Fit for Purpose Regulation

IVD Overview

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The value of in vitro diagnostics

Diagnostics can play a leading role in the fight against disease and in meeting increasingly complex healthcare challenges.

Diagnostics account for

~ 70%

of clinical decision making
At about

~ 2%

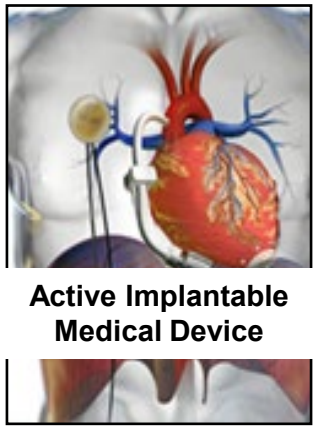
of the healthcare costs.

1. Earlier diagnosis improves COVID-19 prognosis: a nationwide retrospective cohort analysis, June 9, 2021.
2. Effect of delay in diagnosis on transmission of COVID-19, February 25, 2020.

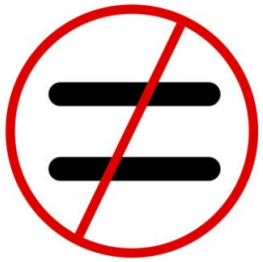
Design Fit for Purpose Regulation

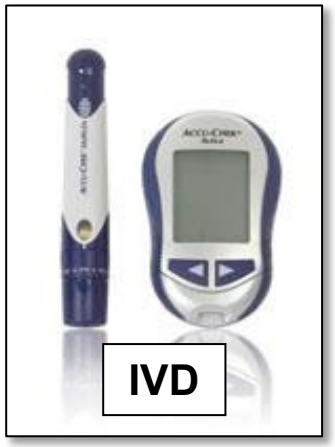
IVDs fundamentally differ form traditional Medical Devices, Vaccines, and Drugs

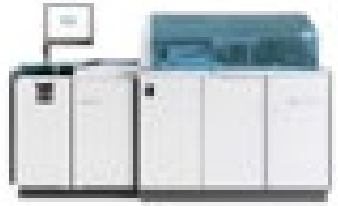
Medical Device



Active Implantable Medical Device





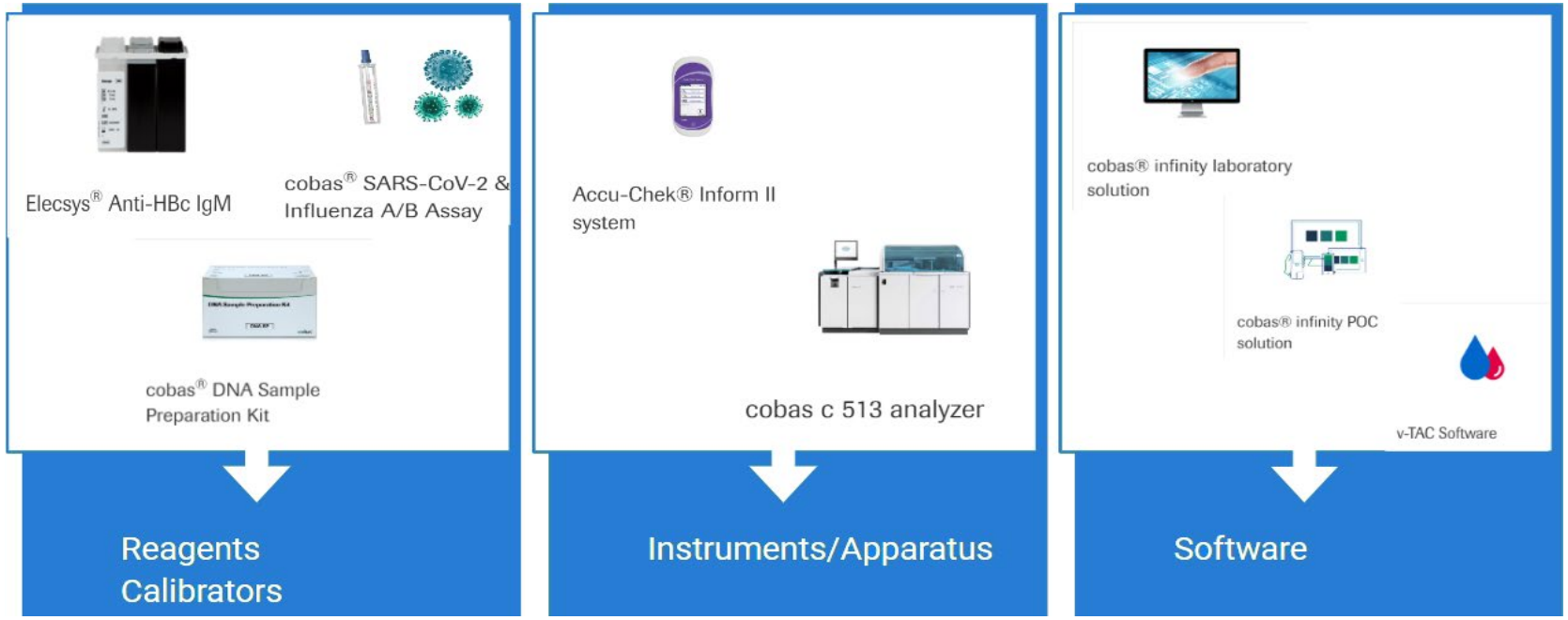


- IVDs are not ingested.
- IVDs do not treat patients, they are non-invasive tests used on biological samples (e.g. blood, urine, tissue, etc.)
- IVDs never come into contact with patients. IVDs always interact exclusively with samples taken from the patient to obtain information of relevance.
- The risks posed by IVDs to patients are based on the information they provide.

IVD Definition

IMDRF definition of 'IVD'

*'**In Vitro Diagnostic (IVD) Medical Device:** 'means a medical device, whether used alone or in combination, intended by the manufacturer for the **in-vitro examination of specimens derived from the human body** solely or principally to **provide information** for **diagnostic**, **monitoring** or **compatibility purposes**.*(GHTF/SG1/N071:2012)'

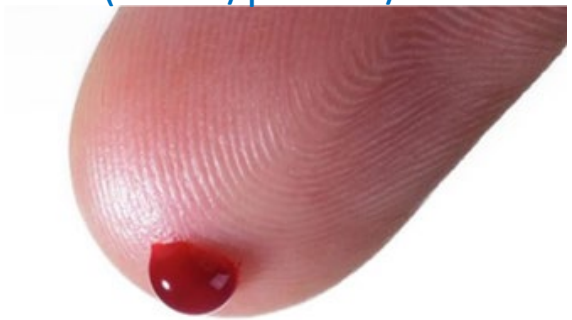


IVD medical devices include reagents, calibrators, control materials, specimen receptacles, software, and related instruments or apparatus or other articles and are used, for example, for the following test purposes: diagnosis, aid to diagnosis, screening, monitoring, predisposition, prognosis, prediction,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

Reference: IMDRF Essential Principles of Safety and Performance of Medical Devices and IVD Medical Devices http://www.imdrf.org/docs/imdrf/final/technical/imdrftech-181031-grrp-essential-principles-n47.pdf

IVD Medical Devices

Test of human specimens
(blood/plasma/urine etc.)



Sample collection tubes

HIV test kits

IVD kit, reagents

Pregnancy test kits

Instruments for sample preparation

*Pictures are taken from Fine Art America, QIAGEN, Qingdao lifecare Trade Co. Ltd.

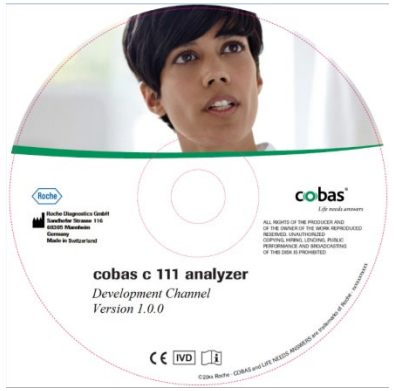
Accessory to an IVD medical device

Accessory for an IVD Medical Device: article intended explicitly by its manufacturer to be used together with an IVD medical devices:

- to enable the IVD medical device to achieve its intended purpose
  or
- to augment or extend the capabilities of the IVD medical device in the fulfilment of its intended purpose.

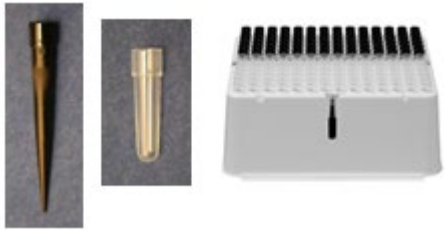
(ISO 18113-1:2009)

IVD Accessories



Software

specifically intended by its manufacturer to be used with a defined automated IVD instrument



Tips and Cups

Cleaning Solution

Classification

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

WG/N64FINAL:2021 Principles of In Vitro Diagnostic (IVD) Medical Devices Classification

WG/N41FINAL:2017 -Software as a Medical Device (SaMD)

Overview of Medical device Classification Principles

Purpose and Criteria

Purpose

"*Regulatory controls are* ***intended to safeguard the health and safety*** *of patients, users and other persons by ensuring that manufacturers of IVD medical devices* ***follow specified procedures*** *during design, manufacture and marketing. The* ***risk presented*** *by a particular device* ***depends substantially on its intended use and intended user*** *.*

Source - Principles of Medical Devices Classification IMDRF IVD working group Final Document :2021

Risk-based classification for IVDs

is one of the **regulatory controls** to safeguard the health and safety of patients, users, and other persons.

IVD Classification Criteria

Intended purpose/ Indication for use as specified by the manufacturer (Diagnosis, Aid to Diagnosis, Screening, Prognosis or monitoring)

User & expertise

The technical- scientific- or medical knowledge of the intended User (lay person or healthcare professional)

Importance

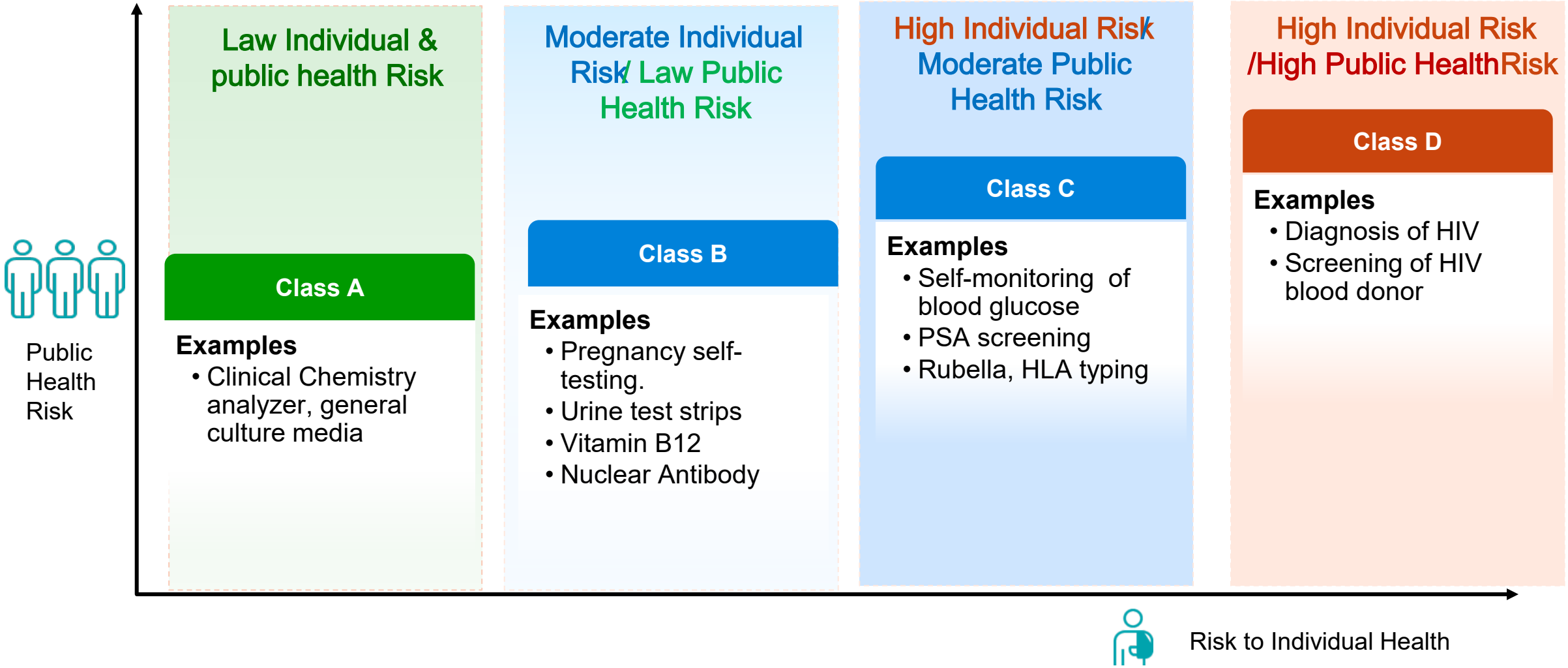
of the information to the diagnosis e.g. when combined with other test results, signs & symptoms, history of disease etc.

Impact

of the result **(true or False)** to the individual and /or to public health

Overview of IVD Classification Principles

Risk-Based IVD Classification System



See also section 6.0 Recommendations and Factors Influencing IVD Medical Device Classification in the IMDRF guidance IMDRF/IVD WG/N64 FINAL: 2021 Principles of In Vitro Diagnostic (IVD) Medical Devices Classification http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-wng64.pdf

Conformity Assessment

GHTF/SG1/N78:2012
Principles of Conformity Assessment for Medical Devices

IMDRF/GRRP WG/N47FINAL:2018
Essential Principles of Safety and Performance of Medical Devices and IVD Medical Devices

Conformity Assessment:

Systematic examination of evidence generated, and **procedures** undertaken **by the manufacturer**, under requirements established by the Regulatory Authority, to determine that a medical device is safe and performs as intended by the manufacturer and, therefore, conforms to the Essential Principles of Safety and Performance of Medical Devices and IVD Medical Devices

GHTF/SG1/N78:2012
Principles of Conformity Assessment for Medical Devices

IMDRF Classification Rules are Tightly Read with GHTF "Principles of Conformity Assessment for IVDs"

- "The inter-relationship between device class and conformity assessment is critical in establishing a consistent approach across all countries/regions adopting GHTF principles, so that the premarket approval process and evidence requirements for a particular IVD medical device are acceptable globally."[1]
- GHTF Conformity Assessment Elements:
  - i. Quality management system (QMS),
  - ii. System for post-market surveillance,
  - iii. Technical documentation,
  - iv. Declaration of conformity, and
  - v. Registration of manufacturers and their medical devices by the Regulatory Authority.

GHTF Principles of Conformity Assessment for In Vitro Diagnostics, accessed August 14, 2023

IMDRF Classification Rules are Tightly Read with "IMDRF Essential Principles of Safety and Performance"

- "Medical devices and IVD medical devices should achieve the performance intended by their manufacturer and should be designed and manufactured in such a way that, during intended conditions of use, they are suitable for their intended purpose."
- "They should be safe and perform as intended, should have risks that are acceptable when weighed against the benefits to the patient, and should not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons."

IMDRF Essential Principles of Safety and Performance for Medical Devices and IVDs, accessed August 14, 2023

IMDRF Classification Rules are Tightly Read with "Principles of Conformity Assessment for IVDs"

- Essential Principle requirements are based on internationally accepted standards.
- IMDRF Emphasized that evidence requirements generally increase with the risk classification.
- IMDRF also offers a MD and IVD TOC , aiming to steer pre-market submissions towards harmonized submissions across the globe.
- The US FDA – Health Canada ESTAR Pilot (based on MD IMDRF TOC); continues to drive convergence and opportunities to implement work-sharing and other reliance pathways. (Brazil and Australia also interested to join the pilot)

Health Canada and FDA eSTAR Pilot

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UPDATE – January 27, 2023: Health Canada and the FDA launch eSTAR pilot

Health Canada and U.S. Food and Drug Administration's joint eSTAR pilot has reached its total of 9 participants. Requests to participate in the pilot are no longer being accepted.

Convergence to International Pre- Market Evidence Requirements

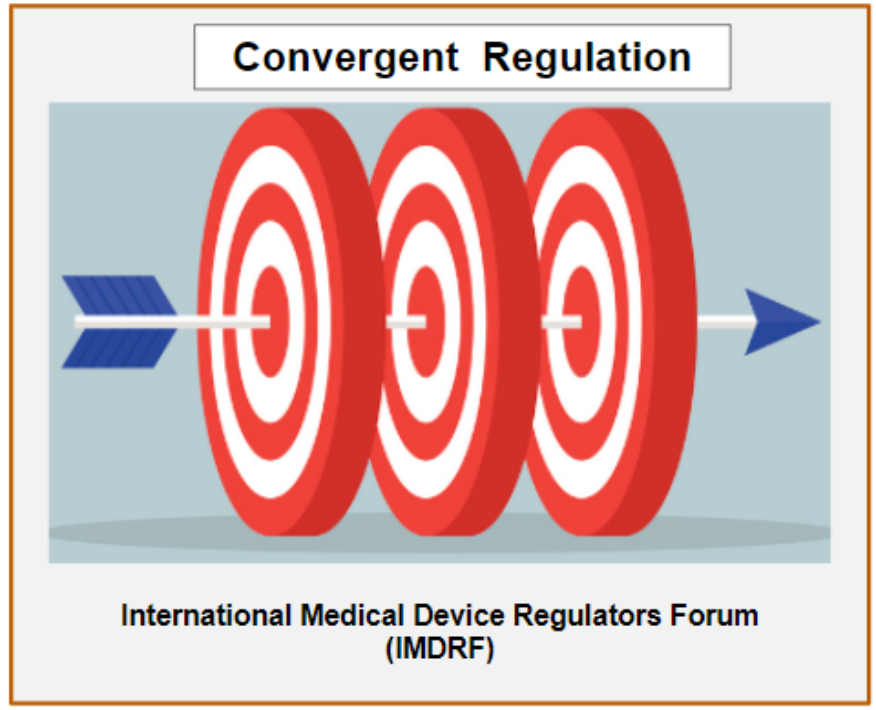
Acceptance of global clinical data

- In country testing is not an IMDRF recommendation. Rather IMDRF seeks to achieve convergence to requirements so that wherever possible, "[T]he premarket approval process and evidence requirements for a particular IVD medical device are acceptable globally".
- WHO recommend a risk based approach:
  - "In-country clinical investigations (that is, systematic clinical investigation in the country in which market authorization is being sought) should not generally be a requirement." Page 239.
  - "In deciding whether to authorize a medical device, the NRA may consider the acceptance of data from clinical investigations conducted outside its jurisdiction, provided that the applicant has demonstrated that the data are adequate and were obtained in accordance with applicable global and national standards and in accordance with the characteristics of the population within the authority's jurisdiction." Page 201-02.
  - "Regarding an issue raised during public consultation concerning the necessity for lot verification testing of medical devices, the Committee agreed that, although important, such a requirement should be based on an assessment of risk." Page 22.
  - "Countries may implement a system of risk-based lot verification of high-risk IVDs (Class D), either before distribution to users, post distribution or before they are put into service." Page 207.

- WHO Global Model Regulatory Framework, May 2023

Regulatory Frameworks to Benefit the Patient

- **Regulatory convergence to internationally established best practices:**
  - Expedites access to medical products
  - Reduces unnecessary complexity in the regulatory process
  - Reserves resources & helps combat raising cost in healthcare
- **Convergence to internationally established IVD classification:**
  - Ensures alignment of downstream processes and evidence requirements
  - Allows more effective capacity building
  - Facilitates the ability to leverage smart regulation (e.g., reliance)



In order to strengthen the regulatory capacity for oversight of medical products globally, WHO encourages international cooperation among regulatory authorities in all its forms, including convergence, harmonization, information- and work-sharing, reliance and recognition.

-World Health Organization, Regulation and Prequalification, accessed August 12, 2023

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