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Medical laboratories — Guidance on application of ISO 15189 in anatomic pathology

Laboratoires médicaux — Recommandations pour l'application de l'ISO 15189 en anatomopathologie

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Foreword

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The procedures used to develop this document and those intended for its further maintenance are described in the ISO/IEC Directives, Part 1. In particular, the different approval criteria needed for the different types of ISO document should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2 (see www.iso.org/directives).

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This document was prepared by Technical Committee ISO/TC 212, *Medical laboratories and in vitro diagnostic systems*.

Any feedback or questions on this document should be directed to the user's national standards body. A complete listing of these bodies can be found at www.iso.org/members.html.

Introduction

Anatomic pathology (AP) is the branch of medicine that examines tissue samples and cells by microscopy and other methods. AP seeks to answer clinical questions (e.g. Is it neoplastic? Is it malignant? Where does it arise? How can it be treated?) by rendering a diagnosis that allows the patient's caregiver to treat the patient's condition, predict the condition's response to treatment and make a judgement about the condition's prognosis.

AP comprises three activities: examination of tissue obtained from the body by biopsy, surgery or autopsy; examining exfoliated or aspirated single cells, circulating tumour cells, or groups of cells whose architectural context is often lost; and examination of deceased persons, usually to confirm or document a cause of death, or the extent of known or previously undiagnosed conditions.

Ancillary techniques such as immunohistochemical stains, (fluorescence) in-situ hybridization studies, molecular testing and advanced genomic and proteomic studies (e.g. next-generation sequencing, mass spectrometry) have complemented or even been incorporated into AP. The arrival of image analysis tools, machine learning algorithms and artificial intelligence systems will introduce new examinations to AP laboratories with a new set of risks and opportunities (e.g. automated quality control).

AP is different from other laboratory medicine specialties such as chemistry, microbiology, or haematology in several aspects. First, samples submitted for evaluation are often solid and, in many instances, unique (i.e. if the sample is exhausted or lost, it cannot be replaced by another sample) and indivisible (i.e. a part taken from the primary sample cannot be expected to have the same properties as the primary sample). Second, the structural integrity at the macroscopic scale determines diagnostic features such as margins status or orientation. Third, the examination process almost always requires at least two separate activities, macroscopic and microscopic examination, that occur at different times. Fourth, processing the sample involves many, often unrepeatable, manual steps, that introduce several risk points along the process. Finally, the analytical examination process is interpretive, performed by humans with intra- and inter-observer variability, and with no universally accepted biological reference intervals.

ISO 15189, can be applied to, and encompasses AP. This document provides guidance for AP laboratories on how the requirements contained in ISO 15189 can be met. Like ISO 15189, this document applies to both the resource and process aspects as well as the governance and management aspects of AP. ISO 15189 defines medical laboratory as an entity performing examinations of materials derived from the human body for the purpose of providing information for a diagnosis.

In AP, examination is not synonymous with diagnosis. An examination has the objective of determining the value or characteristics of a property. The result of an examination in AP can influence, and even be the sole determinant, of a diagnosis. In many instances, however, a diagnosis rests not only on the result of the AP examination but also the clinical setting and results of other examinations (e.g. medical laboratory, imaging). Rendering a diagnosis constitutes practice of medicine. While this document must not infringe on the practice of medicine, it reminds users that the practice of AP is inseparable from the activities and requirements addressed by ISO 15189 and strives to promote the welfare of patients.

This document does not impose new or more stringent requirements than ISO 15189. Instead, this document attempts to clarify the requirements by providing examples of process actions and risks, using language and concepts familiar to the AP laboratory. The left column in each table refers to the subclauses in ISO 15189 for which guidance is offered. Not every subclause of ISO 15189 is addressed, only the subclauses for which clarification or guidance was thought to be of benefit. The tables in this document are not comprehensive lists of actions and risks. They are examples of actions and risks, and conformance with every item in these tables does not imply conformance with ISO 15189.

This document is aligned with ISO 15189 and assumes basic familiarity with central themes of ISO 15189, including process and risk management, corrective action for nonconforming work, internal auditing, and effective management reviews.

Medical laboratories — Guidance on application of ISO 15189 in anatomic pathology

1 Scope

This document provides guidance to anatomic pathology (AP) laboratories on implementing a management system to meet requirements for quality and competence of ISO 15189.

NOTE International, national, or regional regulations or requirements can also apply to specific topics covered in this document.

2 Normative references

The following documents are referred to in the text in such a way that some or all of their content constitutes requirements of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 15189:2022, *Medical laboratories — Requirements for quality and competence*

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO 15189 and the following apply.

ISO and IEC maintain terminology databases for use in standardization at the following addresses:

— ISO Online browsing platform: available at https://www.iso.org/obp

— IEC Electropedia: available at https://www.electropedia.org/

3.1
anatomic pathology
AP
branch of medicine that evaluates tissue and cellular samples

Note 1 to entry: This branch of medicine is also referred to as histopathology or cellular pathology.

3.2
cytopathology
subspecialty of *anatomic pathology* (*AP)* (3.1) that evaluates features at the cellular level

3.3
diagnosis
identification of a health or disease state

Note 1 to entry: A diagnosis can be based on examination results and the disease state's signs or symptoms. A diagnosis typically classifies the disease state into separate and distinct categories or subclasses that allow medical decisions about treatment and prognosis to be made.

Note 2 to entry: Diagnosis is not synonymous with examination.

Note 3 to entry: A diagnosis is rendered by a trained, competent and authorized person. In most instances, this person is a pathologist.

3.4
examination
set of operations having the objective of determining the numerical value, text value or characteristics of a property

Note 1 to entry: An examination may be the total of a number of activities, observations or measurements required to determine a value or characteristic (e.g. dissection, microscopic examination and immunohistochemical stains can be necessary to determine whether a neoplasm extends to the margin of a surgical specimen).

Note 2 to entry: Laboratory examinations that determine a numerical value of a property are called "quantitative examinations"; those that determine the characteristics of a property are called "qualitative examinations".

[SOURCE: ISO 15189:2022, 3.8, modified — Note 1 to entry has been modified; Note 3 to entry has been removed.]

3.5
frozen section
intra-operative consultation
rapid *examination* (3.4) of a tissue sample during surgery to help with intra-operative decision making

3.6
laboratory user
individual or entity requesting services of the medical laboratory

Note 1 to entry: Laboratory user can include patients, clinicians, surgeons, practitioners, requestors and other persons, laboratories or institutions that send samples for examination.

[SOURCE: ISO 15189:2022, 3.16, modified — Note 1 to entry has been modified.]

3.7
gross examination
macroscopic examination
examination (3.4) to determine and record the characteristics and features of a tissue sample, and includes dissection of a tissue sample, often performed to select samples for microscopic evaluation from a primary sample

Note 1 to entry: Features of a tissue sample can include size, weight, visual description and lesions, such as tumours.

Note 2 to entry: Gross examination includes tissue transfer of small biopsies not needing dissection due to size.

3.8
pathologist
medical doctor practicing pathology

Note 1 to entry: Pathologists include general and specialized pathologists (e.g. cytopathologist) who perform examinations, render diagnoses and provide advisory services to laboratory users.

Note 2 to entry: In some countries, settings or situations, individuals other than pathologists can perform examinations, render diagnoses and provide advisory services to laboratory users (e.g. cytotechnologists, biomedical scientists).

3.9
primary sample
specimen
discrete portion of a body fluid or tissue or other sample associated with the human body taken for *examination* (3.4), study or analysis of one or more quantities or characteristics to determine the character of the whole

Note 1 to entry: The International Medical Device Regulators Forum (IMDRF) uses the term specimen in its harmonized guidance documents to mean a sample of biological origin intended for examination by a medical laboratory.

Note 2 to entry: Sample, according to ISO 15189, refers to one or more parts taken from a primary sample. Both definitions apply to anatomic pathology (AP), but primary sample and sample are often used synonymously. Users may use the specific term, especially when that distinction is required. Using specimen instead of primary sample or sample is acceptable.

Note 3 to entry: In AP, a sample is often called a specimen and these words can be considered synonymous.

[SOURCE: ISO 15189:2022, 3.25, modified —Notes 2 and 3 to entry were added.]

4 General requirements

4.1 Anatomic pathology (AP) laboratory

An AP laboratory, like other sections of the medical laboratory, uses materials derived from the human body for the purpose of providing information for the diagnosis, management, prevention, and treatment of disease in, or assessing the health of, human beings. The AP laboratory also provides advisory services, including the interpretation of results and offering advice on further examinations and other appropriate actions.

AP operates in close association with surgeons and interventionalists who perform operations and obtain biopsy samples. Surgeons and interventionalists are technical experts who obtain tissue for diagnostic purposes, but treatment decisions are often made by other members of the healthcare team. Thus, AP has several users: the patient, the person obtaining the tissue and the person using the tissue examination results to direct treatment.

The tissue obtained from patients can be used for rendering a diagnosis and also for biomedical research. Therefore, addressing impartiality, confidentiality and patient needs in AP requires consideration of various stakeholders (Figure 1). Several interests within and outside the AP laboratory deserve attention when building the AP management system and risk management plan.

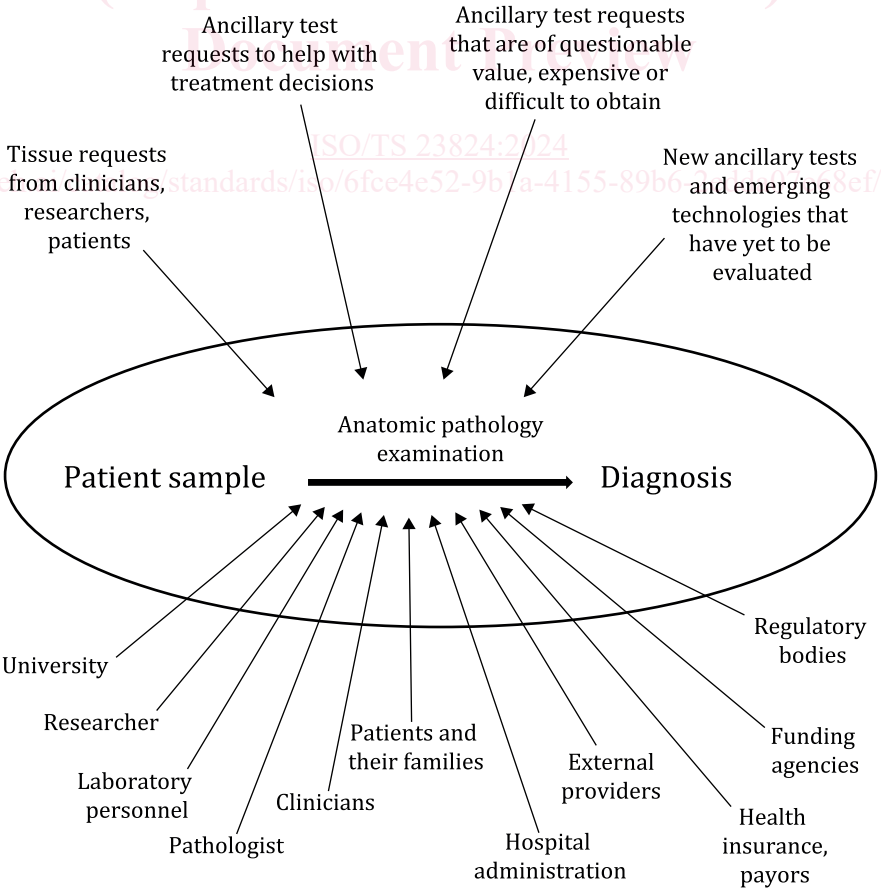

Figure 1 — Outside interests influencing anatomic pathology (AP) processes

4.2 Examples of process actions and risks for general requirements of ISO 15189

Table 1 shows examples of actions that can meet the ISO 15189:2022, Clause 4 requirements as applied to the AP laboratory's processes and also shows examples of risks in the AP laboratory for those processes.

NOTE 1 The actions and risks listed here are not comprehensive, but merely examples for guidance. Conformance with every item in Table 1 does not imply conformance with ISO 15189.

NOTE 2 ISO 22367 provides details for managing risk in medical laboratories.

Table 1 — Examples of process actions and risks for ISO 15189:2022, Clause 4

ISO 15189:2022 subclause	Actions for process management to meet ISO 15189:2022 requirements in the AP laboratory	Examples of risks in the AP laboratory
4.1 Impartiality	— Manage the professional and personal relationships of personnel with manufacturers and suppliers of instruments, reagents, antibodies, probes, etc. — Assess the influence of the several roles in an academic organization (e.g. research, teaching, clinical care) or across several organizations on patient care and take action to remove any conflicts of interest.	— Pathologists assuring impartiality can themselves be subject to conflicts of interest. — Research applications or methodologies that can inappropriately influence patient care. — Purchasing decisions driven by an individual instead of a group. — Financial compensation for expert witness activity that provides an incentive for one examination or diagnosis over another. — Not removing a pathologist from a case or project if impartiality is threatened.
4.2 Confidentiality	— Know the contractual arrangements that allow the laboratory to release confidential information and develop a process for when and how to notify the patient. NOTE Contractual arrangements in AP can be a formal or legal arrangement to share personal information with research organizations, insurance companies, consultants or other third parties. — Remove patient identification from samples (paraffin blocks, slides) that are used for research.	— Security of slide or tissue transport between different sites. — Potential litigation from patient or patient advocate when patient samples are used without consent. — Unintended release of patient information with research samples. — Consent not retrievable for use of materials in the future. — Cases or material taken out of the laboratory (e.g. for referral examinations or reporting at another site or at home) can lead to inadvertent breach of patient confidentiality if materials are lost or stolen.

Table 1 *(continued)*

ISO 15189:2022 subclause	Actions for process management to meet ISO 15189:2022 requirements in the AP laboratory	Examples of risks in the AP laboratory
4.3 Requirements regarding patients	— Specify who is responsible for acquiring informed consent for the use of samples beyond routine laboratory examinations. — Specifically include AP in a patient's consent for research. — Establish a point of contact for patients to communicate with AP. — When reviewing examinations for appropriateness and necessity, include gross examination (e.g. sampling protocols), microscopic examinations (e.g. application of interpretive guidelines and reporting schemes), and other examinations (e.g. predictive marker or genomic testing). — Decide when it is appropriate to disclose to patients any incidents that resulted or could have resulted in patient harm. — Provide reports for patients who have died since the sample was obtained. — Share any ethical considerations with patients.	— Prioritizing AP service to the submitting physician instead of service to the patient. — Performance or selection of an examination based on cost or payment. — Obtaining referral examinations based on routines and traditions rather than what is best for the patient. — Discrimination based on patient ability to pay for examinations.

5 Structural and governance requirements

5.1 Structure of a management system

Two kinds of structures are implied in the management system requirements of ISO 15189:

a) the laboratory's organizational structure (e.g. leadership, laboratory sections);

b) the structure of the management system.

Organizational structure is often displayed graphically, such as in an organizational chart that shows people and laboratories connected by lines in a hierarchy.

Management system structure comprises mission and vision statements, policies, objectives, processes, and procedures. Laboratory management defines the goals in a set of policies. Processes transform the intent of the policies into actions for the work needed to achieve the objectives. The laboratory's stated objectives typically measure progress towards goals to achieve and are the "outcome measures" of laboratory processes and procedures. Records can provide evidence of whether processes have been implemented and are effective.

The laboratory can use two kinds of metrics. First, measuring whether the objectives were met indicates the overall success of the process, but does not detail its functionality. An objective can be met by chance with a non-functioning process or by process errors that cancel each other. Second, measuring quality indicators at different stages of the process provides information about process performance.

EXAMPLE Showing that every report includes all immunohistochemical stains performed can tell the laboratory that the objective was met. However, also showing that half the reports were revised by the pathologist to add missing stains, shows that the reporting process is flawed, and the reporting of stains is easily missed, resulting in extra work for the pathologist and introducing unnecessary risks, such as overworked pathologists and inaccurate charging.