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Manufacturers' considerations for in vitro diagnostic medical devices in a public health emergency

Aspects à prendre en compte par les fabricants de dispositifs médicaux de diagnostic in vitro en situation d'urgence de santé publique

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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 documents 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

During a pandemic, accurate identification and isolation of infected individuals is an effective initial response to secure public health and safety before vaccines are available. The coronavirus disease of 2019 (COVID-19) posed an unprecedented public health emergency, causing many countries to impose restrictions on travel and daily activities to slow the spread of infection. An example where the spread of COVID-19 infection was demonstrated to have been slowed before vaccines became available has been published.[1] Here, a series of interventions, such as the urgent introduction of appropriate emergency use in vitro diagnostic (emergency use-IVD) medical devices, aggressive testing, rigorous contact tracing, etc., were applied in the early stage of the pandemic. Such a series of interventions effectively slowed the spread of infections and succeeded in maintaining public health and safety without the collapse of intensive care capabilities.

Often, regulatory authorization of in vitro diagnostic (IVD) medical devices takes months to a year or more to review and approve under a traditional regulatory pathway. Following a global infectious disease outbreak such as severe acute respiratory syndrome (SARS) or Middle East respiratory syndrome (MERS), the need for an accelerated regulatory pathway to facilitate the introduction of emergency use-IVD medical devices was recognised. While such pathways (i.e. emergency use authorization processes) have been implemented, the processes for authorization are neither well established nor harmonized.[2-14]

While some international guidance is available for the minimum requirements for an IVD medical device in a public health emergency, the regulatory requirements can differ from one jurisdiction to another. For example, information on the quality system (e.g. ISO 13485), developmental history, or raw materials/manufacturing methods are required when a manufacturer applies for the accelerated regulatory pathway in some countries but not in others. Also, some countries require a stability shelf life claim, but the level of evidence required to demonstrate stability during the initial application varies by region.[2,11,16,17] In an urgent situation such as a pandemic, the application of non-standardized requirements can impede implementation of the use of emergency use-IVD medical devices that are critical in protecting global public health.

This document provides minimum requirements, which span pre-market to post-market activities, to accelerate the availability of IVD medical devices in a public health emergency.

Manufacturers' considerations for in vitro diagnostic medical devices in a public health emergency

1 Scope

This document provides guidance to manufacturers on the minimum requirements for the lifecycle management of in vitro diagnostic (IVD) medical devices that are developed in preparation for and in response to a public health emergency involving infectious agents requiring immediate availability of authorized IVD devices.

NOTE This document does not replace existing national (or regional) regulatory pathway requirements for IVD medical devices under non-emergency situations. The regulatory authorization process of emergency use-IVD medical devices is country-specific and it includes:

— following a risk management process;

— monitoring the device's post-market performance and quality assurance;

— implementing a communication system.

2 Normative references

There are no normative references in this document.

3 Terms and definitions

For the purposes of this document, the following terms and definitions 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
adverse event
untoward medical occurrence, inappropriate patient management decision, unintended disease or injury, or untoward clinical sign in subjects, users, or other persons, with any connection to study related activities, whether or not related to the *IVD medical device* (3.9) under investigation

Note 1 to entry: Adverse events can be caused by, for instance, insufficient or inadequate instructions for use, deployment, installation, operation, or any malfunction of the IVD medical device under investigation.

Note 2 to entry: This definition includes the malfunction or deterioration of a device which has not yet caused death or serious injury, but which can lead to death or serious injury.

Note 3 to entry: This definition is not intended to be used in determining whether an event is reportable to a regulatory authority.

Note 4 to entry: For users or other persons, this definition is restricted to events related to investigational IVD medical devices.

Note 5 to entry: False negative or false positive results are not considered adverse events unless, in an interventional study, inappropriate patient management decisions are made based on those false results.

[SOURCE: ISO 20916:2019, 3.2]

3.2
analytical performance
ability of an *IVD medical device* (3.9) to detect or measure a particular analyte or measurand

Note 1 to entry: In metrological terms, this is referred to as performance of a measuring instrument or measuring system.

[SOURCE: ISO 18113-1:2022, 3.2.3, modified — in the definition, "or measurand" was added; Note 1 to entry was added.]

3.3
analytical sensitivity
quotient of the change in a measurement indication and the corresponding change in a value of a quantity being measured

Note 1 to entry: The sensitivity of a measurement procedure can depend on the value of the quantity being measured.

Note 2 to entry: The change considered in the value of the quantity being measured shall be large compared with the resolution.

Note 3 to entry: The analytical sensitivity of a measuring system is the slope of the calibration curve.

Note 4 to entry: Analytical sensitivity should not be used to mean detection limit or quantitation limit and should not be confused with diagnostic sensitivity.

Note 5 to entry: In metrological terms, this is referred to as measurement sensitivity.

[SOURCE: ISO 18113-1:2022, 3.2.4, modified — the preferred term "sensitivity of a measurement procedure" was removed; Note 5 to entry added.]

3.4
clinical performance of an IVD medical device
clinical performance
ability of an *IVD medical device* (3.9) to yield results that are correlated with a particular clinical condition or physiological/pathological process/state in accordance with the intended use (clinical test purpose, target population and intended user)

Note 1 to entry: In accordance with intended use, clinical performance can include expected values, diagnostic sensitivity and diagnostic specificity based on the known clinical condition or physiological/pathological process/state of the individual, and negative and positive predictive values based on the prevalence of the disease.

[SOURCE: ISO 20916:2019, 3.10, modified — the preferred term "clinical performance" was added.]

3.5
clinical performance study
study undertaken to establish or confirm the *clinical performance of an IVD medical device* (3.4)

Note 1 to entry: Testing performed pre-market that is not designed to address clinical performance of an IVD medical device is not considered a clinical performance study (e.g. customer feedback studies, external analytical performance studies, research studies).

[SOURCE: ISO 20916:2019, 3.11]

3.6
complaint
electronic or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, usability, safety or performance of a medical device that has been released from the organization's control or related to a service that affects the performance of such medical devices

Note 1 to entry: This definition of "complaint" differs from the definition given in ISO 9000:2015.

[SOURCE: ISO 13485:2016, 3.4]

3.7
infectious agent
pathogen
infectious micro-organism or agent, such as a virus, bacterium, protozoan, prion, viroid, or fungus that can cause disease

[SOURCE: ISO/TS 16975-4:2022, 3.16, modified — Note 1 to entry has been removed.]

3.8
intended use
objective intent of an IVD *manufacturer* (3.11) regarding the use of a product, process or service as reflected in the specifications, instructions and information supplied by the IVD manufacturer

Note 1 to entry: Intended use statements for IVD labelling can include two components: a description of the functionality of the *IVD medical device* (3.9) (e.g. an immunochemical measurement procedure for the detection of analyte "x" in serum or plasma), and a statement of the intended medical use of the examination results.

Note 2 to entry: The intended use can include the indications for use.

[SOURCE: ISO 18113-1:2022, 3.1.37]

3.9
in vitro diagnostic medical device
IVD medical device
medical device, whether used alone or in combination, intended by the *manufacturer* (3.11) for the in vitro examination of specimens derived from the human body solely or principally to provide information for diagnostic, monitoring or compatibility purposes

Note 1 to entry: IVD medical devices include reagents, calibrators, control materials, specimen receptacles, software, and related instruments or apparatus or other articles and are used, for example, for the following test purposes: diagnosis, aid to diagnosis, screening, monitoring, predisposition, prognosis, prediction, determination of physiological state.

Note 2 to entry: In some jurisdictions, certain IVD medical devices can be covered by other regulations.

[SOURCE: ISO 18113-1:2022, 3.1.33]

3.10
leftover specimen
leftover sample
unadulterated remnants of human derived specimens collected as part of routine clinical practice and after all standard analyses have been performed

Note 1 to entry: Such specimens/samples would be otherwise discarded as there is no remaining clinical need for them.

Note 2 to entry: This can include specimens collected for research or other purposes not connected to the *clinical performance study* (3.5) in question.

[SOURCE: ISO 20916:2019, 3.25]

3.11
manufacturer
natural or legal person with responsibility for design and/or manufacture of a medical device with the intention of making the medical device available for use under that person's name, whether or not such a medical device is designed and/or manufactured by that person or on that person's behalf by another person(s)

Note 1 to entry: Provisions of national or regional regulations can apply to the definition of manufacturer.

Note 2 to entry: 'Design and/or manufacture' can include specification development, production, fabrication, assembly, processing, packaging, repackaging, labelling, relabelling, sterilization, installation, or remanufacturing of a medical device; or putting a collection of devices, and possibly other product, together for a medical purpose.

Note 3 to entry: An authorized representative, distributor or importer who only adds its own address and contact details to the medical device or the packaging, without covering or changing the existing labelling, is not considered a manufacturer.

Note 4 to entry: Any person who assembles or adapts a medical device that has already been supplied by another person for an individual patient, in accordance with the instructions for use, is not the manufacturer, provided the assembly or adaptation does not change the intended use of the medical device.

Note 5 to entry: to the extent that an accessory is subject to the regulatory requirements of the *IVD medical device* (3.9), the person responsible for the design and/or manufacture of that accessory is considered to be a manufacturer.

[SOURCE: ISO 18113-1:2022, 3.1.42]

3.12
pandemic
epidemic occurring worldwide, or over a very wide area, crossing international boundaries and usually affecting a large number of people

[SOURCE: ISO 6028:2023, 3.3]

3.13
post-market surveillance
systematic process to collect and analyse experience gained from medical devices that have been placed on the market

[SOURCE: ISO/TR 20416:2020, 3.2]

3.14
post-production
part of the life cycle of the medical device after the design has been completed and the medical device has been manufactured

EXAMPLE Transportation, storage, installation, product use, maintenance, repair, product changes, decommissioning and disposal.

[SOURCE: ISO 14971:2019, 3.12]

3.15
public health emergency
extraordinary event which is determined to constitute a public health risk to regions or countries through the international spread of disease and to potentially require a coordinated international response

[SOURCE: WHO/IHR:2005[18]]

3.16
quality management
management with regard to quality

Note 1 to entry: Quality management can include establishing quality policies and quality objectives, and processes to achieve these quality objectives through quality planning, quality assurance, quality control, and quality improvement.

[SOURCE: ISO 9000:2015, 3.3.4]

3.17
risk management
systematic application of management policies, procedures and practices to the tasks of analysing, evaluating, controlling and monitoring risk

[SOURCE: ISO/IEC Guide 63:2019, 3.15]