International Organization for Standardization
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Международная организация по стандартизации

STRATEGIC BUSINESS PLAN – ISO/TC 194, BIOLOGICAL AND CLINICAL EVALUATION OF MEDICAL DEVICES – 2024 version

Executive summary

The focus of ISO/TC 194 is the biological and clinical evaluation of medical devices, i.e., ISO/TC 194 develops standards for the biological evaluation and testing of medical devices and materials contacting the human body and for the clinical investigation and evaluation of medical devices. The standards developed by ISO/TC 194 are horizontal standards which can be suitable for all medical devices.

The key benefits expected are contributions to:

- Improvements in the quality and the safety of medical devices worldwide and to
- Protection of the patient by providing an appropriate and adequate basis for evaluating and certifying medical devices.

The work of ISO/TC 194 is expected to facilitate growth and security in the global market economy by developing and sharing appropriate high-quality medical device standards.
Furthermore, ISO/TC 194 has the goal to replace animal-based testing procedures with alternative methods whenever appropriate.

1 Introduction

1.1 ISO technical committees and business planning

The extension of formal business planning to ISO Technical Committees (ISO/TCs) is an important business review activity. The aim is to align the ISO work programme with expressed business environment needs and trends and to allow ISO/TCs to prioritize among different projects, to identify the benefits expected from the availability of International Standards, and to ensure adequate resources for projects throughout their development.

1.2 International standardization and the role of ISO

The foremost aim of international standardization is to facilitate the exchange of goods and services through the elimination of technical barriers to trade.

Three bodies are responsible for the planning, development and adoption of global International Standards: ISO (International Organization for Standardization) is responsible for all sectors excluding Electrotechnical, which is the responsibility of IEC (International Electrotechnical Committee), and most of the Telecommunications Technologies, which are largely the responsibility of ITU (International Telecommunication Union).

ISO is a legal association, the members of which are the National Standards Bodies (NSBs) of some 164 countries (organizations representing social and economic interests at the international level), supported by a Central Secretariat based in Geneva, Switzerland.

The principal deliverable of ISO is the International Standard.

An International Standard embodies the essential principles of global openness and transparency, consensus and technical coherence. These are safeguarded through its development in an ISO Technical Committee (ISO/TC), representative of all interested parties, supported by a public comment phase (the ISO Technical Enquiry). ISO and its Technical Committees are also able to offer the ISO Technical Specification (ISO/TS), the ISO Public Available Specification (ISO/PAS) and the ISO Technical Report (ISO/TR) as solutions to market needs. These ISO products represent lower levels of consensus and therefore do not have the same status as an International Standard.

ISO also offers the International Workshop Agreement (IWA) as a deliverable which aims to bridge the gap between the activities of consortia and the formal process of standardization represented by ISO and its national members. An important distinction is that the IWA is developed by ISO workshops and fora, comprising only participants with direct interest, and so it is not accorded the status of an International Standard.

2 ISO/TC 194 business environment

2.1 Business environment description

The following political, economic, technical, regulatory, legal and social dynamics describe the business environment of the industry sector, products, materials, disciplines or practices related to the scope of this ISO/TC, and they may significantly influence how the relevant standards development processes are conducted and the content of the resulting standards:

The market for medical devices is a global market and is changing constantly due to the vast number of medical devices and the continuous development of new products and new materials (e.g., polymers, metals, ceramics and materials of human or animal origin). Major factors potentially impacting the development of medical device markets include, but are not limited to, the following:

- Industry concentration into larger units.
- Demographic changes, particularly in the developed nations of the western world. A continuing trend is for the proportion of the elderly in the population to increase, thereby increasing the demand for medical devices worldwide.
- The establishment in 1994 of the World Trade Organization, which supports, as the basis for international trade, the development of international standards.
- The issue common to all healthcare categories, of constantly rising patient expectations, with only the best available solution being acceptable. The best available solution should reflect an understanding of physical differences between genders, ethic groups, and age groups.
- Mutual recognition of conformity assessments by different authorities facilitating market approval or clearance.
- Litigation following patient injury is rapidly increasing in some parts of the world, and compliance with international standards is increasingly being used to support arguments on the adequacy or otherwise of medical devices in courts of law.

The focus of ISO/TC 194 is biological and clinical evaluation of medical devices. ISO/TC 194 develops standards for:

- The overall framework of biological and clinical evaluation;
- Practices and test methods which support biological and clinical evaluations and related reporting;
- Good Clinical Practice (GCP) for clinical investigations of medical devices in human subjects.

The standards developed by ISO/TC 194 are horizontal standards which can be suitable for all types of medical devices and, with respect to biological evaluation, medical device materials, in the context of their use. The standards generally do not include acceptance criteria, which are context specific. Some standards provide best practice methods that may help define the acceptance criteria e.g., statistical methods under GCP.

Interested parties for the various device types may vary but they include, in general: regulatory authorities, manufacturers of medical devices, SME's and their trade associations, clinical and other healthcare practitioners of various disciplines, patients, contract research organizations (CROs), test houses, scientific research institutes (academic institutions and other stakeholders) and consumers.

The value of ISO/TC 194 standards cannot be directly related to the economic value of the medical device production and trade but is rather more related to the therapeutic benefits arising from access to those devices, the associated device risks and the clinical evidence gaps related to the medical devices and their use.

Risks related to biological safety or failure to demonstrate adequate clinical evidence of safety and performance for medical devices used as indicated in humans are relevant

worldwide. The aim of ISO/TC 194 is to have optimal alignment with all interested member bodies.

The feasibility of worldwide alignment is dependent on many highly variable aspects, not limited to: legislation, political factors, responsibilities of authorities having jurisdiction and manufacturer compliance.

The environments in which ISO 10993, ISO 22442, ISO 14155 and related documents are used is characterized by the legislation and by market aspects.

Standards development is stimulated by global harmonization agreements between regulatory bodies for medical devices; for example, by the International Medical Devices Regulatory Forum (IMDRF) comprising regulatory authorities from some jurisdictions. IMDRF takes a direct interest in the development and implementation of TC/194 standards and promotes their use amongst members.

Regulatory requirements from global regulatory regions often influence the content of standards.

2.2 Business environment quantitative indicators

The following list of quantitative indicators describes the business environment in order to provide adequate information to support ISO/TC 194 actions:

Every country has a medical device market divided into two categories:

- Professional Use: by clinical practitioners;
- Consumer use: by lay users, usually in the home environment.

Manufacturers and suppliers range from large multinational corporations to small and medium enterprises. The industry is global, with substantial manufacturing and development presence worldwide.

The market is generally highly regulated. Much of the world's population has limited access to medical devices for economic reasons. Efforts are made by non-for-profit organizations to improve access to medical devices compliant with these standards.

The market environment in which ISO/TC 194 operates is the result of the value now attaching to medical devices throughout the world. This has led to an increasing demand for medical devices.

Interest in medical device technology, including the use of artificial intelligence and machine learning in medical devices, is great and, in most countries, medical device uses and innovations are growing. The growing international trade in medical devices is stimulating the ongoing standardization work of ISO/TC 194.

ISO/TC 194 standards cover biological and clinical evaluations related to medical device safety and performance or effectiveness and these standards include practices and test methods to support medical device development in compliance with international legal, regulatory and other requirements.

3 Benefits of ISO/TC 194 standards

The key benefits expected from ISO/TC 194 standards are contributions to:

- Improve quality, safety and clinical performance of medical devices;
- Improve patient access to medical devices;
- Increase internationally harmonized technical requirements;
- Facilitate the global, state-of-the-art, medical device trade;
- Improve ethical benefits and scientific evidence worldwide;
- Improve methods to demonstrate globally-marketed medical device safety and performance in response to standardization; and to
- Address animal welfare concerns (e.g., ISO/TC 194/WG 3 is developing and publishing ISO 10993-2 to specify minimum requirements for animals used in biological testing, establishing guidelines to respect life, minimize suffering and to

reduce both the number of animal experiments and the number of animals used during medical device development for human uses).

ISO/TC 194 standards are widely recognized in many jurisdictions although local interpretations and specific international regulatory requirements may still vary. Mutual legislative agreements between governments continue to develop as harmonized standards facilitate improved biological and clinical evaluations to improve medical device quality and safety and to expedite time to market and reduce costs for all medical devices used globally.

Focusing on new and innovative directions in medical device regulations, biomaterial development, medical device design, biological and clinical evaluation includes:

- Using a structured plan;
- Characterizing materials, additives and leachable substances;
- Designing, applying and interpreting appropriate toxicity and biocompatibility tests;
- Characterizing and assessing tissue response and biological/toxicological risk; and
- Demonstrating acceptable clinical and biological risks in relation to the clinical benefits.

Public demand for and awareness of standardized medical device biological and clinical test and evaluation methods is growing, especially for the thousands of new and innovative medical devices and materials entering the global healthcare markets every year.

4 ISO/TC 194 representation and participation

Active membership and participation are described on the committee website at https://www.iso.org/committee/54508.html.

Basically, active ISO/TC 194 participants include:

- A wide array of clinical, scientific and engineering professionals,
- Manufacturers and manufacturers' associations,
- CROs, test houses and certification bodies,
- Regulators, and
- Academic experts and physicians/users.

5 ISO/TC 194 objectives and strategies

5.1 ISO/TC 194 defined objectives

The ISO/TC 194 main objective is to draft suitable, internationally-applicable standards for biological and clinical evaluation of medical devices.

ISO/TC 194 contributes directly to public health and well-being by developing medical device standards used by manufactures to ensure their medical devices do not compromise biological and clinical safety during the intended patient use. Its activities are intended to encourage and support innovation and ethical practices in the development and provision of medical devices through operational guidance to manufacturers that is applicable throughout the lifespan of a product.

ISO/TC 194 global outcomes include:

- Improved protection of patient and user health and safety ;
- More consistent biological evaluations and clinical investigations;
- Improved protection of patient and user rights and well-being;
- More consistent reference materials;
- More consistent terms and definitions;
- Better international alignment on medical device verification and validation requirements;
- More effective and efficient standards development;

- Reduced trade barriers.

A) Revision coordination

The ISO/TC 194 investigates the need to adapt published standards to the most recent views in development of biological and clinical evaluations.

B) Implementing criteria for acceptance of New Work Items (NWI's)

The ISO/TC 194 accepts NWI's for the ISO/TC 194 work programme after carefully considering many factors including, but not limited to:

- health risks arising from the use of medical devices, including those arising from hazardous materials of construction and manufacturing processes;
- market need to standardize a specific subject;
- feasibility in terms of expertise, availability of experts, valid test methods, etc. and
- availability and adequacy of other standards including, product standards containing specific requirements for specific application areas, monographs, etc.

C) (Re-)activation liaisons

While ISO biological evaluation and clinical investigation standards were prepared in the past, other (vertical) standards were also developed and ISO/TC 194 works diligently to advise other ISO technical committees on aspects concerning relevant biological and clinical evaluation details and to align requirements in vertical standards to those in horizontal standards to ensure an optimal use of ISO 10993 series, ISO 14155, ISO 22442 and other related standards by other technical committees and to minimize the necessity for additional requirements.

5.2 ISO/TC 194 work strategies

ISO/TC 194 includes nineteen working groups intending to meet annually during five days ending with the plenary meeting and preceded by a meeting of the Chairman's Advisory Group.

ISO 10993, ISO 14155, ISO 22442 and other related standards describe procedures to generate systematic approaches to biological and clinical evaluation, including minimum evaluation requirements. Within these standards, the processes required to manage biological and clinical risks are defined and standardized. These standards also specify the rationales behind and the selection of specific tests and evaluation methods. Specific standards provide test methods (*in vitro* and *in vivo*) or provisions necessary for test application including, but not limited to: sample preparation, reference materials, toxicokinetic studies, animal welfare, human subject protection requirements, etc.

These standards strive to prevent unnecessary testing by focusing on the necessary testing requirements and ISO/TC 194 has adopted the following strategies to continue striving for excellence in international standards development:

- Maintain, and where necessary add to, current liaisons with ISO/TC 76, ISO/TC 84, ISO/TC 106, ISO/TC 121, ISO/TC 150, ISO/TC 157, ISO/TC 172, ISO/TC 173, ISO/TC 198, ISO/TC 210, ISO/TC 212, ISO/TC 229, ISO/TC 304 and IEC/TC 124.
- Continue working in close co-operation with CEN/TC 206, CEN/TC 352 and use Vienna agreement processes to develop common documents with CEN.
- Continue with current WG structure as justified by the work programme to develop standards in discrete biological and clinical evaluation areas.
- Continue with one advisory group responsible for recommending the standardization strategy (WG 15), and one overall management group (the Chairman's Advisory Group).
- Continue annual plenary meetings for working group business to be transacted and supplemented with email/telephone discussions and other virtual or face-to-face meetings held only when needed and justified.
- Ensure NWI proposals are properly justified to meet market needs and ISO/TC

194 objectives.
- Continue critical existing standards reviews and rationalize or withdraw standards when justified.

6 Factors affecting ISO/TC 194 work programme

Keeping ISO/TC 194 standards internationally consistent and up to date is challenging especially since ISO/TC 194 is focused on areas of rapid scientific development. Early revision of published standards has been required on several occasions in order to keep the whole standards package aligned. Interrelated projects have required target dates to be modified frequently in order to mutually explain the new developments in the interlinked standards.

Critical success factors require the continued motivation of all parties concerned to achieve the common goals.

For ongoing standards writing, critical success factors include commitment to the work programme, development of available resources and coordination of activities.

7 ISO/TC 194 structure, current projects and publications

The ISO/TC 194 webpage is found at: ISO/TC 194 on ISO Online and includes the following linked information:

- About (Secretariat, Committee Manager, Chair, Date of creation, Scope, etc.)
- Contact details
- Structure (Subcommittees and working groups)
- Liaisons
- Meetings
- Tools

The work programme is provided including published standards and standards under development along with reference information (e.g., Glossary of terms and abbreviations used in ISO/TC Business Plans and General information on the principles of ISO's technical work).