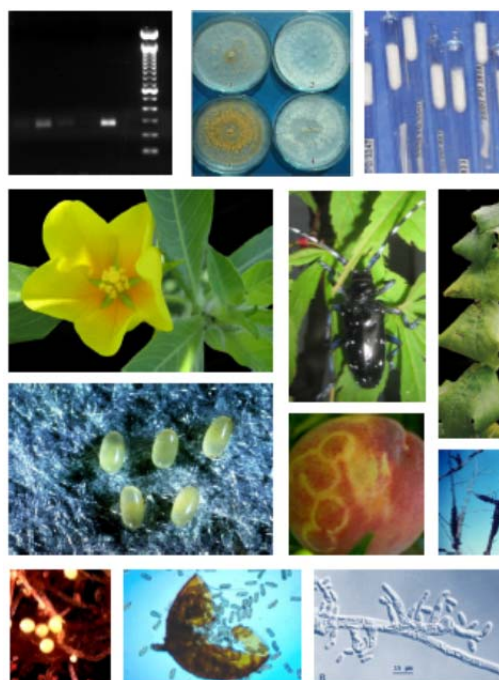




Draft review of quality control standards applied in the main EU reference collections of quarantine organisms.



1. Introduction

As part of the questionnaire produced under Q-Collect WP2 and distributed under WP7, a number of questions were devised to obtain current information regarding the use of quality standards across the various reference collections of quality organisms in each of the disciplines (viruses/viroids, phytoplasmas, bacteria, fungi/omycetes, nematodes, insects/mites and invasive plants). The results obtained at the end of month 12 are summarised here and following consultation amongst the various project partners at the project workshop in Kleinmachnow (27-28th November, 2014) and subsequent revisions via email, a final version is anticipated in month 15 (December, 2014). This review also summarises the formal quality standards covering areas of work relevant to reference collections and will consider EPPO guidelines and standards relating to identification of specimens as well as requirements for quality management and accreditation in diagnostic laboratories. The information will be used to assess where quality standards are currently missing or could be improved and to recommend minimum standards to be adopted by collections providing reference materials of quarantine organisms (as live or dead specimens, DNA or associated data) for use in EU diagnostic and research laboratories.



2. Status of quality control in EU reference collections of quarantine organisms

The results from the questionnaire highlighted a wide variation in current quality standards across 110 EU reference and research collections, 84% of which contained quarantine or relevant related organisms.

2.1. Accreditation

Of 106 respondents, 50% reported that their host institutes/laboratories had a formal quality system covering maintenance of the collection. Of these, 33 collections were officially accredited or certified, representing 9 collections of bacteria, 5 of fungi, 6 of insects, 3 of invasive plants, 4 of nematodes, 4 of phytoplasmas and 5 of viruses/viroids (Fig. 1). A total of 30 collections indicated that some procedures in their host laboratories conformed to ISO 17025, although the detail of the relevance of these accredited procedures to the maintenance of the collections or the provision of materials was not determined and requires further interpretation. Surprisingly, only 8 collections reported accreditation to ISO 9001 standard, covering general management, control of standard operating procedures and records, although this should be inferred as a necessary precursor to ISO 17025 certification. To date there appears to be only one collection accredited to ISO 17025 together with ISO Guide 34:2009 for the production of reference materials. The ISO 17025 standard is not automatically the relevant standard for reference material and collections.

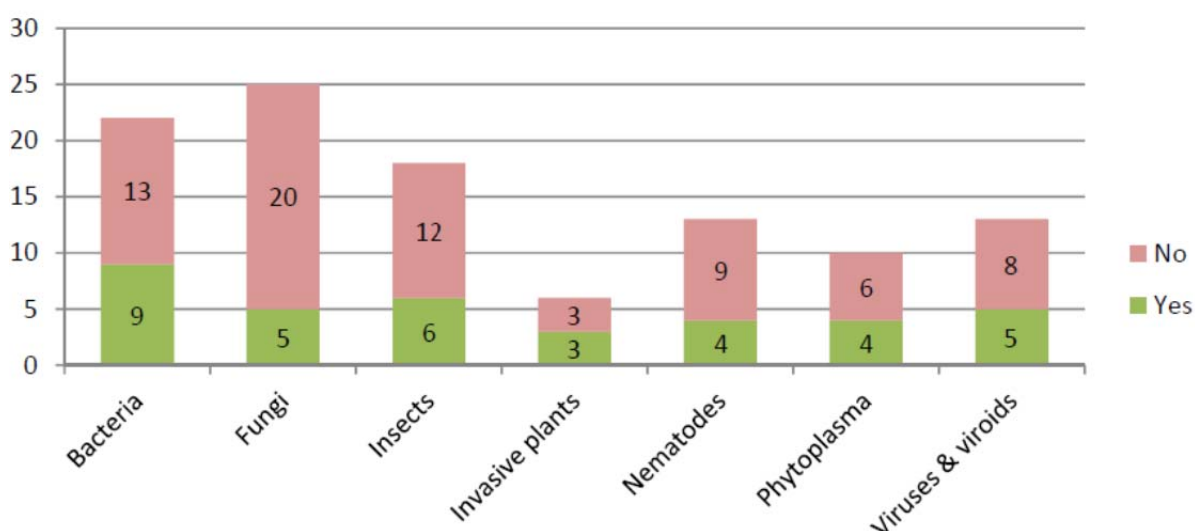


Fig 1. Number of collections with accredited/certified quality systems.



Of the 53 responding collections with no official accreditation, over 60% used validated methods or published keys for initial identification of specimens. Less than 50% applied document controls or monitored performance of laboratory equipment used in identification or preparation of reference materials. Less than 40% monitored training of personnel, customer complaints or preventative actions and less than 30% used calibrated equipment, monitored corrective actions or performed management reviews. Around 10% or less maintained any quality or technical records or performed internal audits (Fig. 2).

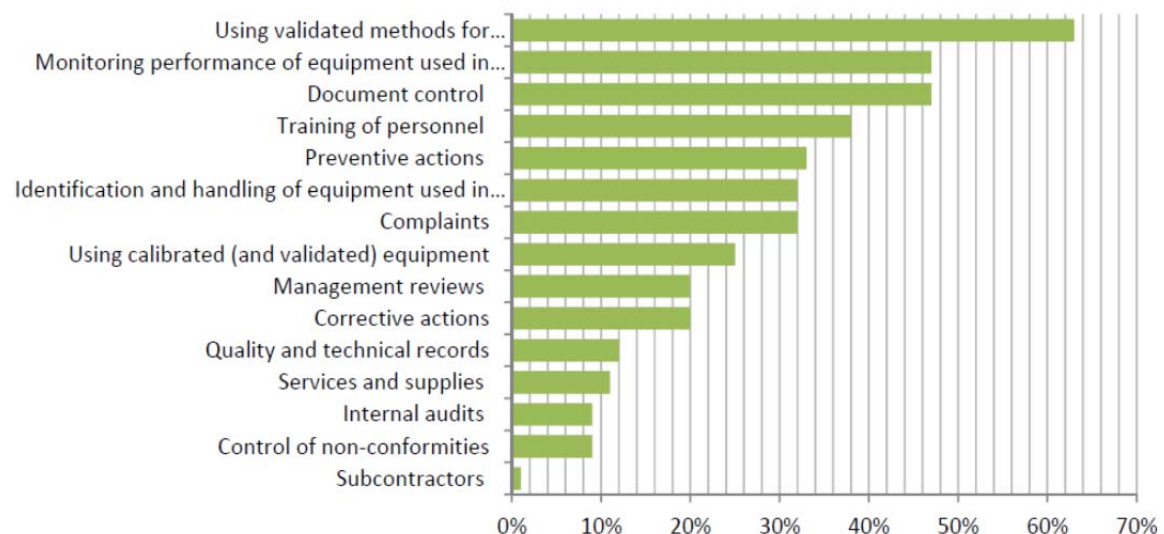


Fig. 2: Quality controls applied in non-accredited collections

2.2. Procedures and record keeping

Less than half of the collections maintained a catalogue of their accessions, although around two-thirds could provide at least a partial list of the specific quarantine and related organisms held. Since the definition of catalogue was unclear in the questionnaire, further investigation is required to determine the type of inventory of the contents of each collection and whether or not these are registered and publically available or only for internal use. Where the contents of collections were reported as catalogued, the breadth of information stored to describe each accession varied between collections (Fig. 3).

Almost all collections could provide a list of scientific names for the organisms in the collection. A high proportion (>70%) of collections used recognised (published or widely adopted) procedures for identification and authentication of quarantine organisms and had internally documented procedures and records for primary identification of specimens (Fig 4). The proportion reporting documented standard operating procedures (SOPs) and data for classical morphological identification, DNA/RNA sequencing, phenotyping methods or pathogenicity



determinations was 59%, 52%, 38% and 33% respectively. Further discussion is required to determine the minimum type and level of information which should be maintained for collections from the different disciplines.

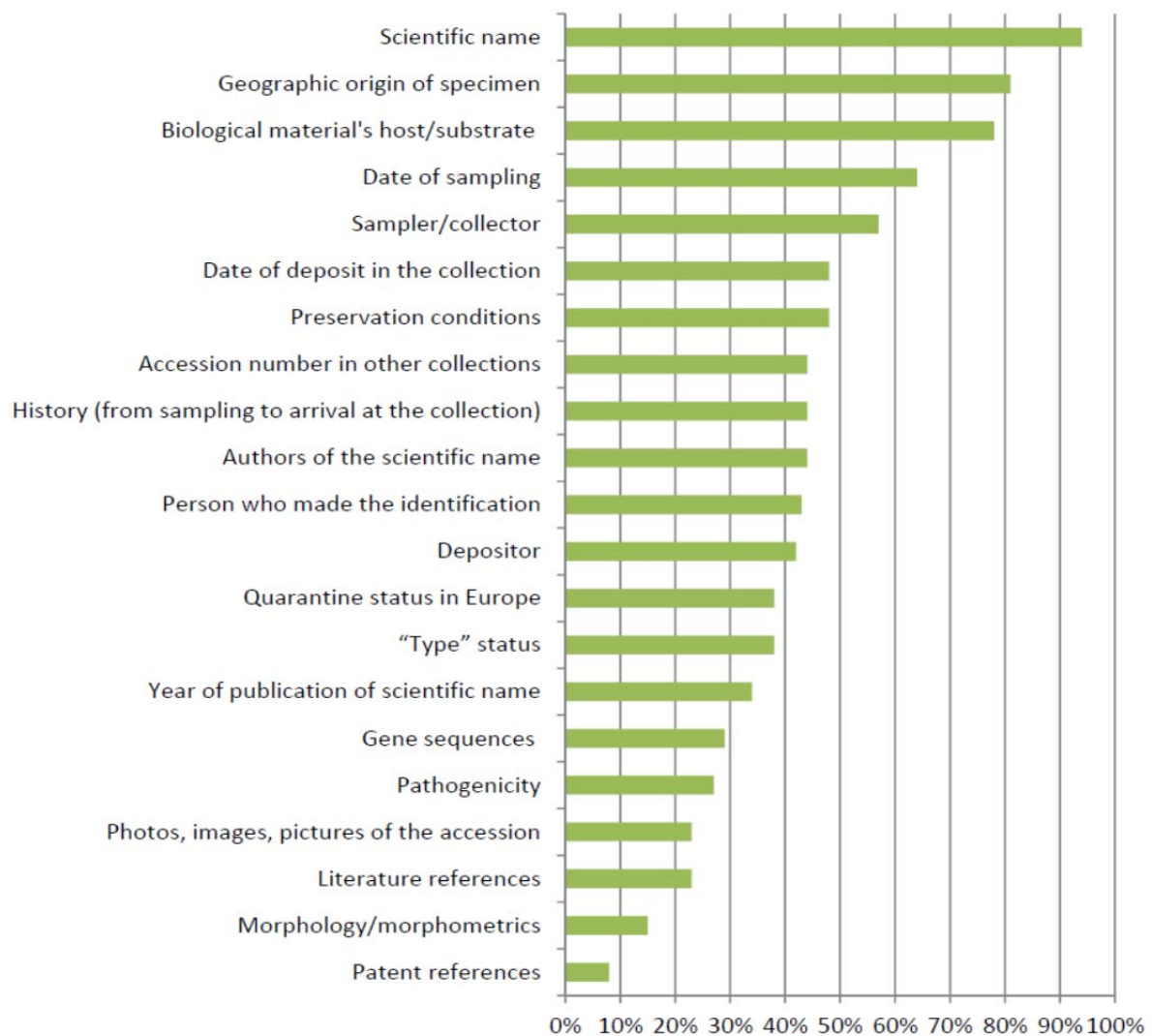


Fig. 3: Proportion of collections maintaining different accession data

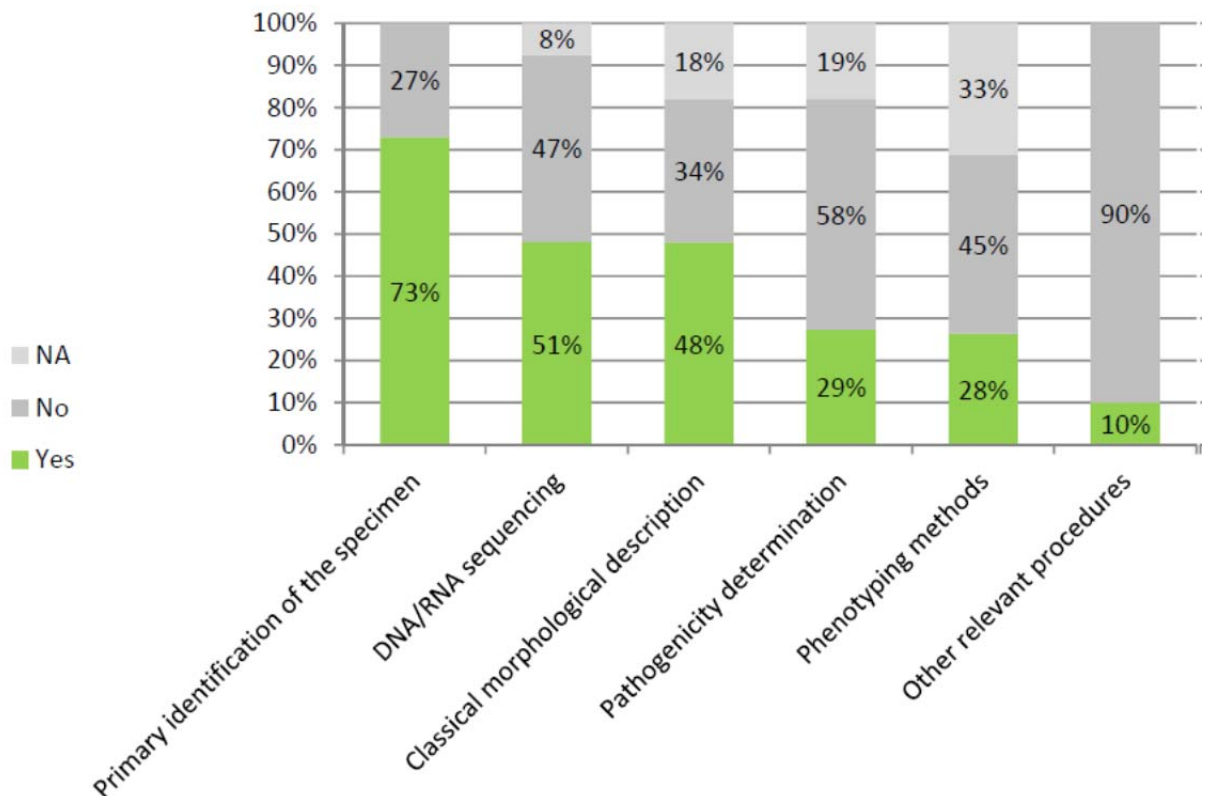


Fig. 4: Proportion of collections with standard operating procedures and records (where relevant) regarding characterisation of specimens (NA = not applicable).

The collections also varied in their keeping of procedures and records relating to handling, storage and external supply of specimens (Fig. 5). More than half of collections, where procedures were considered relevant, maintained SOPs and records with respect to storage conditions, assignment of unique identification numbers, preservation methods, periodic assessment of specimen authenticity, isolation methods and prevention of contamination. Fewer than half of the collections, where procedures were considered relevant, maintained SOPs and records regarding external supply of specimens (including labelling, shipment, packaging, assessment of authenticity and quality following exchange of specimens and homogenisation of reference materials).

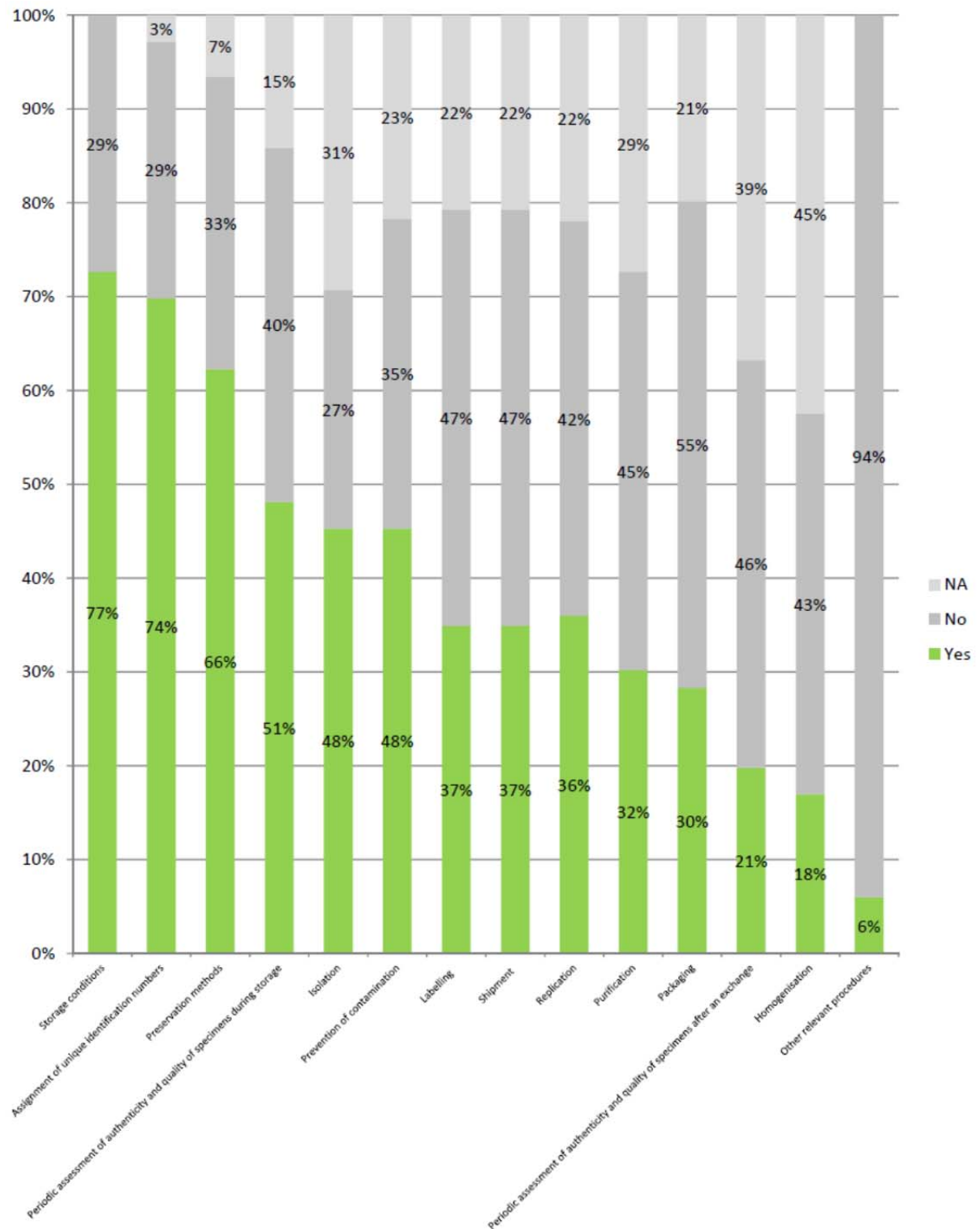


Fig. 5: proportion of collections with standard operating procedures and records regarding handling, storage and external supply of specimens.



Characterisation of specimens was reported to be performed by an expert in 82% of cases, although the definition of expert varied, mostly referring either to specialists with a higher degree, with some years of experience or specifically dedicated to working on the collection (Fig. 6). Some collections reported that experts could be identified as competent under accredited quality systems.



Fig 6: Description of experts used to characterise specimens in 82% of collections.

3. Relevant formal quality standards for accreditation

3.1. ISO 9001 – a generic management standard covering all aspects of the management of quality with potential for covering management of the complete workflow of a collection. This could include maintenance and storage of procedures and data regarding submission of material, establishment of identity and purity, maintenance of the specimens and the distribution of the material when requested by breeders and researchers. Third party verification of compliance with this standard is carried out by a Certification Body and does not cover technical competence but may in specific cases involve assessment by technically competent assessors.



- 3.2. ISO 17025** – a technical standard demonstrating the competence of the laboratory to conduct specific procedures. For example, It may potentially cover specific testing activities associated with the management of biological material, including establishing genetic purity and freedom from contamination. Procedures accredited to this standard are usually fixed in scope, although a flexible scope accreditation may be possible where similar procedures are used for different biological materials. Third party verification of compliance with this standard is carried out by a national Accreditation Body and involves a technical assessment by experts.
- 3.3. ISO Guide 34:2009** - Biological reference materials produced under an ISO Guide 34:2009 accredited process offer confirmed identity, well-defined characteristics and an established chain of custody, all qualities essential to their effectiveness as biological standards in research and development. This Guide specifies general requirements in accordance with which a reference material producer has to demonstrate that it operates, if it is to be recognized as competent to carry out the production of reference materials. It is intended for use by reference material producers in the development and implementation of their management system for quality, administrative and technical operations. Reference material customers, regulatory authorities and accreditation bodies may also use it in confirming and recognizing the competence of reference material producers. This guide is currently under revision to become a standard on its own and may be most suited for application in reference collections.

4. Relevant EPPO guidelines and standards

4.1. Identification methods

EPPO standards on diagnostics provide all the information necessary for a named pest to be detected and positively identified by an expert (i.e. a specialist in the relevant discipline). There are currently diagnostic protocols for around 120 of the 353 organisms (34%) currently recommended for regulation as quarantine pests under the EPPO A1 and A2 lists (<http://www.eppo.int/QUARANTINE/quarantine.htm>) (Fig. 7).

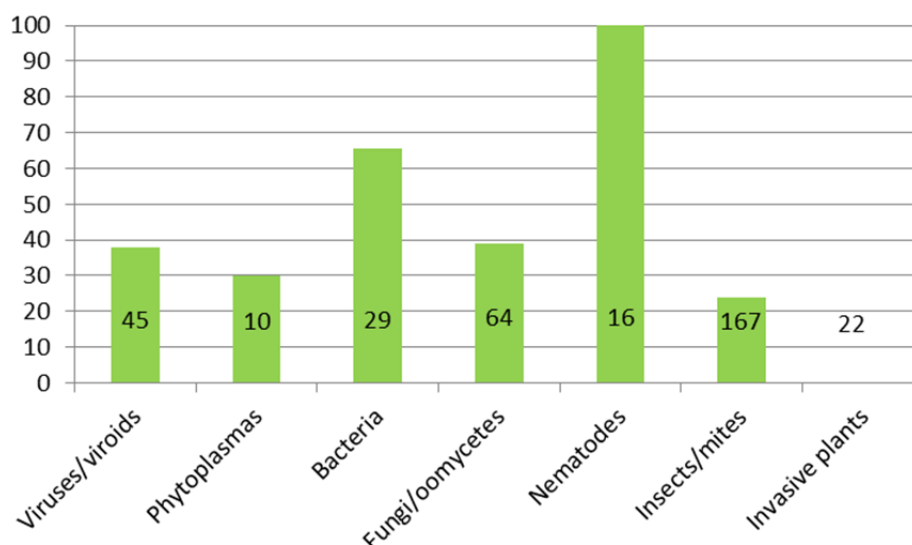


Fig. 7: Proportion of pests recommended for regulation as quarantine pests with EPPO standard diagnostic protocol.

The preparation of protocols involves close collaboration between different EPPO Panels composed of diagnostic experts nominated by the NPPOs of the EPPO member countries. These include panels on Diagnostics and Quality Assurance, Diagnostics in Bacteriology, Diagnostics in Entomology, Diagnostics in Nematology and Diagnostics in Virology and Phytoplasmaology.

Each protocol gives details on internationally accepted and/or validated procedures for detection and identification of the pest and comparisons with similar species which may lead to misidentification. A list of institutes or individuals where further information on the organism can be obtained is provided (also available via the EPPO database of diagnostic expertise at <http://dc.eppo.int>). Information on access to reference materials from established collections or individual experts is also provided.

4.2. Quality standards

The EPPO panel on Diagnostics and Quality Assurance oversees the quality aspects of all of the diagnostic protocols and has produced two standards concerning the management and operations of diagnostic laboratories, which are also relevant to the application of quality management systems within reference collections:



- **PM 7/84(1) Basic requirements for quality management in plant pest diagnosis laboratories.**

This standard describes basic management and technical requirements to assist laboratories to design a quality management system. For management, these include:

- Availability of appropriate resources
- Purchase of appropriate supplies
- Clear definition of responsibilities and tasks
- Recognition and prevention of conflicts of interest
- Documentation and assessment of training
- Availability of standard operating procedures (SOPs)
- Verification of appropriate quality standards of subcontracted work
- Confidentiality agreements with clients
- Suitable complaints procedures
- Procedures to record and correct non-compliances
- Suitable documentation and archiving
- Periodic review of the system

Technical factors affecting the reliability of the laboratories include:

- Availability and competence of personnel
 - Training programmes and records
 - Proficiency testing
- Laboratory infrastructure
 - Appropriate containment for quarantine organisms
 - Avoidance of cross contamination
 - Suitable environmental conditions (laboratory and storage)
 - Appropriate space and number of laboratories
 - Maintenance and cleaning of facilities
 - Facilities for safe preparation and disposal of materials
- Methods and procedures
 - Identification, authenticity, storage and distribution methods
 - Accepted international, national or regional standards
 - Availability of documented SOPs, technical manuals
 - Fit for purpose and reviewed
 - Availability of data from method comparisons/validation
- Equipment
 - Labelling and listing of essential equipment
 - Operating instructions and training
 - Calibration and maintenance records



Additional considerations specific for reference collections include:

- Type of reference materials to be considered
 - Reference material – documented authenticity and chain of succession from a recognised source.
 - Other reference material – appropriate for use with correct diagnostic features
 - Fit for purpose – e.g. for controls in detection or identification, calibration, validation, method comparison, proficiency testing.
 - Live cultures, infected plant material, DNA/RNA, mounted specimens, prepared microscope slides, images of diagnostic quality.
- Documentation/procedures
 - Catalogue of specimens with relevant key data for internal and external information
 - SOPs on identification and authentication methods
 - SOPs on preservation and storage methods
 - Data storage and retrieval methods
 - Customer communication methods
 - Procedures for specimen distribution/sharing
- **PM 7/98(2) Specific requirements for laboratories preparing accreditation for a plant pest diagnostic activity.**

This standard describes additional specific requirements for laboratories applying for accreditation against the ISO Standard 17025 on “General requirements for the competence of testing and calibration laboratories”. Such accreditation is granted and maintained after independent audits by the national accreditation body. Accreditation may be fixed or flexible in scope. A clearly and unambiguously defined procedure is accredited under fixed scope, whereas, a flexible scope allows the laboratory to report accredited results of tests which are not explicitly stated in the scope but represent either:

- Optimisation of a given test
- Modification of an existing test to broaden its application (e.g. for use in a new matrix)
- Inclusion of a test which is equivalent to one which is already accredited.

Flexible scope places more responsibility on the laboratory to demonstrate that tests are validated, suitable for circumstances of use and are performed competently and consistently.



EPPO standard PM 7/98(2) provides guidance on the validation of methods for detection and identification of quarantine pests. Where applicable, guidance is given on requirements for test validation in preparation for accreditation. Validation includes provision of data for the following performance criteria:

- Analytical sensitivity
- Analytical specificity
- Repeatability
- Reproducibility

Not all test methods included in EPPO diagnostic protocols are validated. Where surveys have shown that certain identification tests are widely used within the various disciplines, they are listed in Appendix 1 of the standard. In these cases, the tests are considered by experts to give appropriate confidence regarding repeatability and reproducibility, although accredited laboratories are still expected to produce validation data on analytical sensitivity and specificity. Validation of identification methods based on morphological and morphometrical methods is not subject to the same requirements since expert judgement is based on the use of documented keys, descriptions, specimens and voucher images which are internationally recognised by experts.

- **EPPO Standard PM 3/64 Intentional import of organisms that are plant pests or potential plant pests.**

EPPO Standard PM 3/64 provides guidelines for authorizing and managing import of living plant pests and minimizing any risks associated with their maintenance and disposal. These guidelines are therefore highly relevant to the safe maintenance of reference collections of viable quarantine plant pests. Of the collections participating in the WP2 questionnaire, 84% responded that they were aware of this standard. Guidelines are presented on procedures for:

- Applying to the NPPO for permission to import
- Performing a risk analysis on the pest to be imported in line with ISPM 11
- Assessment of the risk by the NPPO and decision on whether to import and the requirement for import and holding licences.
- The level of containment required in relation to the risk and methods for safe disposal after the required period of use.