International standards management and a practical application at a national level

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MEDICAL DEVICE REGULATORY CONVERGENCE PROJECT (MDRC)

GOOD REGULATORY PRACTICES & TECHNICAL COMPETENCIES

South Africa Health Products Regulatory Authority (SAPHRA) & Regulated Sector

16th November 2023

Simone Rudolph-Shortt

MDMSA
Medical Device Manufacturers of South Africa

ISOhealthSA
Rudolph-Shortt Consultancy cc t/a

Medical Device Manufacturers of South Africa

- The INDEPENDENT, FOCUSED & DISTINCT voice and driver for local production initiatives, activities, actions and excellence

.. With member participation to achieve continued stakeholder support, commitment and drive for manufacturing in South Africa and Africa

… CIPC registered as a Non for Profit Company (NPC)

Who are MDMSA

- MDMSA is the Medical Device Manufacturer's of South Africa.
- We are an association of member companies that manufacture medical devices locally, service companies or suppliers involved in the value chain of local medical devices locally; including consultancies and academia within South Africa.
- MDMSA represents numerous organisations with diverse disciplines such as wound management, instrumentation, orthopaedics, single-use technology, consumables, capital equipment and digital health technologies.

Medical Device Manufacturers of South Africa

MANUFACTURING

Manufacturing is the making of goods using raw materials or component parts or assembly of a product to sell to a customer.

Production management is the study (practices) of planning, designing, and production systems and subsystems to achieve the goals of an organization.

There are three primary functions in any business company

1. production (Operations)
2. Marketing
3. Finance

Manufacturer definition

- ISO13485 & GHTF [SOURCE: GHTF/SG1/N055:2009, 5.1]
- 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 his name; whether or not such a medical device is designed and/or manufactured by that person himself or on his behalf by another person(s)

- Note 1 to entry: This “natural or legal person” has ultimate legal responsibility for ensuring compliance with all applicable regulatory requirements for the medical devices in the countries or jurisdictions where it is intended to be made available or sold, unless this responsibility is specifically imposed on another person by the Regulatory Authority (RA) within that jurisdiction.
- Note 2 to entry: The manufacturer’s responsibilities are described in other GHTF guidance documents. These responsibilities include meeting both pre-market requirements and post-market requirements, such as adverse event reporting and notification of corrective actions.
- Note 3 to entry: “Design and/or manufacture”, as referred to in the above definition, may 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 products, together for a medical purpose.
- 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: Any person who changes the intended use of, or modifies, a medical device without acting on behalf of the original manufacturer and who makes it available for use under his own name, should be considered the manufacturer of the modified medical device.
- Note 6 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 7 to entry: To the extent that an accessory is subject to the regulatory requirements of a medical device, the person responsible for the design and/or manufacture of that accessory is considered to be a manufacturer.

EU MDR definitions

It is the manufacturer that defines intended use and label / IFU

- (12) ‘intended purpose’ means the use for which a device is intended according to the data supplied by the **manufacturer** on the **label**, in the **instructions for use** or in promotional or sales materials or statements and as **specified by the manufacturer** in the clinical evaluation;
- (13) ‘label’ means the written, printed or graphic information appearing either on the device itself, or on the packaging of each unit or on the packaging of multiple devices;
- (14) ‘instructions for use’ means the information provided by the manufacturer to inform the user of a device's intended purpose and proper use and of any precautions to be taken;

Activities of manufacturers

- Place the product in the market
- Compliance to the essential principles of Safety and Performance
- Compliance to regulatory pre and post market requirements (labelling, safety and performance principles – GMP
- Operational production and market access interventions; QMS

“essential principals”

MDR art135. Importers shall ensure that, while a device is under their responsibility, storage or transport conditions do not jeopardise its compliance with the general safety and performance requirements set out in Annex I and shall comply with the conditions **set by the manufacturer,** where available.

ANNEX I GENERAL SAFETY AND PERFORMANCE REQUIREMENTS CHAPTER I GENERAL REQUIREMENTS

1. Devices shall **achieve the performance intended by their manufacturer** and shall be designed and manufactured in such a way that, during normal conditions of use, they are suitable for their intended purpose. They shall be safe and effective and shall not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons, provided that any risks which may be associated with their use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety, taking into account the generally acknowledged state of the art.

5.2.2 Declaration of conformity

- One element of a global regulatory model for medical devices is that the **manufacturer** attests that its medical device complies fully with all applicable Essential Principles for Safety and Performance and draws up a written 'Declaration of Conformity'.

Title: Principles of Conformity Assessment for Medical Devices

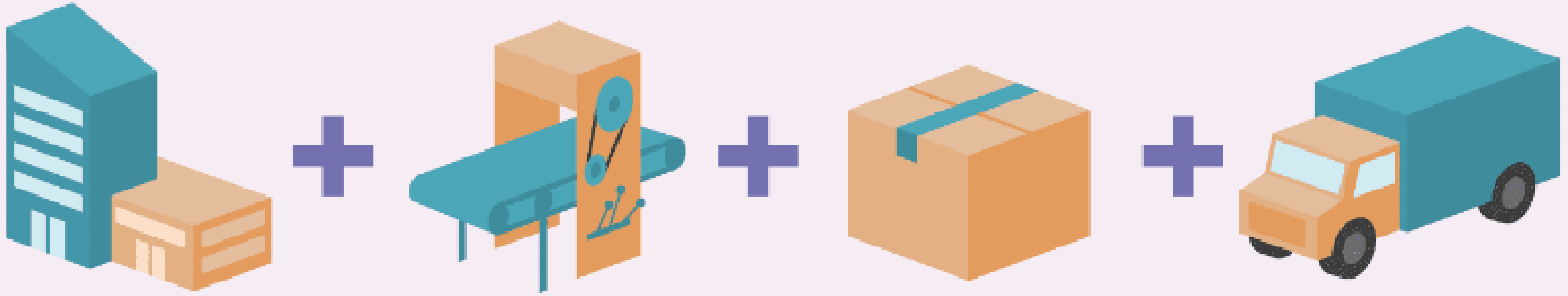
Authoring Group: Study Group 1

Endorsed by: The Global Harmonization Task Force

Date: June 26, 2006

SUPPLY CHAIN

- A supply chain is the network of all the individuals, organizations, resources, activities and technology involved in the creation and sale of a product.
- A supply chain encompasses everything from the delivery of source materials from the supplier to the manufacturer through to its eventual delivery to the end user



Procurement

Avoid duplicate procedures in different departments.

Manufacturing

Improving quality and precision prevents defects and returned goods.

Warehousing

Keep inventory levels as low as is reasonable.

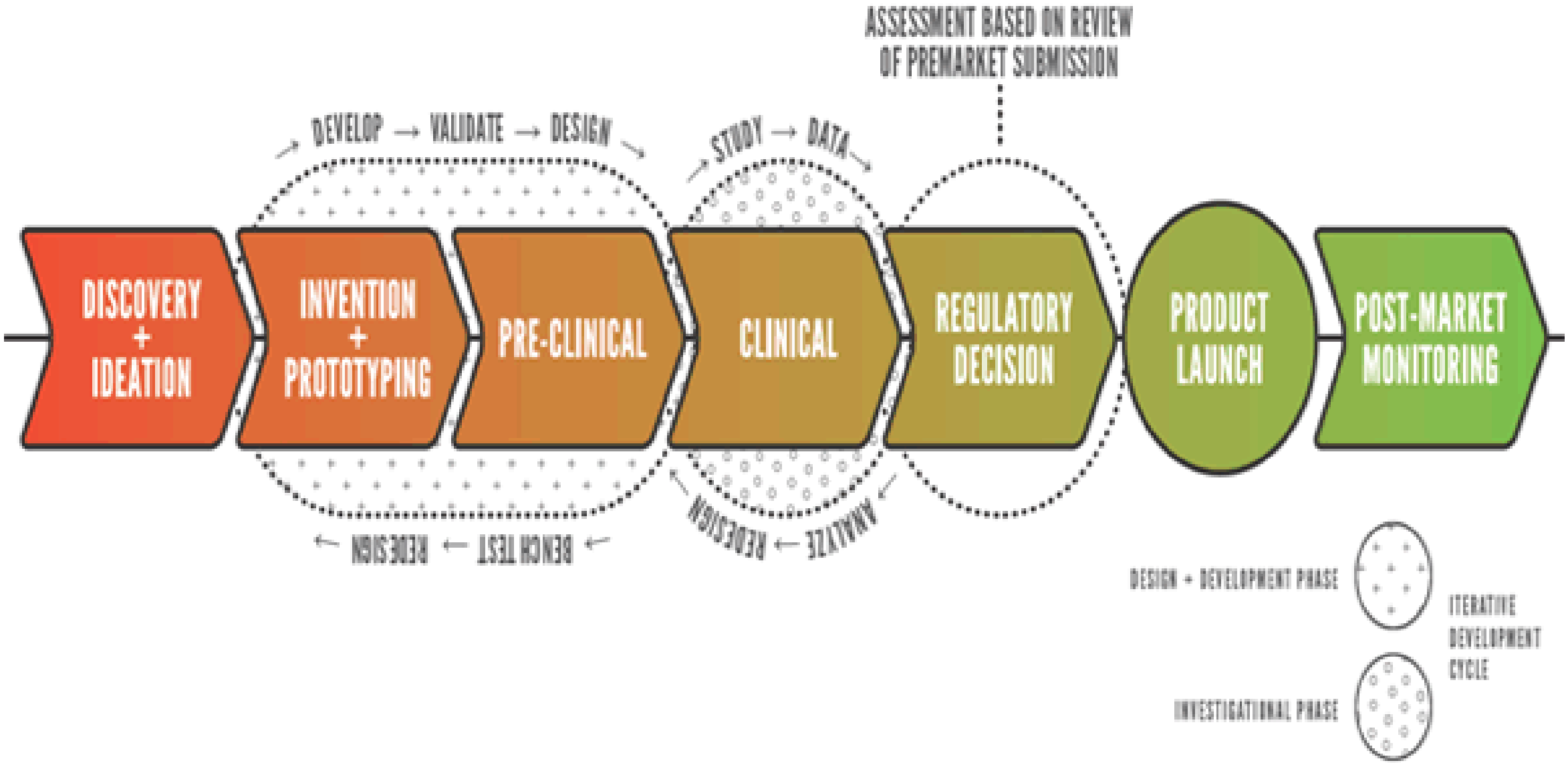
Transportation

Consolidate multiple products into a single shipment.

MANUFACTURER obligations

- Manufacturer QMS (ISO13485)
- Follow clause 7.3 Design & Development
- Design with Safety & Performance evidence
  - Plan, process and record a product, process and market risk assessment
  - Compliance to essential principles of safety and performance
    - Compliance to “common specifications”
    - Compliance to GMP (ISO13485, 14971)
  - Performance compliance to technical standards
    - Verification and validation protocols (plans) and records
    - Stability studies and lifetime / storage conditions / expiry dates
  - Clinical evidence plan and evaluation report
- Technical File
  - Label, Instructions for use, Training requirements

Regulatory roadmap



CONFORMITY ASSESSMENT

Class of Medical Device	Most commonly used conformity assessment procedures	Declaration of Conformity reference
Class A	Part 6 (Declaration of Conformity Procedures Not Requiring Assessment)	Part 6, clause 6.6
Class A (measuring) and Class B (non-sterile)	Part 6 (Declaration of Conformity Procedures Not Requiring Assessment) + Part 5 (Product Quality Assurance Procedures)	Part 6, clause 6.6
Class A (sterile) and Class B (sterile)	Part 6 (Declaration of Conformity Procedures Not Requiring Assessment) + Part 4 (Production Quality Assurance Procedures)	Part 6, clause 6.6
Class C	Part 1 excluding Clause 1.6 (Full Quality Assurance Procedures)	Part 1 clause 1.8
Class D	Part 1 (Full Quality Assurance Procedures) + Clause 1.6 (Examination of Design)	Part 1 clause 1.8
Systems or Procedure Packs	Part 7 (Procedures for Medical Devices Used for a Special Purpose)	Part 7, clause 7.2

The following conformity assessment procedures are rarely used as they are generally more expensive for manufacturers, but are options that can be considered:

Part 2 (Type Examination) for specific models of Class C, Class D, (including Active Implantable devices), in conjunction with Part 1 or Part 3 or Part 4 or Part 5.

Part 3 (Verification Procedures) for non-sterile Class A measuring and Class B devices or, when used in conjunction with Part 2, for non-sterile Class C and Class D devices.

CONFORMITY ASSESSMENT

- Conformity assessment is based on risk classification conducted before and after a medical device is placed on the market, and post-market and are intended to provide the **objective evidence of safety, performance, and benefits and risks** to maintain public confidence surveillance of device
- SA: "conformity assessment" means the systematic examination of evidence generated and procedures **undertaken by the manufacturer, to determine that- a medical device or IVD is safe and performs as intended and that the medical device or IVD fulfils the Essential Principles of Safety and Performance** for Medical Devices or IVDs, as determined by the Council;

Common specifications

- '"common specifications' [..] means a set of technical and/or clinical requirements, other than a standard, that provides a means of complying with the legal obligations applicable to a device, process or system."
    - MDR, IVDR
- Common Specifications (CS). Article 9 only allows for an exemption if manufacturers "*can duly justify that they have adopted solutions that ensure a level of safety and performance that is at least equivalent thereto*"

Common Specifications in EU exist for:

- Clinical investigation, clinical evaluation and / or clinical follow-up after placing on the market ISO14155
- Risk management IS)14971
- Performance assessment and performance testing after having placed the device on the market
- General safety and performance requirements, including physical and chemical characterization, microbiological and biocompatibility tests as well as mechanical, electric, electronic or non-clinical toxicology studies ISO16142
- Technical documentation
- Processing (including verification, validation, quality management)
- Reporting

Types of SABS Standards

1. Prescriptive specifications
   - Obligate product characteristics, e.g. device dimensions, biomaterials, test or calibration procedures, as well as definitions of terms and terminologies.
2. Design specifications
   - Set out the specific design or technical characteristics of a product, e.g. operating room facilities or medical gas systems.
3. Performance specifications
   - Ensure that a product meets a prescribed test, e.g. strength requirements, measurement accuracy, battery capacity, or maximum defibrillator energy.
4. Management specifications
   - Set out requirements for the processes and procedures companies put in place, e.g. quality systems for manufacturing or environmental management systems.

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SABS

Our legislative mandate

The SABS was established by the Standards Act, 1945 (Act 24 of 1945)

SABS exists as a public entity under the Standards Act, 2008 (Act 8 of 2008)

The objectives of SABS are as follows:

- Develop, promote and maintain South African National Standards (SANS)
- Promote quality with respect to commodities, products and services
- Render conformity assessment services and matters connected therewith

International Membership

ISO IEC PASC PACIFIC AREA STANDARDS CONGRESS ARSO SMIIC AFSEC

Accreditation of SABS

sanas South African National Accreditation System

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SABS

How standards are developed

SABS is the only organisation in South Africa with the mandate to develop, promote and maintain national standards

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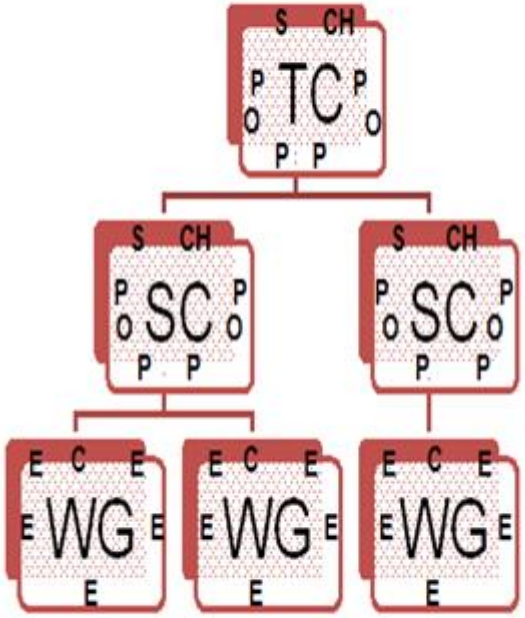
SABS

Guiding principles

- International Principles
- Governance process
- SABS Norm
- Alignment to ISO and IEC programme of work
- Maintenance
  - Reaffirmations
  - Withdrawal
  - Amendments
  - Revisions



List of standards

- https://www.emergobyul.com/blog/2013/01/us-fda-publishes-revised-list-recognized-medical-device-standards

Areas in which more up-to-date standards have replaced previous versions include:

Biocompatibility	Materials
Cardiovascular	OB-GYN/Gastroenterology
Dental/ENT	Ophthalmic
General	Orthopedics
General Hospital/General Plastic Surgery	Sterility
In Vitro Diagnostics	

New entries to the FDA's list of standards have also been added in the following areas:

Cardiovascular	OB-GYN/Gastroenterology
Dental/ENT	Ophthalmic
General	Orthopedic
General Hospital/General Plastic Surgery	Radiology
In Vitro Diagnostics	Software/Informatics
Materials	Sterility

List of Standards

- https://www.govinfo.gov/content/pkg/FR-2013-01-15/pdf/2013-00605.pdf

that involve the initial addition of standards not previously recognized by FDA.

TABLE 2—MODIFICATIONS TO THE LIST OF RECOGNIZED STANDARDS

Old recognition No.	Replacement recognition No.	Title of standard [1]	Change
		A. Biocompatibility	
2–156		AAMI/ANSI/ISO 10993–1:2009 Biological evaluation of medical devices—Part 1: Evaluation and testing within a risk management process.	Extent of recognition.
2–178	2–191	ISO 10993–12 Fourth edition 2012–07–01 Biological evaluation of medical devices—Part 12: Sample preparation and reference materials.	Withdrawn and replaced with newer version.
2–184	2–192	USP 35–NF30:2012<87> Biological Reactivity Test, In Vitro—Direct Contact Test.	Withdrawn and replaced with newer version.

List of Standards

- https://ec.europa.eu/growth/content/new-lists-harmonised-standards-medical-devices-oj-c-389-17-november-2017_en

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Contents

The AFRICAN scene

- Countries Regulators e.g
  - South Africa SAHPRA, Rwanda FDA, Tanzania Medicines and Medical devices Authority TMDA, Uganda National Drug Autority (NDA), Nigeria National Agency for Food and Drug Administration, Kenya Pharmacy and Poisons Board (PPB), Botswana BOMRA
  - Africa Medical Devices Forum (AMDF) was Pan African Harmonization Working Party (PAHWP)
  - Local Standards authorities e,g, ISO (SABS South Africa, Botswana BWA (Botswana Bureau of Standards)) to ARSO (African Organisation of Standards) and Electrotechnical Commission (IEC), and the International Telecommunication Union (ITU),

AUDA-NEPAD
AFRICAN UNION DEVELOPMENT AGENCY

ARSO

Africa Medical Devices Forum (AMDF)
formerly Pan-African Harmonization Working Party (PAHWP)
ARSO – African Organisation of Standards

- For harmonized framework of regulation of medical devices and in vitro diagnostics in Africa based on the WHO global model for Medical Devices Regulatory Framework Model
- establishes basis for reliance and recognition, requirements for manufactures
- ARSO to harmonise African Standards, Conformity Assessment & Procedures in order to reduce Technical Barriers to Trade and therefore promote Intra African and International Trade as well as enhance the industrialization of Africa
- Collaboration with other harmonization initiatives such as AHWP, IMDRF, ASEAN (Association of Southeast Asian Nations), APEC (Asia-Pacific Economic Cooperation) and any other interested partner enhanced.

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Simone, chairperson MDMSA, a SA local manufacturer & the leading consultant and facilitator on health products Establishment Licencing, Quality Management Systems [ISO13485], Design Project Management & Technical Documentation and Infrastructure (cleanroom, equipment & production) design, installation and validation