Implementation of Good Regulatory Practices within the Medical Device Regulatory Process including Use of International References & Standards for Medical Technology

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Background

The **World Health Organization** (WHO) urges public health authorities around the world to economize their limited public health resources by relying on international standards as a basis for national regulations and by relying on the conformity assessment results of other jurisdictions. The government funds required to develop a regulation in isolation, to test a product that has already been tested, or to certify products or processes that have already been certified are funds that a health agency can use to strengthen post-market surveillance, to digitize import review procedures, to modernize IT infrastructure, or to upgrade regulatory inventory.

Medical Device Sector Regulatory Convergence is a concerted public-private effort to systematically pursue and maximize alignment of medical device sector-specific technical regulations, standards and conformity assessment criteria to internationally harmonized global standards.

According to the WHO, more them two million different types of medical devices circulate on the world market, categorized into more than 22,000 groups of generic devices. The regulation of medical devices contributes to the reduction of potential risks arising from their use and allows the population access to safe, effective and high quality medical devices, contributing to better public health outcomes.

On the control of these products , it is important to implement a globally aligned approach that, at the same time, contributes to the access of safe products and do not impede innovation or create unnecessary barriers to trade.

In addition, the **World Trade Organization Technical Barriers to Trade (WTO/TBT) Agreement** aims to ensure that technical regulations, standards, and conformity assessment procedures are non-discriminatory and do not create unnecessary obstacles to trade. At the same time, it recognizes WTO members' right to implement measures to achieve legitimate policy objectives, such as the protection of human health and safety, or protection of the environment. The TBT Agreement strongly encourages members to base their measures on international standards as a means to facilitate trade. Through its transparency provisions, it also aims to create a predictable trading environment.

Good Regulatory Practices (GRP) refers to a formalized, mandatory, whole-of-government policy, that defines the common and transparent rules by which regulatory agencies develop technical regulations for all regulated sectors (i.e., cross-sector, transverse, horizontal, foundational) following international standards. GRP is the quality control mechanism for the development of regulations, ensuring on a continuous and systematic basis that government rules are relevant, of the highest quality, cost-effective, internationally aligned and least economically restrictive amongst alternatives of the same purpose.
International Standardization refers to the work conducted within international Standards Developing Organizations (SDOs) to develop and maintain the globally harmonized documents that define the ever-evolving technical criteria underpinning medical device design, performance, safety, interoperability, cyber-security, and regulation.

In the context of the MDRC, the following definitions and conventions will be used:

Tier 1 – Foundational Good Regulatory Practices – GRP (Whole of Government / Cross-Sectoral)

Tier 2 – Medical Device Specific Regulatory, Standards and Conformity Assessment Convergence

2a – Implementation of Good Regulatory Practices within the Medical Device Regulatory Process including Systemic and Prioritized Use of International References & Standards for MedTech

2b – Use of Specific International References & Standards for Medical Technologies

The proposed scope of MDRC work with PPB is focused on Tier 2 (a and b).

Assessment Topics:

Tier 2a – Implementation of Good Regulatory Practices within the Medical Device Regulatory Process including Systemic and Prioritized Use of International References & Standards for MedTech

Elements of Good Regulatory Practices[1]:

1. Ensuring transparency and stakeholder involvement in the development of standards, technical regulations and conformity assessment procedures:
   a) Producing regulatory forecasts.
   b) Maintaining a National Register of existing regulations.
   c) Publishing a proposed regulation for public comment.
   d) Publishing evidence or regulatory analysis that supports a proposed regulation.
   e) Providing a reasonable time period for public comment on a proposed regulation and making such comments publicly available.
   f) Taking into account and responding to public comment on a proposed regulation.
   g) Publishing final regulations and ensuring a reasonable period for the entry into force of regulations.
   h) Allowing for any interested person to submit to a regulatory authority written suggestions for the issuance, modification, or repeal of a regulation.

[1] APEC-OECD Integrated Checklist on Regulatory Reform

2. Maintaining internal processes or mechanisms that provide for consultation, coordination, and review among domestic authorities in the development of regulations, including for the purposes of ensuring consistency with international trade agreements and avoiding unnecessary burdens and duplication.

3. Using evidence-based decision-making and regulatory analysis:
   a) Relying on valid, reliable data and sound science.
   b) Placing risk assessment and risk management at the core of regulatory decision-making.
   c) Using evidence-based decision-making.
   d) Assessing the impact of regulations, including conducting Regulatory Impact Assessments (RIAs). Considering benefits and costs of the selected and other feasible alternatives, including the relevant impacts (such as economic, social, environmental, public health, and safety effects) as well as risks and distributional effects over time, recognizing that some costs and benefits are difficult to quantify or monetize.

4. Using international standards (as defined in the WTO/TBT Committee Decision) as the basis for regulations.

5. Leveraging international conformity assessment mechanisms.

6. Providing for independent judicial review of regulation.

7. Undertaking retrospective review of regulations for possible modification or repeal.

8. Establishing a Central Regulatory Coordination Body or Structure.

Tier 2b – Use of Specific International References & Standards for Medical Technologies

World Health Organization

1. Global Model Regulatory Framework for Medical Devices Including IVD Medical Devices (all), including:

Stepwise Approach (Section 4 – page 21)

Reliance and Recognition (Section 4.11 – page 21)

4.2 Basic-level controls and their enforcement (page 23)

4.2.1.2 – *"…The preferred, but optional, way by which the manufacturer may demonstrate conformity with the Essential Principles is to apply voluntary international standards that are appropriate and relevant. The law should include provisions allowing the regulatory authority to formally recognize such standards for that purpose (see section 4.3.1.3)…"*

4.3.1.3 – *"…At the expanded level, the regulatory authority may wish to establish a procedure to identify national versions of international standards that it accepts as providing presumption of compliance to*

specific Essential Principles, i.e. "recognized standards". Preference for recognition should be given to international standards, e.g. those of the International Organization for Standardization (ISO)and the International Electrotechnical Commission (IEC), regional standards and the national versions of international standards. It is also important that national standards correspond to the current version of international standards. As international standards are periodically revised, national standards will have to be revised accordingly and the authority should establish a transition period for manufacturers to adopt the new versions. To maintain the necessary flexibility in utilizing standards, it is better to adopt a system of recognizing standards through guidance documents or guidelines than placing the standards into legislation; they can then be updated to stay current and can be revised much faster than legislation can be updated.

2. Good regulatory practices in the regulation of medical products
…" A sound regulatory framework, including international norms and standards, and the recruitment and development of competent staff are necessary but not sufficient conditions to ensure "good oversight". All individuals in regulatory authorities should be guided by GRP in setting appropriate requirements and formulating decisions that are clear, transparent, consistent, impartial, proportionate, timely and based on sound science. Regulated parties and other stakeholders also play important roles in ensuring a clear, efficient regulatory environment so that quality-assured medical products are available to patients."

3. Good reliance practices in the regulation of medical products: high level principles and considerations
" WHO supports reliance on the work of other regulators as a general principle in order to make the best use of available resources and expertise. This principle allows leveraging the output of others whenever possible while placing a greater focus at national level on value-added regulatory activities that cannot be undertaken by other authorities, such as, but not limited to: vigilance, market surveillance, and oversight of local manufacturing and distribution. Reliance facilitates timely access to safe, effective, quality-assured medical products (see section 3. Scope) and can support regulatory preparedness and response, particularly during public health emergencies. Good reliance practices (GRelP) are anchored in overall good regulatory practices (GRP) (1), which provide a means for establishing sound, affordable, effective regulation of medical products as an important part of health system strengthening. If implemented effectively, GRP can result in consistent regulatory processes, sound regulatory decision-making, increased efficiency of regulatory systems and better public health outcomes. NRAs are encouraged to adopt GRP to ensure that they are using the most efficient regulatory processes possible."

4. Guidance for post-market surveillance and market surveillance of medical devices, including in vitro diagnostics
"Post-market surveillance is a set of activities conducted by manufacturers, to collect and evaluate experience gained from medical devices that have been placed on the market, and to identify the need to take any action. Post-market surveillance is a crucial tool to ensure that medical devices continue to be safe and well performing, and to ensure actions are undertaken if the risk of continued use of the medical device outweighs the benefit. The evaluation of post-market surveillance experiences can also highlight opportunities to improve the medical device."

International Medical Device Regulators Forum (IMDRF)

International Medical Device Regulators Forum (IMDRF) documents (all), including:

2a. IMDRF N47 – "Essential Principles of Safety and Performance of Medical Devices and IVD Medical Devices"

Annex A: Use of Standards in Meeting Essential Principles

B. Use of Standards by Regulatory Authorities having Jurisdiction

"These standards should, wherever possible, be standards incorporating the thinking of the global marketplace and help support the development of consistent expectations between Regulatory Authorities having jurisdiction. In the absence of international consensus standards, it may be appropriate for Regulatory Authorities having jurisdiction to accept the use of regional or national consensus standards or industry standards."

2b. IMDRF N51 – "Optimizing Standards for Regulatory Use"

B. Use of Standards by Regulatory Authorities having Jurisdiction

1.2 Role of standards in regulatory processes

2. Although regulatory processes among IMDRF regions differ, RAs [regulatory authorities] share the common objectives to ensure medical device safety and performance and to protect public health. International consensus standards are based upon science, technology and experience and generally reflect the best experience of industry, researchers, consumers, regulators and other experts worldwide. IMDRF members affirm their collective belief that reliance upon consensus standards is a key element of a robust regulatory framework. Appropriate use of standards will promote efficiencies and innovation while facilitating objective assessment of device safety and performance."

GHTF/SG1/N071/2012 – Definition of the terms "Medical Device" and In Vitro Diagnostic (IVD) Medical Device

GHTF/SG1/N055:2009 "Definitions of the Terms Manufacturer, Authorized Representative, Distributor and Importer

GHTF/SG1/N77:2012 - Principles of Medical Devices Classification

WG/N64FINAL:2021 - Principles of In Vitro Diagnostic (IVD) Medical Devices Classification (formerly GHTF/SG1/N045:2008)

IMDRF/GRRP WG/N52 FINAL:2019 Principles of Labelling for Medical Devices and IVD Medical Device

IMDRF/UDI WG/N7FINAL:2013 - UDI Guidance Unique Device Identification (UDI) of Medical Devices

IMDRF MDCE WG/N57FINAL:2019 (formerly GHTF/SG5/N3:2010) - Clinical Investigation

IMDRF MDCE WG/N56FINAL:2019 (formerly GHTF/SG5/N2R8:2007) - Clinical Evaluation

IMDRF MDCE WG/N55 FINAL:2019 (formerly GHTF/SG5/N1R8:2007) - Clinical Evidence - Key Definitions and Concepts

Medical Device Single Audit Program (MDSAP)

The **Medical Device Single Audit Program** is a global approach to auditing and monitoring the manufacturing of medical devices. This program, launched in January 2014, with the participation of Health Authorities from Brazil, Australia, Canada, US and Japan, has the mission of "strategically accelerate international medical device regulatory convergence to promote an efficient and effective

regulatory model for medical devices that is responsive to emerging challenges in the sector while protecting and maximizing public health and safety".

International Standards

ISO Guidance on use of International Standards, among others:

ISO Guide 21-1 "Regional or national adoption of International Standards and other International Deliverables — Part 1: Adoption of International Standards"

0.2 International Standards are widely adopted at the regional or national level and applied by manufacturers, trade organizations, purchasers, consumers, testing laboratories, authorities and other interested parties. Since these standards generally reflect the best experience of industry, researchers, consumers and regulators worldwide, and cover common needs in a variety of countries, they constitute one of the important bases for the removal of technical barriers to trade. This has been explicitly acknowledged in the Agreement on Technical Barriers to Trade of the World Trade Organization (WTO TBT Agreement).

It is important that every effort be made to adopt and use International Standards as regional or national standards and, consequently, to withdraw conflicting regional or national standards as soon as practicable for the reasons mentioned above. Only by developing a global approach can the benefits of standardization be fully realized. However, full adoption may not be practicable in all cases for reasons such as regional or national security, protection of human health or safety, or protection of the environment, or because of fundamental climatic, geographical or technological problems. The WTO TBT Agreement recognizes that these are legitimate reasons for regional or national deviations.

0.3 The adoption of an International Standard as a regional or national standard will be extremely difficult if the regional or national rules or traditions concerning structure and layout of regional or national standards differ from those of the standard being adopted. It is therefore recommended to apply, as far as possible, the ISO/IEC Directives, Part 2, for the preparation of regional and national standards.

Even for the cases referred to in 0.2, every effort should be made to reduce the deviations to a rational minimum. Moreover, where deviations from International Standards exist, it is important to identify the deviations clearly and to state the reasons for the deviations. If International Standards are adopted only by means of a re-edited version, it is extremely difficult to identify the technical deviations owing to the presentation differences (that is differences in the structure and wording) of the original standard. On the other hand, a clearly identified deviation will have a tendency to disappear because as long as it remains visible, the question as to whether it is still necessary will arise repeatedly, while a hidden deviation may not disappear even when no longer justified.

0.4 It is recommended that as much information as possible be given about the correspondence of regional or national standards that adopt International Standards (or are based on them). This information should be displayed in a prominent place on the regional or national standard (preferably on the title page and in the foreword), in standards lists, catalogues, year-books and any other media for retrieval purposes. When quoting an International Standard, at least its number and date of publication should be given. If a regional or national standard does not exist materially (for example, if the International Standard has been adopted by the endorsement method), this information about correspondence should be given in standards listing media as mentioned above."

Basic Standards Package

Over 200 international standards from standards developing organizations (SDOs) are used my medical device regulatory authorities and industry for regulatory purposes.

The MDRC project recommends and contemplates the NRA codified recognition and/or use of the following indicative list of international standards for medical technologies as a foundational basis upon which to build, noting that customizations may be made pending the outcome of the mutually agreed-upon workstreams deriving from the triaged comparison of NRA and COVID-19 needs.

SDO	TC / WG	Secretariat	Standard	Title
ISO	ISO TC 210	US/ANSI/AAMI	ISO 13485:2016	Medical devices — Quality management systems — Requirements for regulatory purposes
	ISO TC 210	US/ANSI/AAMI	ISO 14971:2019	Medical devices — Application of risk management to medical devices
	ISO TC 194	Germany/DIN	ISO 14155:2020	Clinical investigation of medical devices for human subjects — Good clinical practice
	ISO TC 210	US/ANSI/AAMI	ISO 14971:2019	Medical devices — Application of risk management to medical devices
	ISO TC 210	US/ANSI/AAMI	ISO 15223-1:2021	Medical devices — Symbols to be used with medical device labels, labelling and information to be supplied — Part 1: General requirements
	ISO TC 210	US/ANSI/AAMI	ISO/TR 20416:2020	Medical devices — Post-market surveillance for manufacturers
	ISO TC 212	US/ANSI/CLSI	ISO 23640:2011	In vitro diagnostic medical devices — Evaluation of stability of in vitro diagnostic reagents
IEC	IEC TC 62/SC 62A	US/ANSI/USNC	IEC 60601-1-11:2015	Medical electrical equipment — Part 1-11: General requirements for basic safety and essential performance — Collateral standard: Requirements for medical electrical equipment and medical electrical systems used in the home healthcare environment

ASTM International	**ASTM F04.42**		ASTM F 2027-16	Standard Guide for Characterization and Testing of Raw or Starting Materials for Tissue-Engineered Medical Products
	ASTM F04.42		ASTM F2212-20 (ASTM F2212-19)	Standard Guide for Characterization of Type I Collagen as Starting Material for Surgical Implants and Substrates for Tissue Engineered Medical Products (TEMPs)
	ASTM F29.21		ASTM F2761-09 (2013)	Medical Devices and Medical Systems - Essential safety requirements for equipment comprising the patient-centric integrated clinical environment (ICE) - Part 1: General requirements and conceptual model