedure		Classification
significant (> 20 % measurement uncertainty)	→	D

Leading to a 4 level classification system for calibration actions

Example: Risk assessment for instruments

Risk assessment for balances

Calibration actions shall be carried out according to the classification

Actions:

Classification	Actions	Documentations
☐ **A**	daily adjustment and annual inspection	e.g. F 5044
☐ **B**	at least monthly documented control at a measuring point	e.g. F 5043
☐ **C**	at least weekly documented control at two measuring points	e.g. F 5043
☐ **D**	annual calibration (see SOP 6602) and at least weekly documented control at two measuring points	calibration certificate e.g. F 5043

Comments:

_____

Date **Name and signature of the lab manager**

Example: Ensuring the validity of results

Requirments of the new ISO 17025

- Use of reference material or quality control materials
- Use of alternative instrumentation that has been calibrated to provide traceability results
- Functional checks of measuring and testing equipment
- Use of check or working standards with **control charts**
- Replicate tests or calibrations using the same or different methods
- Retesting or recalibration of retained items
- Correlation of results for different characteristics of an item
- Review of reported results
- Intralaboratory comparisons
- Testing of blind samples
- Participation in proficiency testing and interlaboratory comparison other than proficiency testing

Example: Ensuring the validity of results

Requirments of the new ISO 17025

- Use of check or working standards with control charts

Control charts according SHEWHART

QM reference:	SOP_7986_02 – Detection of Erwinia amylovora using Realtime PCR
Organism:	Erwinia amylovora
Reference material:	295/93
Storage place:	box 1
Expiry date:	not defined
Charge:	10/18

	Date	Reference	Ct- value	Cycler
1	16.08.2018	295/93	17,16	Eppendorf
2	20.08.2018	295/93	14,7	Eppendorf
3	23.08.2018	295/93	15,32	Eppendorf
4	27.08.2018	295/93	15,82	Eppendorf
5	29.08.2018	295/93	16,35	MIC
6	31.08.2018	295/93	15,49	Eppendorf
7	03.09.2018	295/93	18,87	Eppendorf
8	06.09.2018	295/93	18,69	MIC
9	10.09.2018	295/93	21,14	MIC
10	18.09.2018	295/93	14,79	Eppendorf
11	24.09.2018	295/93	19,24	MIC
12	01.10.2018	295/93	18,23	MIC
13	03.10.2018	295/93	18,66	MIC
14	05.10.2018	295/93	19,15	MIC
15	12.10.2018	295/93	18,22	MIC
16	15.10.2018	295/93	17,23	MIC
17	29.10.2018	295/93	16,84	Eppendorf

Result	
Mean ct- value:	17.41
Standard deviation:	1.77

Defined value for the use: 17.4 +/- 2

Formular PCR-Nb.: RT_Ea_Tough_63/18

Real-Time PCR Protocol

Organism: Erwinia amylovora

Date:	28.10.2018
Technician:	Hess

SOP:	Identification of phytopathogenic organisms using Realtime PCR
Literature:	Gottsberger, 2007

Reaction mix: Nb. of samples +1: 10

Reference material (Charge): 10/18
Expected ct= 17.4 (+/-2)

Reagenzien	Conz.	µL per reaction	µL for master mix
PCR graduated water		2,5	25
Quanta Tough Mix		5	50
Primer 1	10µM	0,5	5
Primer 2	10µM	0,5	5
Sonde	1µM	0,5	5
Vol Mastermix		9	
Template		1	

Used Cycler:

x	Mastercycler EP
	MBDP-QTC-MIC-02

Type of PCR:

x	Colony PCR
	PCR with extracted DNA
	PCR with plant tissue

Temperature profil:

	Schritt 1		Schritt 2		Schritt 3	
	°C	[min]	°C	[min]	°C	[min]
	95	10:00	95	00:15	60	01:00
Zyklen			45x			

Example: Corrective actions

Requirments of the new ISO 17025

- Take action to control and correct it
- Address the consequences
- Review and analyse the nonconformity
- Determine the cause of the nonconformity (incl. if similar nonconformities exist)
- Implement any action needed
- Review the effectiveness of any corrective action taken

Example: Corrective actions

AGES system for managing corrective actions

- Take action to control and correct it

Implementation of the nonconformity in our corrective action mangegement system

Maßnahmenmanagement

AGES

Status: Meldung abgeschlossen | Fehler | ROER-B5TJAV

ErfasserIn	Renate Oeschlmueller/AGES	*Tel. Nr.*	+43(0)5 0555 32700
Name (EinmelderIn)	Gudrun Lapan	*Tel. Nr.*	+43(0)5 0555 38212
Betreff	LWT 09/2018 - NK01		
Beschreibung	Bei den extern kalibrierten Pipetten wurde eine nicht akkreditierte Kalibrierung durchgeführt --> Pipetten müssen nach einem Intervall im eigenen Ermessen (Risikoanalyse durchführen) mit akkreditierter Kompetenz kalibriert werden und mit einem entsprechenden Prüfbericht dokumentiert werden		

Example: Corrective actions

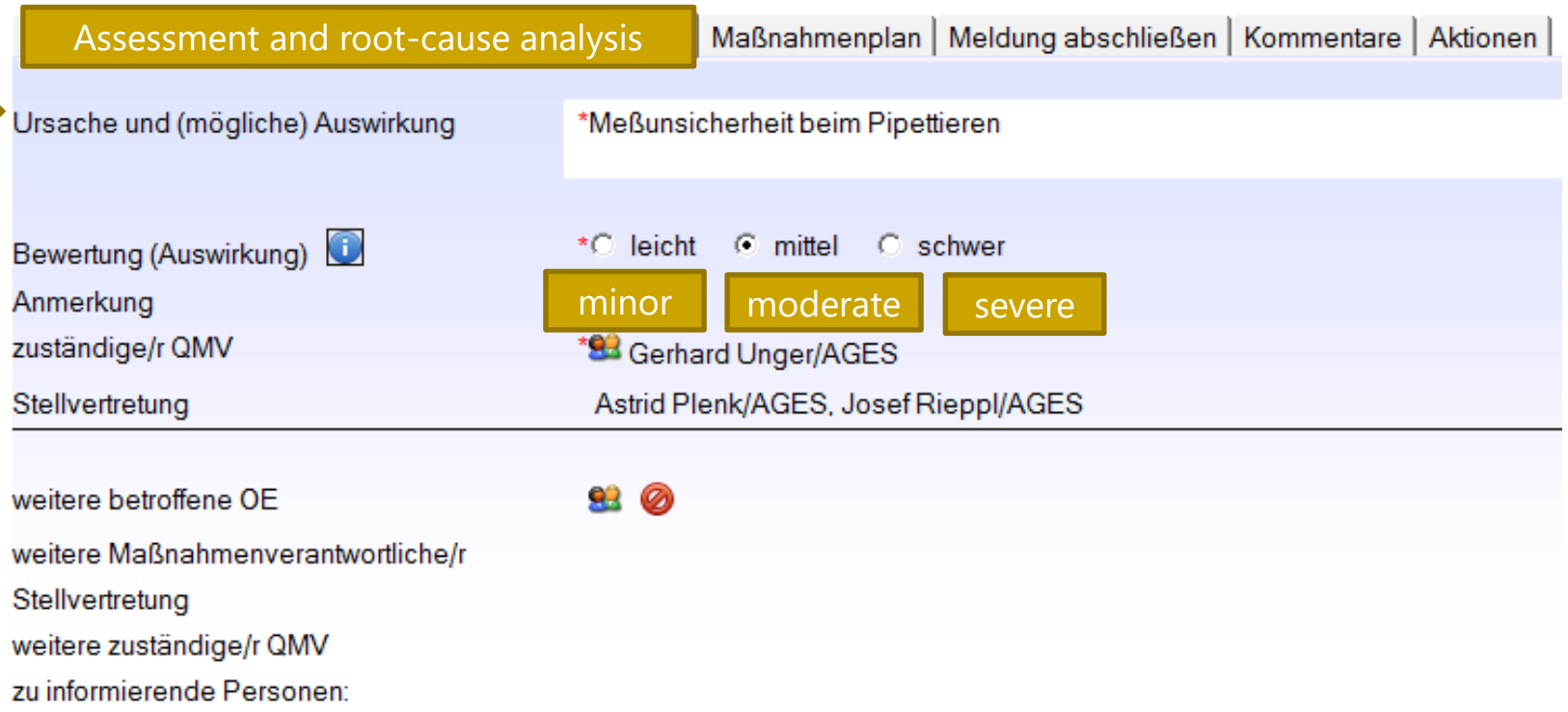
AGES system for managing corrective actions

- Address the consequences
- Determine the cause of the nonconformity (incl. If similar nonconformities exist)

root-cause analysis & possible consequences

quantitative assessment of consequences

Other organisation unit involved or persons to inform?

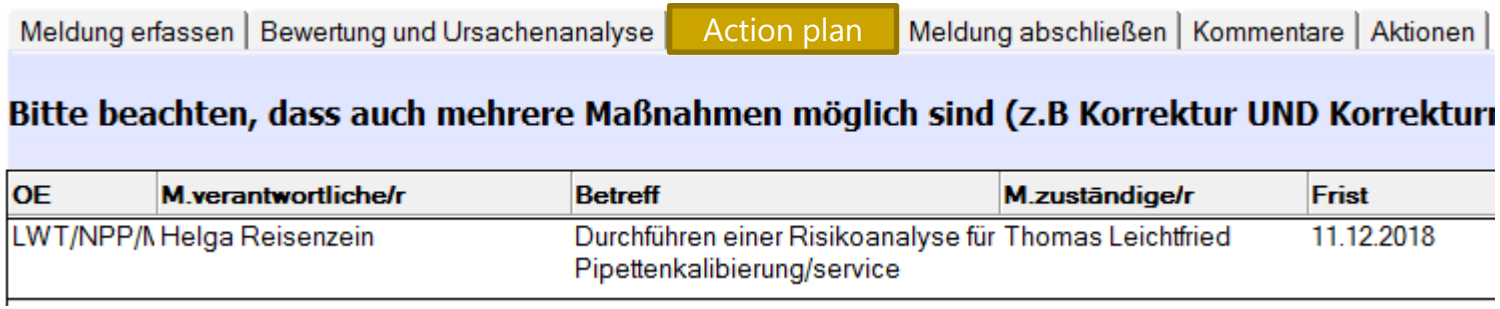


Example: Corrective actions

AGES system for managing corrective actions

- Implement any action needed

What, who, deadline



Example: Corrective actions

AGES system for managing corrective actions

- Implement any action needed
- Review the effectiveness of any corrective action taken

Create the task

Maßnahmentitel	*Durchführen einer Risikoanalyse für Pipettenkalibierung/service
Maßnahme / Beschreibung	Risikoanalyse für gekennzeichneten Pipetten wird durchgeführt und in Liste eingetragen. Eine Liste mit allen gekennzeichneten Pipetten wird erstellt, das Servicedatum eingetragen um einen Überblick über die Intervallzyklen für die Kalibierung zu habenRisikoanalyse für gekennzeichneten Pipetten wird durchgeführt und in Liste eingetragen. Eine Liste mit allen gekennzeichneten Pipetten wird erstellt, das Servicedatum eingetragen um einen Überblick über die Intervallzyklen für die Kalibierung zu haben
Termin (bis wann)	*11.12.2018
Maßnahmenzuständige/r:	Thomas Leichtfried

Implement the action

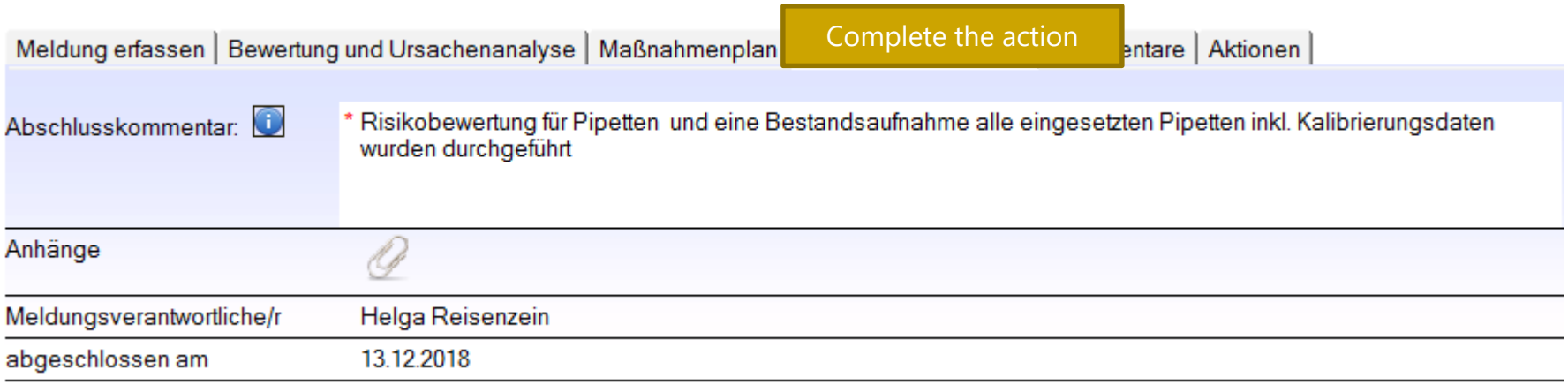
umgesetzt am:	*23.10.2018
Anmerkungen	*Risikoplan erstellt
Anhänge	VM03_Risikobewertung der Pipetten_MBDP.docx

Review the effectiveness of the action

durchgeführt am:	*23.10.2018
Ergebnis:	* wirksam / nicht wirksam
Anmerkungen	
Anhänge	

Example: Corrective actions

AGES system for managing corrective actions



- Database is part with of our email system
- All involved persons are informed about the relevant steps of the process by email

PM 7/98 (2) Specific requirement for laboratories preparing accreditation for a plant pest diagnositc activity

...it´s all about verification and validation...

There is a DIFFERENCE….

To verfiy or validate a test ≠ **quality assured procedure for verification/validation studies**

Validation for a scientific publication	Quality assured procedure
Development of a new test to identify an organism	Development of a new test to identify an organism or identify a organism-test-combination for validation/verification
	Define performance criteria for the purpose/scope
	Make a validation plan
	Authorise the validation plan
Test the analytical sensitivity and specifity	Test the analytical sensitivity and specifity
	Calculate diagnostic sensitivity and specifity
	Test repeatability and reproducability
Publication in a scientific journal	Summarize the results in a validation report
	Statement of the Lab manager on achievment of the scope

There is a DIFFERENCE….

PM 7/98 (2) Specific requirement for laboratories preparing accreditation

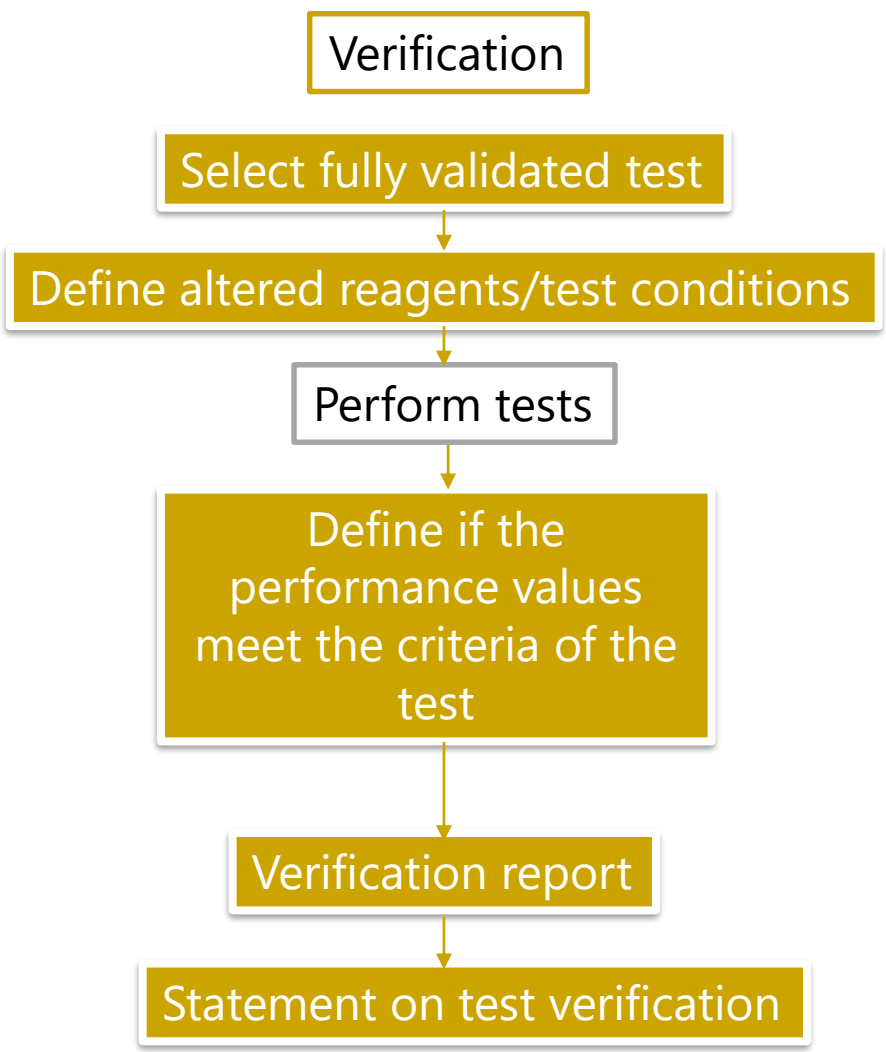
- **Guideline** to establish a

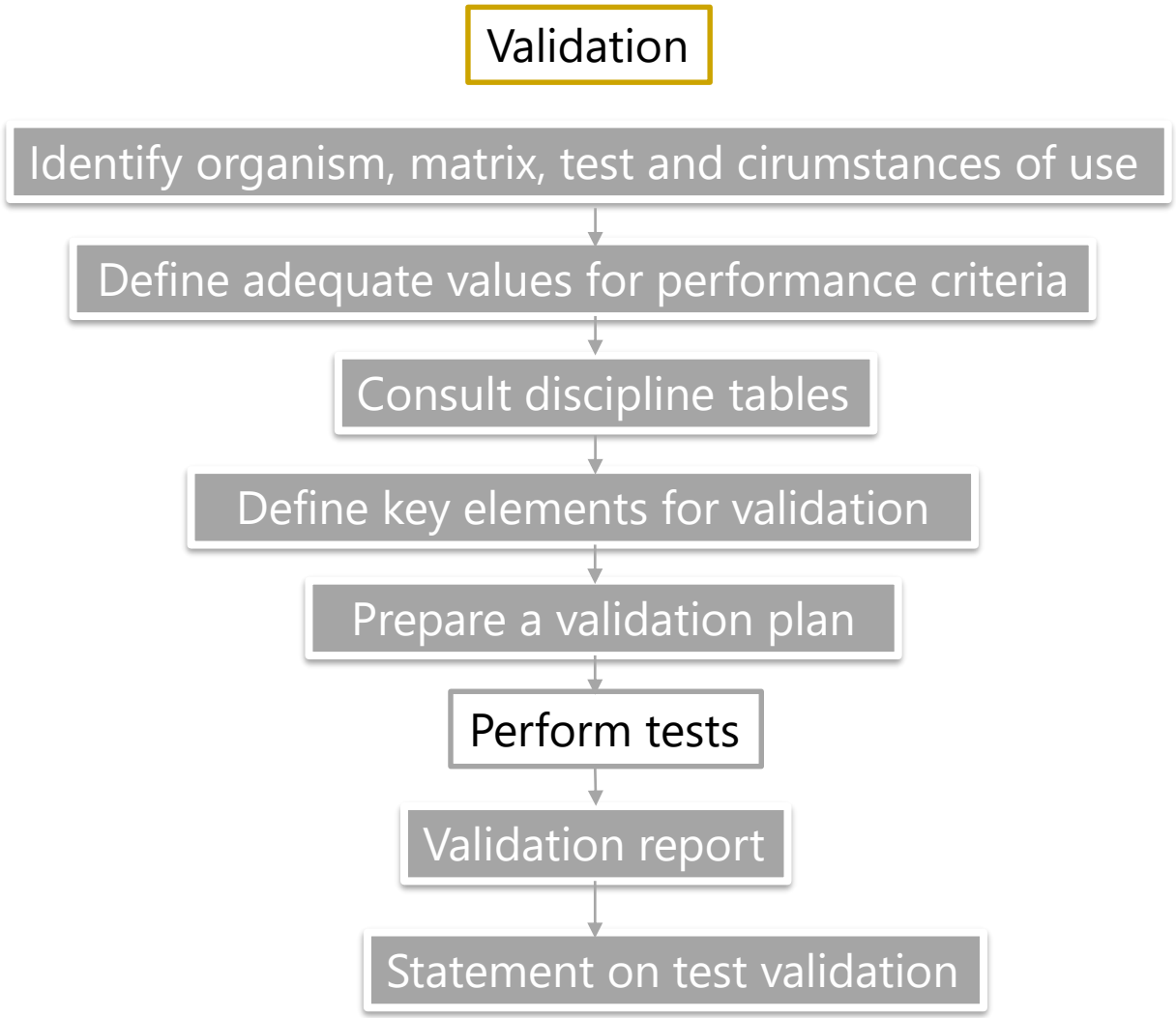
quality assured procedure for

- verfication studies
- validation studies

IMPLEMENTATION of the STANDARD

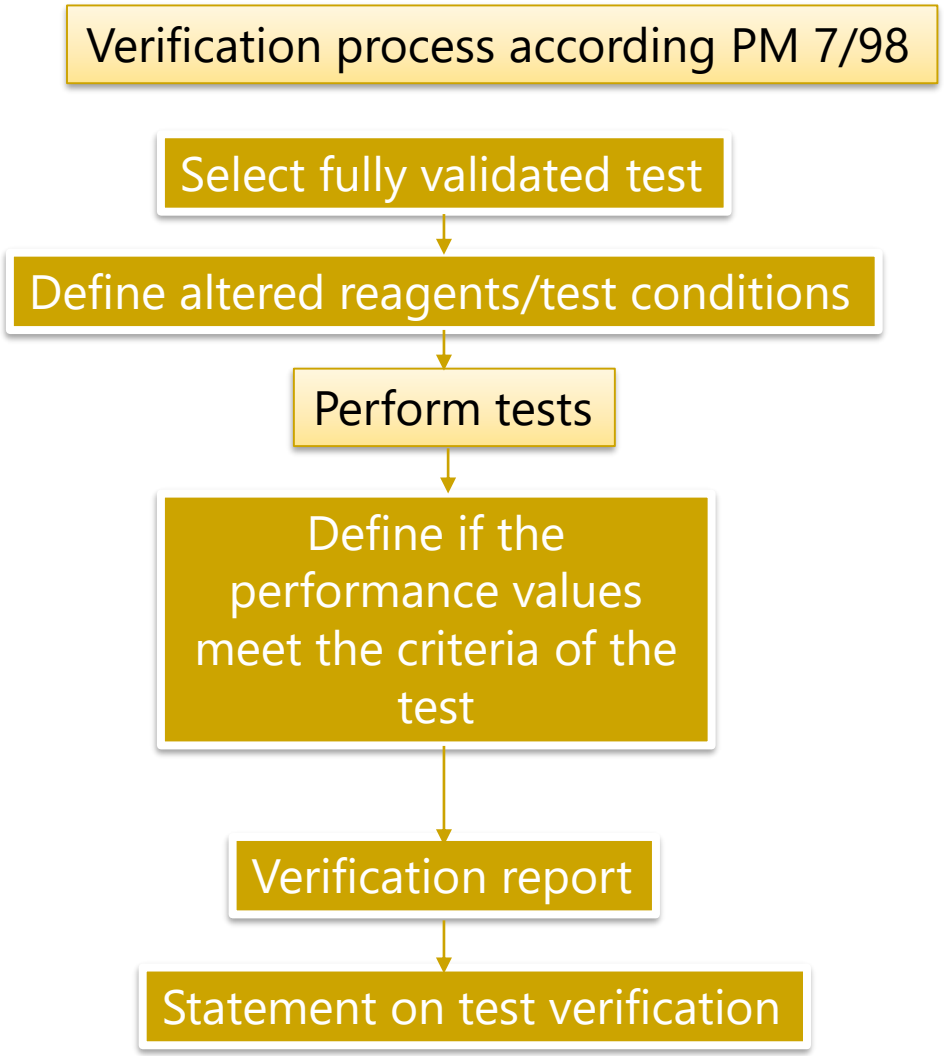
Processes according PM 7/98





IMPLEMENTATION of the STANDARD

Challenges for implementation



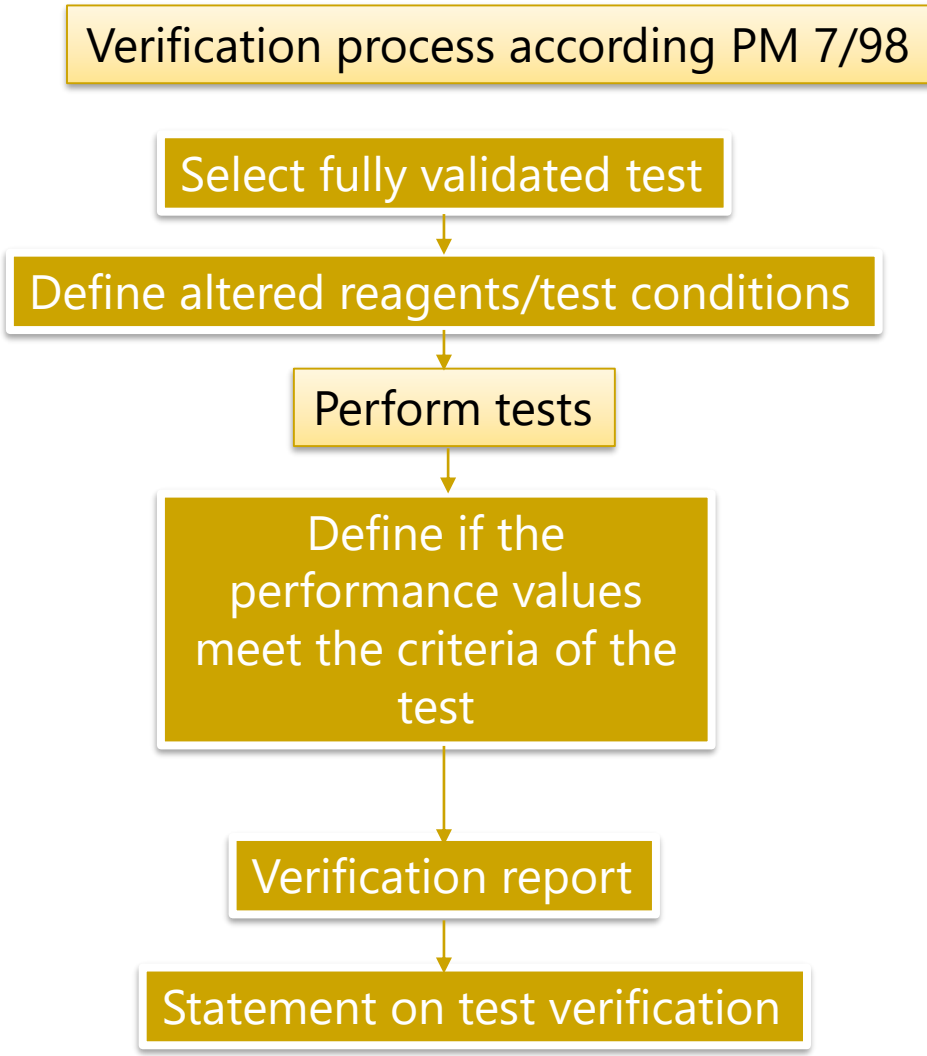
Fully validated tests are not always available

Fully validated tests are frequently not available

Standard	Date of publication	Number of tests	Number of fully validated tests	Number of partly validated tests	Number of tests without validation data
PM7_17_2_Guignardia citricarpa	2009	4	0	0	4
PM 7_2_1_Tobacco ringspot virus	2017	6	0	1 (PCR) 1 (ELISA)	3 (PCR) 1 (bioassay)
PM 7_3_3_Thrips palmi	2018	3	1 (LAMP)	1 (Barcoding)	1 (morphological identification)
PM7_40_4_Globodera rostochiensis and pallida	2017	9	5 (PCR)	1 (PCR)	3 (bioassay, hatching, viability test)
PM7_24_3_Xylella fastidiosa	2018	10	7 (PCR)	3 (serolog. tests)	0
PM7_79_2_Grapevine flavescence dorée	2015	5	5 (PCR)	0	0

IMPLEMENTATION of the STANDARD

Challenges for implementation



Fully validated tests are frequently not available

Various performance criteria are available for one test depending on host, DNA extraction method, spiked or natural infected matrix, available strains etc.

Various performance criteria available

Example: PM 7/24 (3) Xylella fastidiosa and PCR according Minsavage

	Analytical sensitivity	Analytical specifity	Diagnostic sensitivity	Diagnostic specifity	Repeatablity	Re-producibility
Validation data ANSES (DNeasy Plant Mini Kit)	Vitis vinifera: **10^2** cfu/mL Prunus persica: **10^2** cfu/mL Citrus sinensis: **10^3** cfu/mL Coffea arabica: 10^4 cfu/mL	Inclusivity: 100% on 10 targets Exclusivity: 100% on 16 non – target strains	Vitis vinifera: **81%** P. persica: **81%** Citrus sinensis: **82%** Coffea arabica**:** **81%** Coffea canephora: 74%	Citrus sinensis: 100% Coffea arabica: 100% Coffea canephora: 100%	Vitis vinifera: 80% Prunus persica: 92% Citrus sinensis: 98% Coffea arabica: 94%	Not available
Test performance study 2014 (spiked samples, DNeasy Plant Mini Kit)	Vitis vinifera: **10^6** cfu/mL Prunus persica: **10^4** cfu/mL Citrus sinensis: **10^2** cfu/mL Coffea spp: 10^4 cfu/mL **10^6** cfu/mL		Vitis vinifera: **40%** P. persica: **60%** Citrus sinensis: **80%** Coffea spp: **70%** Olea europea: **30%**	100%	95%	84%
Test performance study CREA (CTAB)	Olea europaea: **10^4** cfu/mL	Not available	Olea europea: **47%**	Olea europea: 100%	80% on undiluted DNA 100% on 10fold diluted samples	Olea europea: 60%

Challenges for implementation

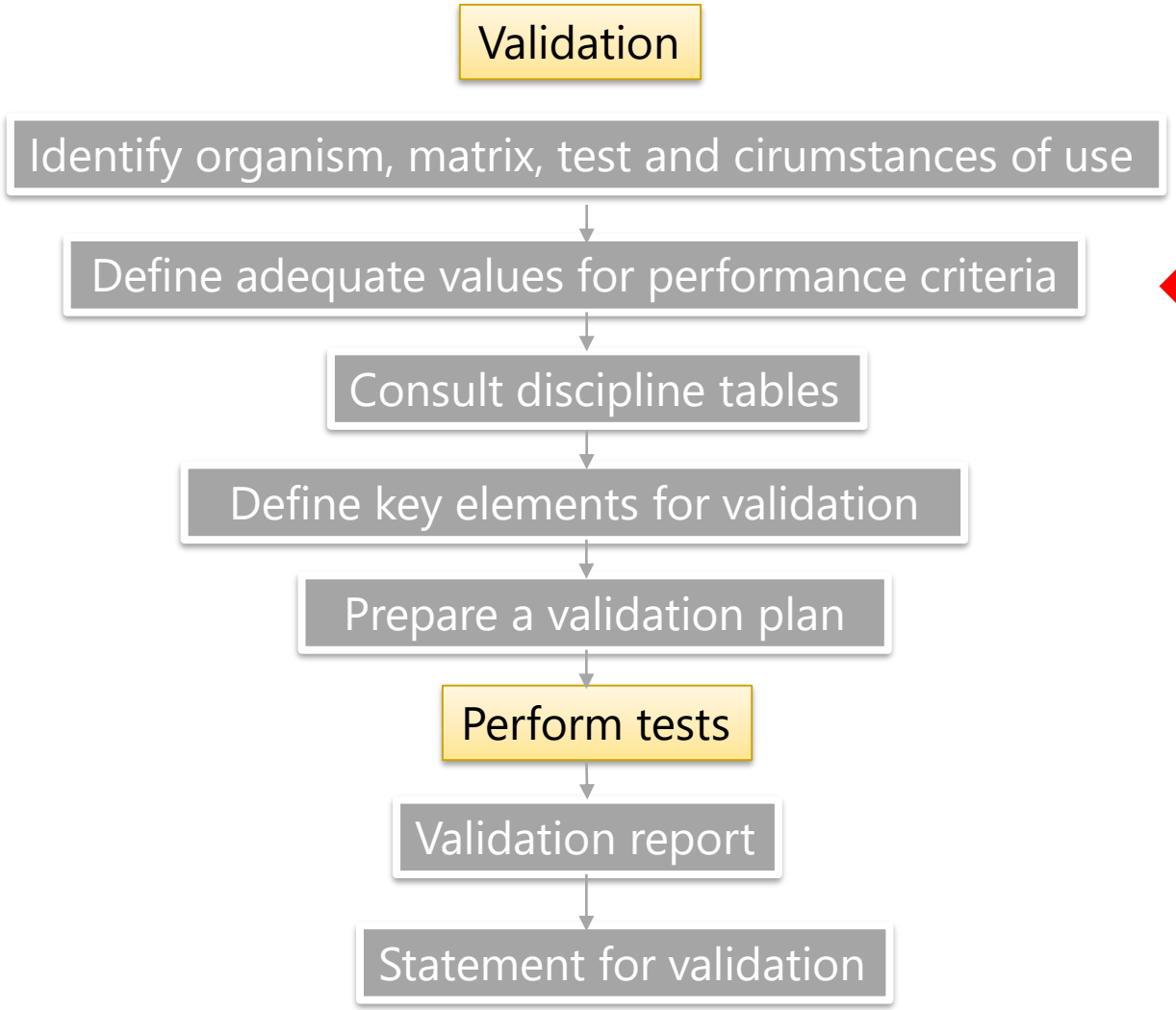
Define if the performance values meet the criteria of the test

Example: Verification of X. fastidiosa, **Vitis vinifera**, conventional PCR according Minsavage

	Original paper by Minsavage	Validation by Harper, 2010	Validation ANSES	TPS, 2014	Range of performance criteria
Analytical sensitivity		**10^2** cfu/mL	**10^2** cfu/mL	**10^6** cfu/mL	**10^2 -10^6** cfu/mL
Analytical specifity			100%		**100%**
Diagnostic sensitivity	100%	**64%**	V. vinifera: **81%**	V. vinifera: **40%**	**40 - 100%**
Diagnostic specifity	100%	100%	100%	100%	**100%**
Repeatablity			V. vinifera: **80%**	**95%**	**80 -95%**
Reproducibility			Not available	84%	**84%**

IMPLEMENTATION of the STANDARD

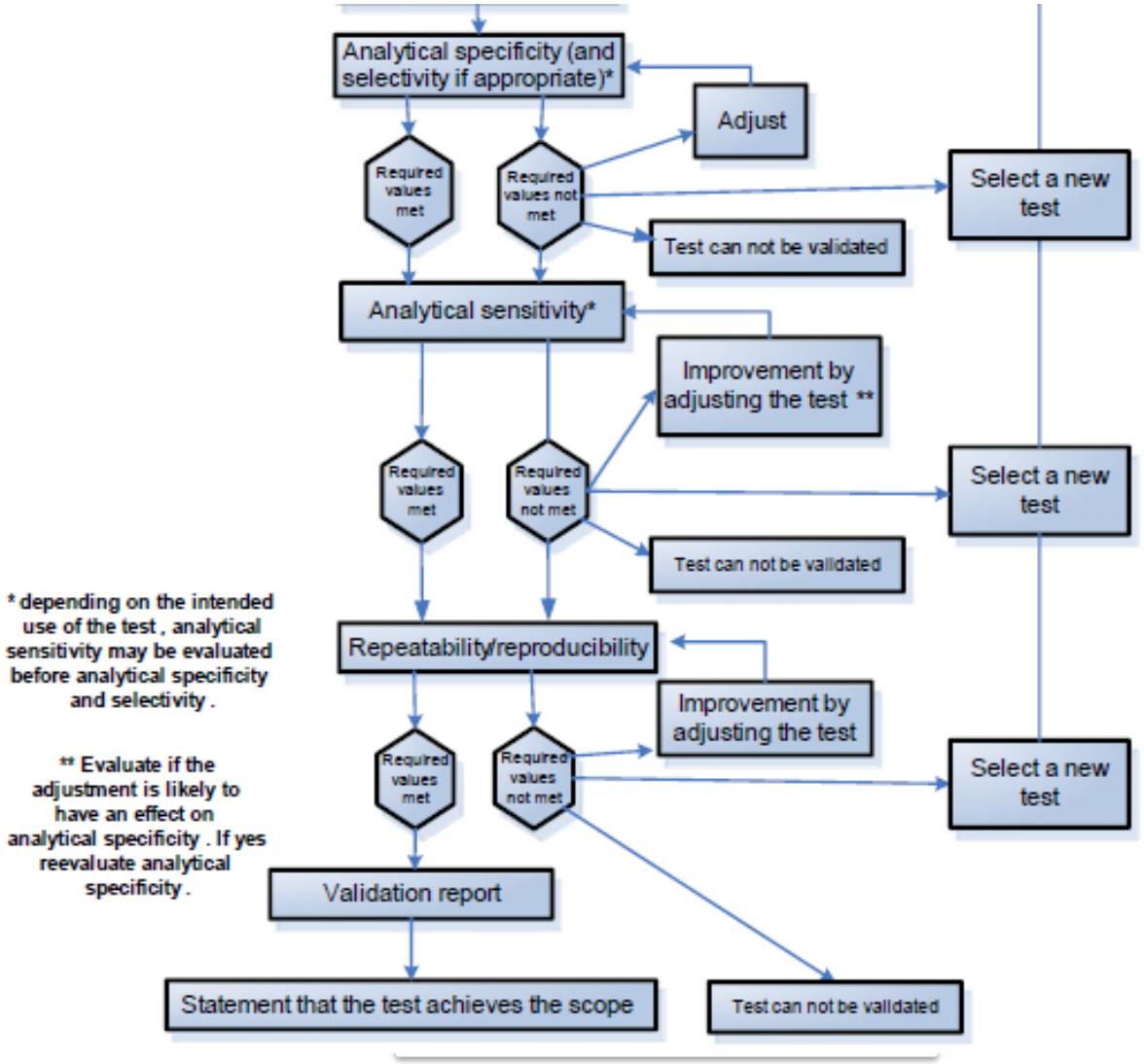
Processes according PM 7/98



To define adequate values for performance criteria **in advance** is difficult and not always possible

IMPLEMENTATION of the STANDARD

Processes according PM 7/98

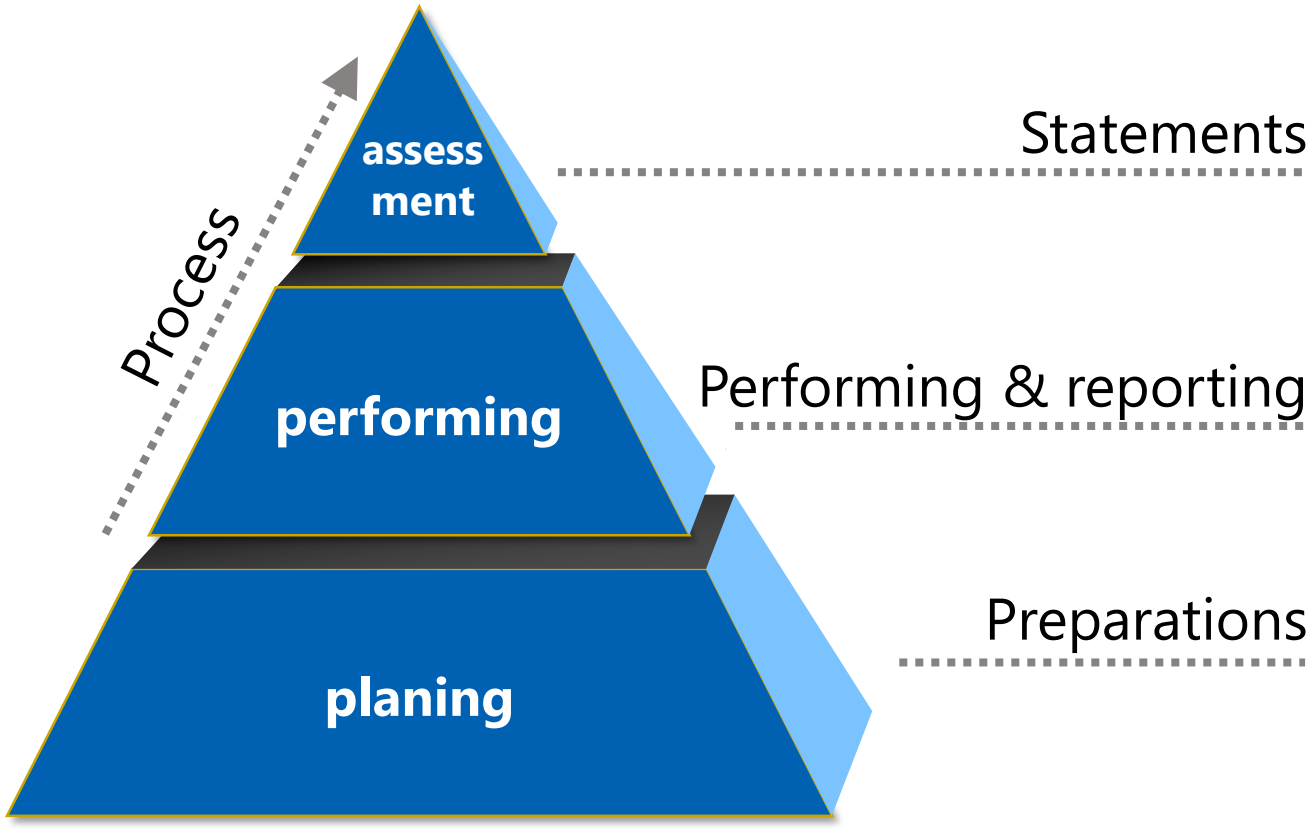


We do not stop the validation and select a new test, but at the end of the validation we check, if we can use the test for the intended purpose or if we can use it for another purpose

IMPLEMENTATION of the STANDARD

Verification and validation process - AGES

PM 7/98 (2) is implementing in a SOP and related technical templates



1. Statement that the validated or verfied test can be used for the intented purpose/scope
2. Statement that the validated or verfied test can not be used for the intented purpose, but for an alternative purpose within the scope.

1. Discussions about organism, test, use, costs
2. Literature search
3. Listing of available performance criteria
4. Preparation of sample set
5. Determination of the exact implementation
6. Authorisation by the lab manager

Challenges are meant to be met and overcome….

The biggest challenges on the way to implementing new standards are how to avoid unnecessary paperwork ….

Source: reporting-dms-metrics

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