Reliance Through the Medical Device Lifecycle

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Examples of how Post Market Reliance can be practiced

Adverse Event Reporting

Leveraging monitoring and safety issues discovered after a product is on the market.

Post Market Changes

Relying on reference authority authorization of a product change after initial approval.

Inspections

Utilizing audit reports from recognized authorities and institutions to streamline inspection process.

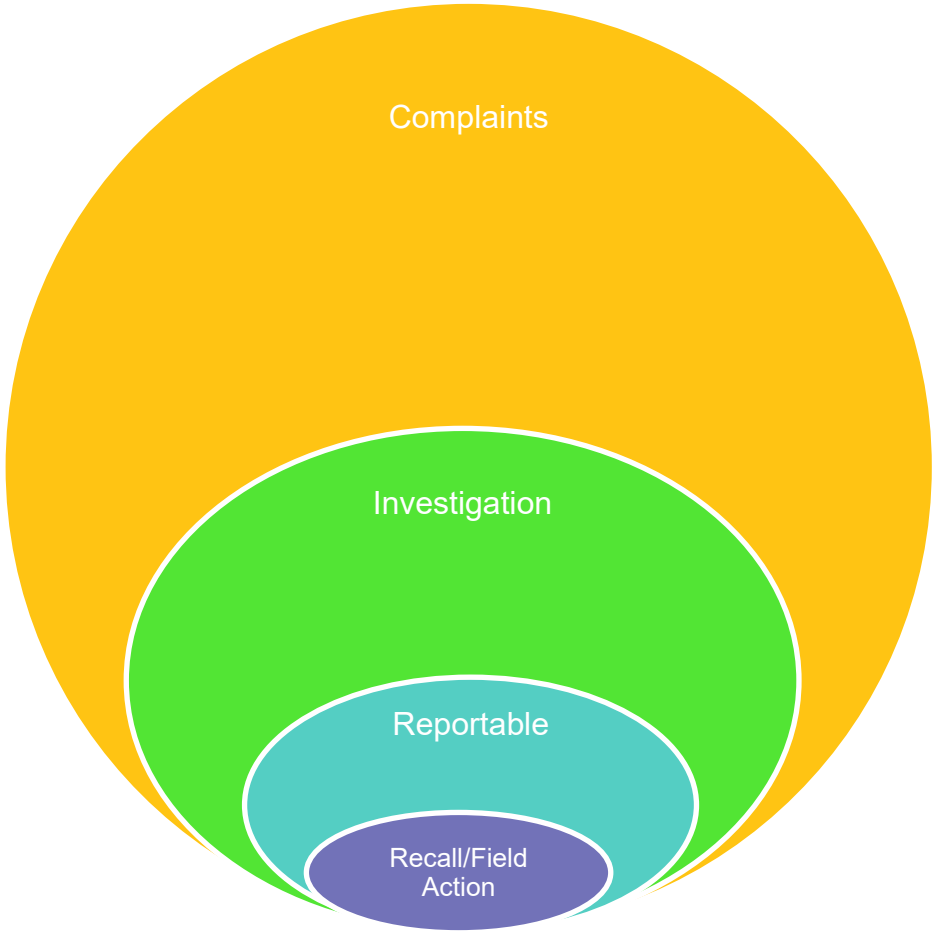
Opportunity: Convergence is needed to fully benefit from reliance in post-market surveillance, product changes, and inspections

Post Market Surveillance including Adverse Event Reporting

Complaint Handling Foundation

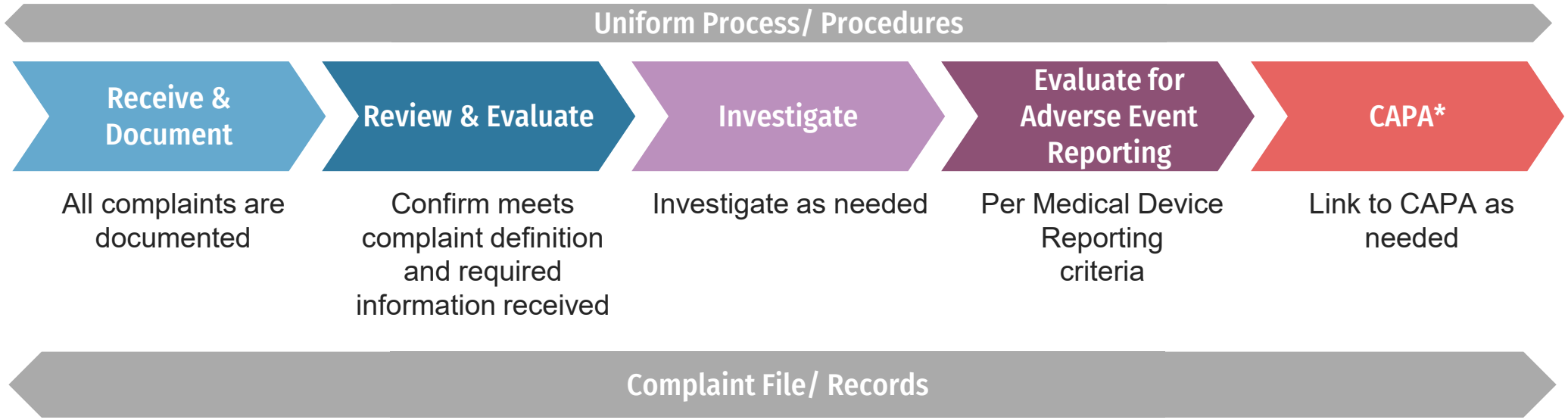
A complaint is any written, electronic, or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, safety, effectiveness, or performance of a device after it is released for distribution.

- Manufacturers should document all complaints and investigate/report, as necessary.
- Not all complaints are reportable (e.g., lack the necessary nexus to the device).
- Not all incidents are reportable (an incident could refer to any possible inquiry including those without an alleged deficiency of the product or safety allegation)



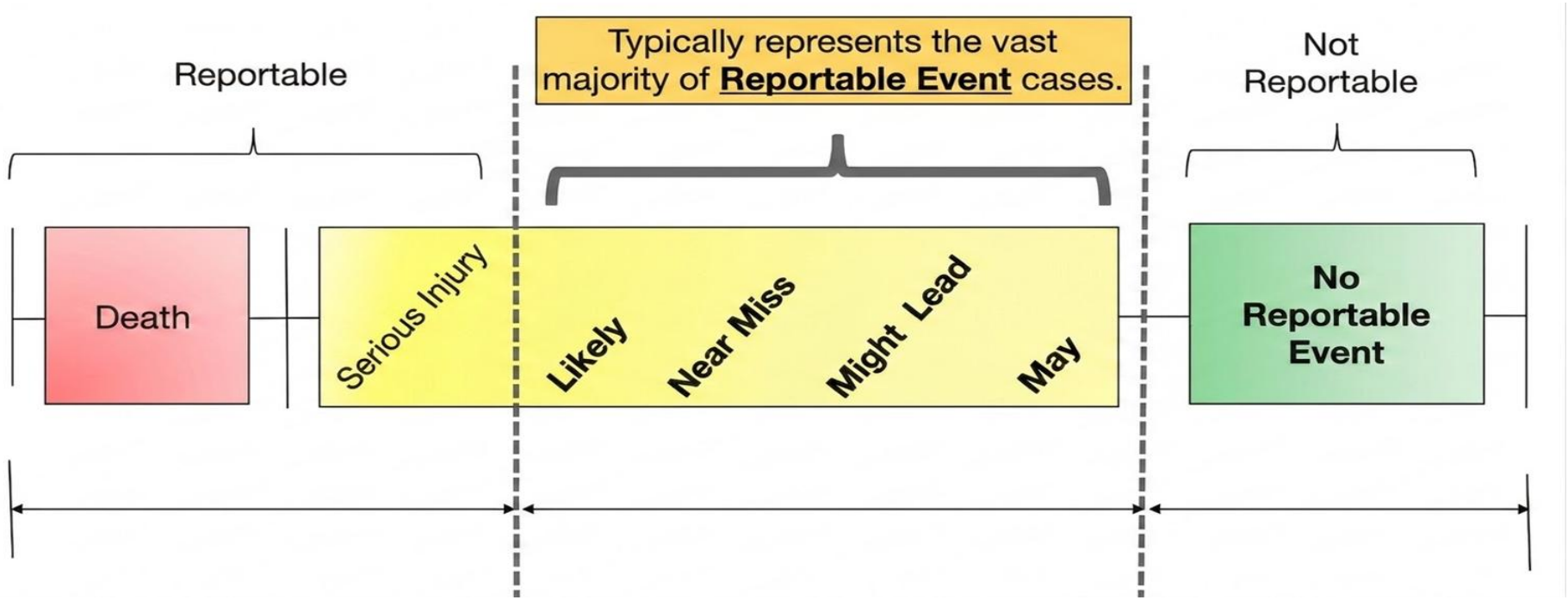
Big Picture Complaints and Reporting

- **ISO 13485:2016, 3.4:** Written, 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.



To fully benefit from reliance convergence is needed

Aligned definitions, terms, timing, criteria and exclusions for Adverse Event Reporting



Challenges in Adverse Event Reporting

Adverse Event reporting **requirements differ across jurisdictions** making it difficult to:

- Collate and compare data
- Accurately predict and prevent patient harm

Varied Terminology

Malfunction • Serious public health threat
Serious Incident • Adverse Incident
Adverse Event • Serious injury • Safety Issue
Event • Sentinel Event • Serious illness
Unanticipated death or unanticipated serious injury
Abnormal use • Near Incident
Use error • Life-threatening

Reporting Thresholds

Might lead to • Likely to lead to
Near Miss • May

Diverse Timelines

Immediate • 2 days • 5 days
10 days • 15 days • 30 days

Of this criteria, what does IMDRF use to describe Adverse Event Reporting?

IMDRF uses the following terms highlighted below

Terminology

Malfunction
Reportable Malfunction
Serious public health threat
Serious Incident
Adverse Incident
Adverse Event
Serious injury
Safety Issue
Event
Sentinel Event
Serious illness
Unanticipated death or unanticipated serious injury
Abnormal use
Near Incident
Use error
Life-threatening illness or injury

Thresholds

Might lead to
Likely to lead
Near Miss
May
Likely

Timing

Immediate*
2 days
5 days
10 days
15 days
30 days

*Immediate adverse event report: For purposes of adverse event reporting, immediately means as soon as possible, but not later than 10 elapsed calendar days following the date of awareness of the event. GHTF/SG2/N54R8:2006, page 5.

IMDRF Criteria for Adverse Event Reportability

- An event occurred. The manufacturer becomes aware of information regarding an event which has occurred with its device;
  - i.e., malfunction, out of specification result, discovery of design flaw, inaccuracy in labeling, use error, the discovery of a serious public health threat;

  AND the manufacturers device is associated with the event;

  AND the event led to one of the following events:

  – Death, Serious Injury; or

  – No death or Serious Injury but the event might lead to D/SI if it were to re occur

…AND no exclusion criteria have been met.

Source: Medical Devices Post Market Surveillance: Global Guidance for Adverse Event Reporting for Medical Devices. **Serious Injury** - Life threatening illness or injury. Permanent impairment of a body function or permanent damage to a body structure. A condition necessitating medical or surgical intervention to prevent permanent impairment of a body function or permanent damage to a body structure.

Death and Serious Injury cases should be **prioritized** from a manufacturer and Regulator perspective.

GHTF/IMDRF Adverse Event Reporting Exemptions

- When an **exemption** is met, the **event is not reportable** even if it met reportability criteria.
- If **exemptions** are **not implemented** or not aligned, reporting across jurisdictions results in **different case reporting**.
- Please refer to Section 4, Exemption Rules of the GHTF/IMDRF Post Market Surveillance: Global Guidance for Adverse Event Reporting for Medical Devices

IMDRF Exclusions
Adverse event caused by **patient condition**
Service **life exceeded**
Design feature protected against adverse event
Negligible likelihood of death or serious injury
Documented expected **foreseeable** side effect
Adverse event described in **advisory notice** (corrective action, recall)
Use error, and no death or actual serious injury
Abnormal use
Those requested and **approved by authority**

IMDRF NCAR Exchange Program Guidance

Reliance example to build on

Exchange Criteria & Scope

- Focuses on two-way communication of serious public health issues.
- Reports are not for single incidents unless they imply significant public health risk.
- Participation is limited to IMDRF Management Committee Regulators.

Confidentiality Protocols

- "Confidential" reports shared only via existing arrangements.
- Authorization required to release any information outside members.
- No patient-identifiable data permitted in any report.

Standardized Reporting Format (Annex 1)

Key Fields & Responsibilities:

- **Author Accountability:** Point of contact ensures accuracy and relevance of content.
- **Manufacturer Consultation:** Manufacturers may be consulted to verify technical accuracy.
- **Unique Numbering:** Uses ISO 3166 country codes (e.g., CA-YYYY-MM-DD-###).

IMDRF NCAR Guidance. Link here, accessed June 2026

IMDRF/NCAR WG/N14(Edition5)

Medical Devices: Post Market Surveillance National Competent Authority Report Exchange Criteria and Report Form

Convergence to IMDRF terms, criteria and timing is essential to fully benefit from reliance in post market

The Path to Easier Reliance

If terms, definitions, criteria, exclusions and timing were harmonized to IMDRF, post market reliance would be significantly streamlined and more effective.

Standardized Reporting

Adoption of a common format for reporting (e.g., IMDRF coding and Reference Authority form) will allow more efficient reporting and post market reliance practices.

Strategic Implementation of IMDRF Coding

Regulators can implement recommended coding structures based on IMDRF. This enables the global study of data, enhancing the ability to predict and prevent patient harm.

Guidance for Regulatory Reform

When developing or reforming requirements or reporting systems, converging to IMDRF Guidance significantly strengthens post-market surveillance reliance.

Transition to Product Changes

Significantly different treatment of product changes between the Reference Agency and the Relying Agency may hinder reliance

Scenario 1: Sufficient Similarity

If regulations for the treatment of product changes is sufficiently similar, Recognition on Reference Authorities is appropriate.

Scenario 2: Significant Difference

However, if there are significant differences in how products changes are treated between the Reference and Relying Agency, an Abridged Assessment may be more appropriate. Keep in mind differences create a barrier.

Strategic Framework

Laws and regulation should authorize the regulator to practice Reliance through the total product lifecycle. Implementing instruments and guidance can create appropriate contours for how reliance on product changes authorizations is practiced.

Why is there a focus on product changes?

The Challenge of Variability

Definitions and the treatment of post market changes **vary across jurisdictions**, creating significant delays.

- Confusion for relying agencies
- Delays & trade barriers in implementation and timely patient access
- Unnecessary operational complexity
- PCCPs?

Terminology Framework

Standard terms for this session:

Significant & Non-significant

Alternate terms recognized:

- Major / Minor
- Substantial / Non-substantial

The same change can receive **very different regulatory treatment**, with no corresponding difference in patient safety.
Implementation timelines vary from immediate to ~18 months

Case Study 1: Shelf-Life Extension Change

(1) Type of change:	(3) Observed regulatory outcomes:
• **Shelf-life extension** from 12 to 18 months of a moderate risk IVD assay with updated stability certificate • **No changes to device** design, materials, intended use, sterilization method, or validation approach	• Change classified variously as non-significant and significant • **Regulatory actions ranged from "no action/ letter to file" to Notification *and even full prior approval*** • **Implementation lead times varied significantly for the same exact product**
(2) Risk profile:	**(4) Key observation:**
• **Intended use was unchanged** • **No identified impact to safety or performance** • Verification completed and no evidence of impact to product or process quality	Despite the low-risk nature of the change to a moderate-risk product under a unified QMS, the shelf-life extension triggered **divergent regulatory pathways**. This led to inconsistent evidence requirements, staggered global implementation, and avoidable delays in testing continuity

Case Study 2: Addition or relocation of an approved sterilization site

(1) Type of change:	(3) Observed regulatory outcomes:
• **Addition or relocation of an approved sterilization site** for a sterile, single-use catheter, using an established sterilization modality and validated process • No changes to device design, materials, intended use, sterilization method, or validation approach	• Change classified variously as non-significant and significant • **Regulatory actions ranged from "no action/ letter to file" to Notification and even full prior approval** • **Implementation lead times varied significantly across the jurisdictions**
(2) Risk profile:	**(4) Key observation:**
• Intended use unchanged • No identified impact to safety or performance • **Sterilization validation accepted as technically adequate across jurisdictions**	Despite a **consistent risk profile and unified QMS**, identical sterilization site changes triggered **widely divergent regulatory pathways**, resulting in duplicative reviews, staggered global implementation, and delays inconsistent product supply

What is the international best practice?

IMDRF currently **lacks** guidance on the treatment of product changes although the IMDRF Industry Group has met with the IMDRF Management Committee multiple times asking for their leadership.

The WHO has guidance on product changes and is considered best practice:

"Once medical devices have been granted market authorization and placed on the market, the manufacturer may introduce changes to the product, its manufacturing process or location, or to the QMS under which it is produced."

Such changes range from:

- ***Minor changes:*** *Little potential to impact safety, performance, or quality.*
- ***Substantial changes****: Likely to affect safety, performance, quality, or conformity with essential principles.*

WHO Recommendations

For Manufacturers

Manufacturers should establish, maintain and apply a procedure for **categorizing and documenting any changes** to the device design/type (including software) and/or QMS as either substantial or not substantial (significant/non-significant). **NOTE: ISO 13485 and MDSAP audits the manufacturers QMS to ensure policies and procedures are in place and followed to document assess product changes.**

For National Regulatory Authorities (NRAs)

The NRA should establish **guidance on changes** (including a definition), and on the tools and processes used to handle such changes. When possible, the NRA should implement **reliance and recognition principles** when evaluating changes.

What does this look like in practice?

Changes to Low-Risk Devices

Regulator review should not be required for changes to low-risk devices. Aligned to best practice on the treatment of pre-market review for low-risk products, changes to low-risk products should be documented internally unless the change ***increases the risk classification***. The inspection process ensures the manufacturers follows established procedures for appropriate classification.

Changes to Higher-Risk Devices

Only changes that are **likely to have a significant impact on safety or performance** should require regulator review. All other changes should be documented internally per the established QMS and subject to inspection. This is consistent with the WHO recommendations.

When regulator review would be required, utilize modernized approaches such as:

- Pre-approved change protocols
- Reliance on Reference Authority authorization of the change
- Pre-certifications for regulated companies
- Reagent Replacement Policy*

*Replacement Reagent and Instrument Family Policy for In Vitro Diagnostic Devices. Link here, accessed June 2026

MDSAP Approach to Change Management

Core Requirement: Formalized Risk Evaluation

MDSAP audits are fundamentally anchored to ISO 13485 compliance, specifically integrating risk management principles into document control, change control, and design changes

Design & Production

Manufacturers must have procedures to review, verify, validate, and approve design changes *before* implementation. The process requires evaluating how these changes might impact the existing risk management file

Supply & Production

If product changes require substituting a material or changing a supplier, manufacturers must assess the risk associated with that new supplier or material

If a manufacturing process changes, the impact on product quality and safety must be assessed

Audit Impact

Throughout MDSAP audits, assessors verify that risk management remains an ongoing activity. When a change is introduced, manufacturers update the risk assessment to prove the benefit-risk ratio remains acceptable

Under MDSAP, manufacturers are expected to maintain objective evidence that the risk of product change was assessed. Failing to appropriately assess and document the risk of a product change can lead to a formal nonconformity

Transition to MDSAP & ISO 13485

Background

Medical Device Manufacturer

- Desires to provide medical devices to many jurisdictions
- Committed to meet requirements of the Authorities
- Focuses on the patient and customer

Without MDSAP & ISO 13485

- Increased audit demands across multiple jurisdictions
- Divergent audit approaches due to unique requirements
- Resource intensive for both authorities and manufacturers

Regulatory Authority & Inspection Types

Four Main Categories of Inspections

Pre-Approval Inspections

To verify that a facility is capable of manufacturing a new, high-risk device in accordance with pre-market application specifications.

Post-Approval / Surveillance

To ensure the facility remains in compliance with regulations *after* a device has been authorized and is on the market.

For Cause Inspections

To investigate a specific problem that has been brought to the regulators' attention.

Compliance Follow-Up

To ensure the facility has adequately resolved violations cited in a previous inspection.

While MDSAP and ISO 13485 reports are accepted, regulators maintain full authority for inspections triggered by specific cause or reason.

The Medical Device Single Audit Program (MDSAP)

Management

Evaluates top management's responsibility, quality policy, planning, resource management, and organizational structures

Design & Development

Audits the full product lifecycle, including planning, inputs, outputs, verification, validation, design transfer, and design changes

Production & Service

Covers environmental controls, infrastructure, equipment calibration, process validations, product identification, traceability, and handling of nonconforming materials

Purchasing Process

Examines supplier evaluation, selection, performance monitoring, and purchasing controls

Measurement, Analysis, and Improvement Process

Reviews mechanisms for customer feedback, internal audits, control of nonconforming product, and CAPA .

Authorization & Registration

Ensures MDs & facility registrations are accurately authorized and documented according to local jurisdictional requirements

Adverse Event Reporting

Audits the procedures and records for reporting AE and issuing field safety corrective actions/advisory notices to authorities

Participating Jurisdictions: USA (FDA), Canada (Health Canada), Australia (TGA), Brazil (ANVISA), and Japan (MHLW/PMDA)

Assesses QMS against ISO 13485:2016 and specific national requirements.

Strategic Benefits of MDSAP

Global Market Access

Satisfy QMS requirements for Australia, Brazil, Canada, Japan, and the USA through a single audit.

Operational Efficiency

Reduces audit burden, minimizes business disruption, and optimizes regulatory resource allocation.

Enhanced Predictability

Prescribed audit model provides clear expectations and standardized nonconformity assessment.

MDSAP Participation Status

Members

- Australia (TGA)
- Brazil (ANVISA)
- Health Canada
- Japan (MHLW/PMDA)
- USA (FDA)

Official Observers

- European Union (EU)
- Singapore (HSA)
- United Kingdom (MHRA)
- WHO IVD Programme

Affiliate Members

- Argentina (ANMAT)
- Israel MoH
- Kenya (PPB)
- Republic of Korea (MFDS)
- Mexico (COFEPRIS)
- South Africa (SAHPRA)
- Taiwan (TFDA)

Global Accessibility

Jurisdictions do not have to be part of MDSAP to benefit from the inspection results. Inspection certificates can be obtained directly from the manufacturer.

Benefiting from ISO 13485 & MDSAP

International Recognition
The gold standard for medical device QMS, accepted globally

Regulatory Compliance
Designed specifically to help organizations demonstrate their ability to meet customer and regulatory requirements

Risk Management
Incorporates a risk-based approach to ensure safety and performance throughout the device lifecycle

Lifecycle Integration
Applies to all stages: design, production, storage, distribution, installation, and servicing

ISO 13485 served as the foundation for MDSAP
ISO 13485 is the base for the Medical Device Single Audit Program.
It is best practice to **accept either MDSAP or ISO 13485 in lieu of** jurisdiction specific audits.

Post Market Reliance in Action!!

Adverse Event Reporting

Converging to IMDRF terms, definitions, criteria, timing, and exclusions will enhance the ability to practice recognition of safety issues discovered after a product is on the market.

Post Market Changes

Taking a risk-based approach to the treatment of product changes as recommended by WHO ensures uninterrupted access to safe and effective MD/IVDs

Inspections

Utilizing shared audit data from MDSAP and ISO 13485 to streamline inspections.

Thank you!!
Gracias!!