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French agency for food, environmental and occupational health & safety

Investigate, evaluate, protect

Flexible scope and accreditation body's requirements: how to answer EU regulation 2017/625 in France

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Workshop Heads of Laboratories, 2019-09-09/11

EU requirements for official controls

EU rule 2017/625 - Article 37 (Official laboratories, but also valid for NRLs)

- 5. The scope of the accreditation of an official laboratory as referred to in point (e) of paragraph 4:
- (a) shall include those methods of laboratory analysis, test or diagnosis required to be used by the laboratory for analyses, tests or diagnoses, when it operates as an official laboratory;

- (b) may comprise one or more methods of laboratory analysis, test or diagnosis or groups of methods;

- (c) may be defined in a flexible manner, so as to allow the scope of accreditation to include modified versions of the methods used by the official laboratory when the accreditation was granted or new methods in addition to those methods, on the basis of the laboratory's own validations without a specific assessment by the national accreditation body prior to the use of those modified or new methods.

Anses - Plant Health Laboratory
Mycology Unit

Nancy / Malzeville

- Mycology Unit is the National Reference laboratory (NLR) for the detection and identification of phytopathogenic fungi

- Accredited since 2006 by the French Accreditation Committee (COFRAC) in accordance with the ISO/IEC 17025:2005 Standard for the detection and identification analyses of phytopathogenic fungi and oomycetes included in quarantine lists

- Since January 2014, the Mycology unit had extended is accreditation with a flexible scope to use tests developed and validated in-house.

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Accreditation scope for NRL in mycologie

- ANSES Plant Health Laboratory - Mycology Unit : designated National Reference laboratory (NLR) for the detection and identification of phytopathogenic fungi since 2007

- Accredited since 2006 by the French Accreditation Committee (COFRAC) in accordance with the ISO/IEC 17025:2005 Standard for the detection and identification analyses of phytopathogenic fungi and oomycetes

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- Since January 2014, the Mycology unit had extended is accreditation with a flexible scope to use molecular tests developed and validated in-house.

- Since August 2018, the Mycology unit operates as EURL in mycology.

Accreditation scope for NRL in mycologie

From the beginning, a standard flexible scope (FLEX1)

- The lower level of flexibility
- No possibility to add new tests without prior external evaluation
- If test relies on recognized methods, possibility to implement new versions of this method without prior evaluation in the framework of this level of flexibility

➢ ***Used for the detection and morphological identification of phytopathogenic fungi***

Since 2014, extended flexible scope (FLEX3)

- The hightest level of flexibility
- Adding new tests without prior external evaluation
- Different sub-levels of flexibility:

  Adoption of test << Adaptation of test<<< Development of test

➢ ***Used for the detection of phytopathogenic fungi by PCR tests developed and characterized in-house.***

Flexible scope of Mycology Unit : general scope

Matrix defined with the AC

Matrice	Organism	Principle of the method
Seeds	Phytopathogenic fungi and oomycetes	Manual extraction of nucleic acids by column absorption. DNA amplification by end (qualitative test)
	Phytopathogenic fungi and oomycetes	Manual extraction of nucleic acids by absorption. DNA amplification by rea (qualitative test)
All parts of plants (except seeds)	Phytopathogenic fungi and oomycetes	Manual extraction of nucleic acids by absorption. DNA amplification by end-poi (qualitative test)
	Phytopathogenic fungi and oomycetes	Manual extraction of nucleic acid y column absorption. DNA amplificati by real-time PCR (qualitative test)
Fungi and oomycetes	Phytopathogenic fungi and oomycetes	Manual extraction of nucleic acids by column absorption. DNA amplification by end-point PCR (qualitative test)
	Phytopathogenic fungi and oomycetes	Manual extraction of nucleic acids by column absorption. DNA amplification by real-time PCR (qualitative test)
DNA	Phytopathogenic fungi and oomycetes	Manual extraction of nucleic acids by column absorption. DNA amplification by end-point PCR (qualitative test)
	Phytopathogenic fungi and oomycetes	Manual extraction of nucleic acids by column absorption. DNA amplification by real-time PCR (qualitative test)

For each line, at least 2 tests included

Adding a new matrice, a new organism or a new principle of detection implies an extension of the accreditation scope (with dedicated evaluation by the AC)

Flexible scope of Mycology Unit : detailed scope

Extract of detailed scope

Matrice	Organism	Principle of the method	Method reference
Seeds of sunflowers	*Plasmopara halstedii*	Detection by grinding, manual extraction, amplification by real-time PCR	MA 032
Leaves, twigs, trunk	*Phytophthora ramorum*	Detection by grinding, manual extraction, amplification by PCR	MOA 018

Why flexible scope ?

Accreditation under flexible scope enables to:

- Include tests for a quick response to requests (e.g. phytosanitary crisis situations or emerging pests)
- Withdraw tests after phytosanitary crisis situations or changes in regulation
- Maintain a quality management system that fulfils the requirements of the ISO/IEC 17025 Standard and that is suitable for the size of the laboratory

Evolution of the extent of flexible scope since January 2014

- Inclusion of new tests: **3**
- Revision of tests: **5**
- Withdrawal of tests: **3**

How do you deal with validation of newly introduced test?

Input

Technical need

Current state of knowledge

Description of methodological project

Ressources and outcomes

Biological materials

Performance criteria to be characterised

Expected performance values

Etablisment of partnership

Statistical tests required

How do you deal with validation ?

Mandatory and optional criteria to be characterized

For each criteria the process provides:

- A definition
- How it will be assessed
- Expected performance values

Mandatory criteria *	Evaluation of the efficacy of a PCR reaction	
	Analytical sensitivity:	Determination of the smallest detectable quantity of the target that it is possible to measure with a defined certainty
	Inclusivity:	Ability of the method to detect the target taxon regardless of geographical origin and host, etc
	Analytical specificity:	Ability of the test to provide a negative result for a non-target organism
	Repeatability:	Consistency between successive and independent results obtained with the same method and using an identical test sample in identical conditions
	Reproducibility:	Consistency between results of individual tests performed on an identical test sample and using the same method obtained by operators using different equipment
	Diagnostic sensitivity:	Proportion of infested or infected samples yielding a positive result with the test of interest
	Diagnostic specificity:	Ability of the test to provide a negative result for a healthy sample
Optional criteria *	Robustness:	Ability of the method to remain unaffected by small deliberate variations in the experimental parameters described in the method.
	Evaluation of the quality of DNA extraction by an external (monoplex) or internal (multiplex) real-time PCR test targeting the 18S gene	
	Ability of the test to be used in multiplex, i.e. to be used in parallel with other PCR tests in real time in the same reaction tube (e.g. test for another target, internal control of DNA extraction, etc.)	
	Evaluation of the minimum number of test samples to be used	
	Ease of use and transfer	
	Estimate of all the costs generated to produce the results: personnel, infrastructure, liquids, consumables, reagents, etc.	

How do you implement quality assurance in the frame of a flexible scope?

	Methodological development projects	Analyses under accreditation
Process and traceability	Specific process and forms for the project description and the characterisation of the method	Existing process and traceability for analysis (extraction, PCR, mycological cultures…)
Staff	Definition of a new function: project leader	Existing process and traceability for operators and technical responsibles persons
Management	Specific process for the management of the detailed scope	Existing process and traceability for quality management system
Equipement Consumables Reagents	The laboratory decided to use of the existing quality management system to perform and to trace PCR or real-time PCR detection analyses	

How do you demonstrate technical expertise for test development?

Qualification and maintenance of operator expertise

- Regular activity of detection with molecular biology techniques and specific demonstration when needed (horizontal demonstration, e.g. running PCR on one pest)
- Various controls (positive, negative, specificity, LOD)
- PT or blind samples
- Supervision of work by the project leader during project review

Qualification and maintenance of project leader expertise

- Qualification criteria based on initial training and professional experiences
- Publication in peer-reviewed journals

Noted as a critical point by the quality assessor

What about flexible scope in other disciplines / techniques?

Example :

For morphological methods (e.g. insects & mites, nematodes, fungi…):

- Difficult to manage a flexible scope, because too demanding
- Insects and mites: hundreds of regulated targets pests
- Numerous types of matrices (e.g. for nematodes or fungi)
- Absence of recognized methods, just literature (keys available)

Huge gap between AB requirements and reasonable technical validation work

Which options:
Scope accreditation limited to higher taxonomic level (e.g. genus)?
Derogation to EU rule and no accreditation in specific cases?
Without accreditation, which confidence in the results of the laboratory?
Impact on trade?

Conclusion

Considering the Plant Health disciplines, diversity and regulations:

- Necessary to be pragmatic (what is achievable)

- Avoid unacceptable requirements that reduce the confidence in accreditation

Common discussion between EU commission, AB and PH labs needed to address this challenge, maybe with a horizontal approach

Thank you for your attention