FIND

CREATING A REGULATORY STRATEGY

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TOPICS

Explore:

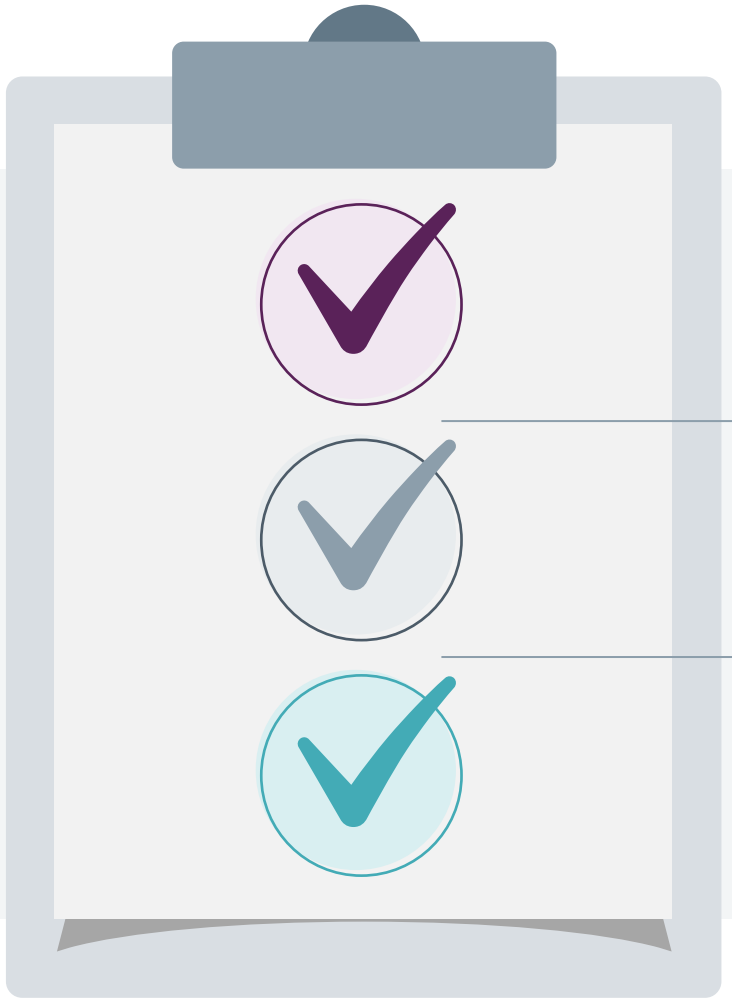
1. What is a Regulatory Strategy
2. The interplay between Market and Product Design Requirements and a robust Regulatory Strategy
3. 10 Steps for Creating a Regulatory Strategy

WHAT IS A REGULATORY STRATEGY?

A regulatory strategy for in vitro diagnostic medical devices (IVDs) is a comprehensive plan outlining the steps necessary to achieve and maintain regulatory approval and compliance for a device.

It includes understanding and addressing regulatory requirements, clinical evidence, quality systems, and market-specific considerations to ensure that IVDs meet all legal and safety standards before being marketed and used in healthcare settings.

IMPORTANCE OF A REGULATORY STRATEGY

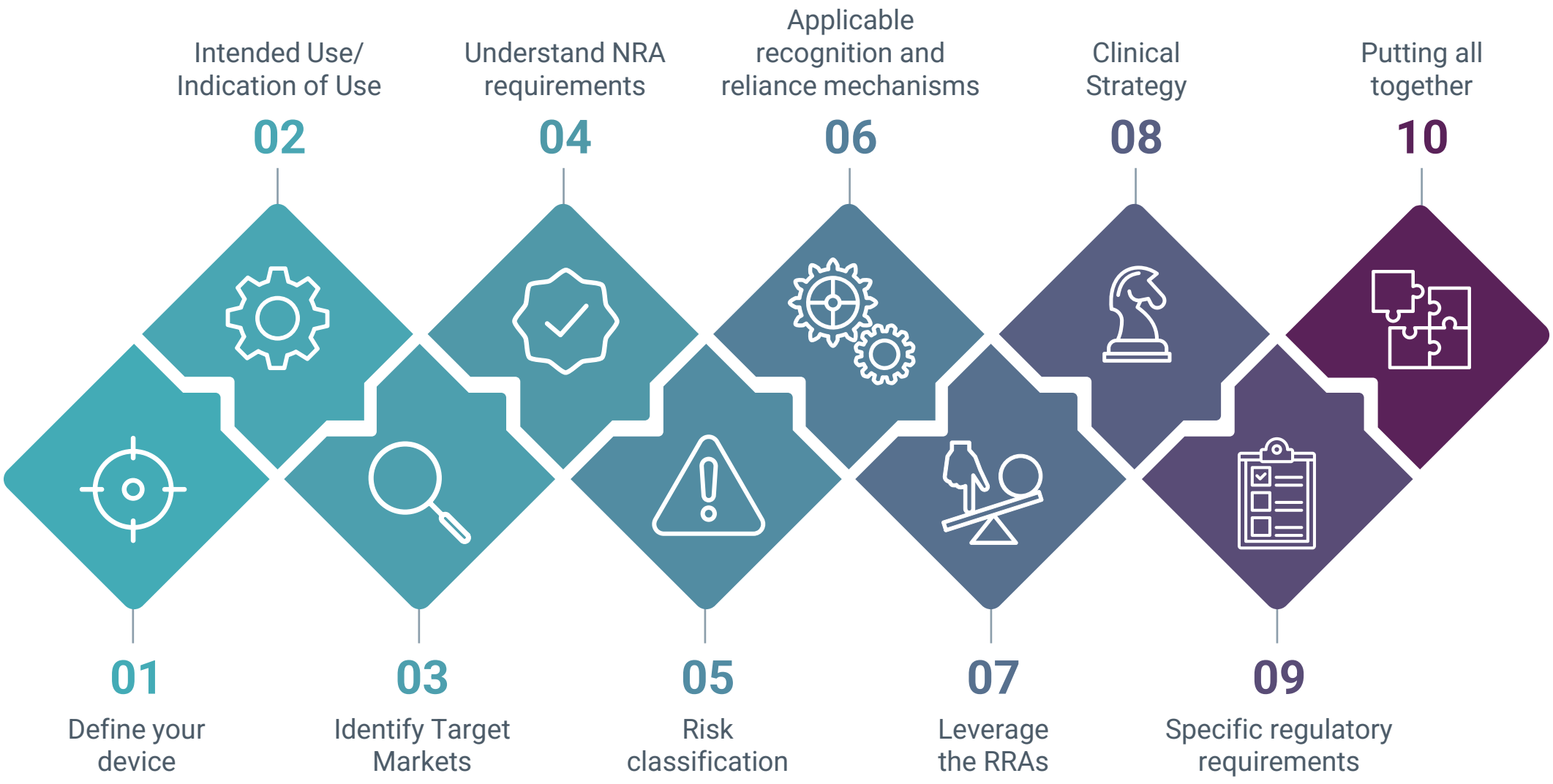


It aims to find the most efficient pathway for market access by first thoroughly understanding the regulatory requirements and pathways specific to each target market

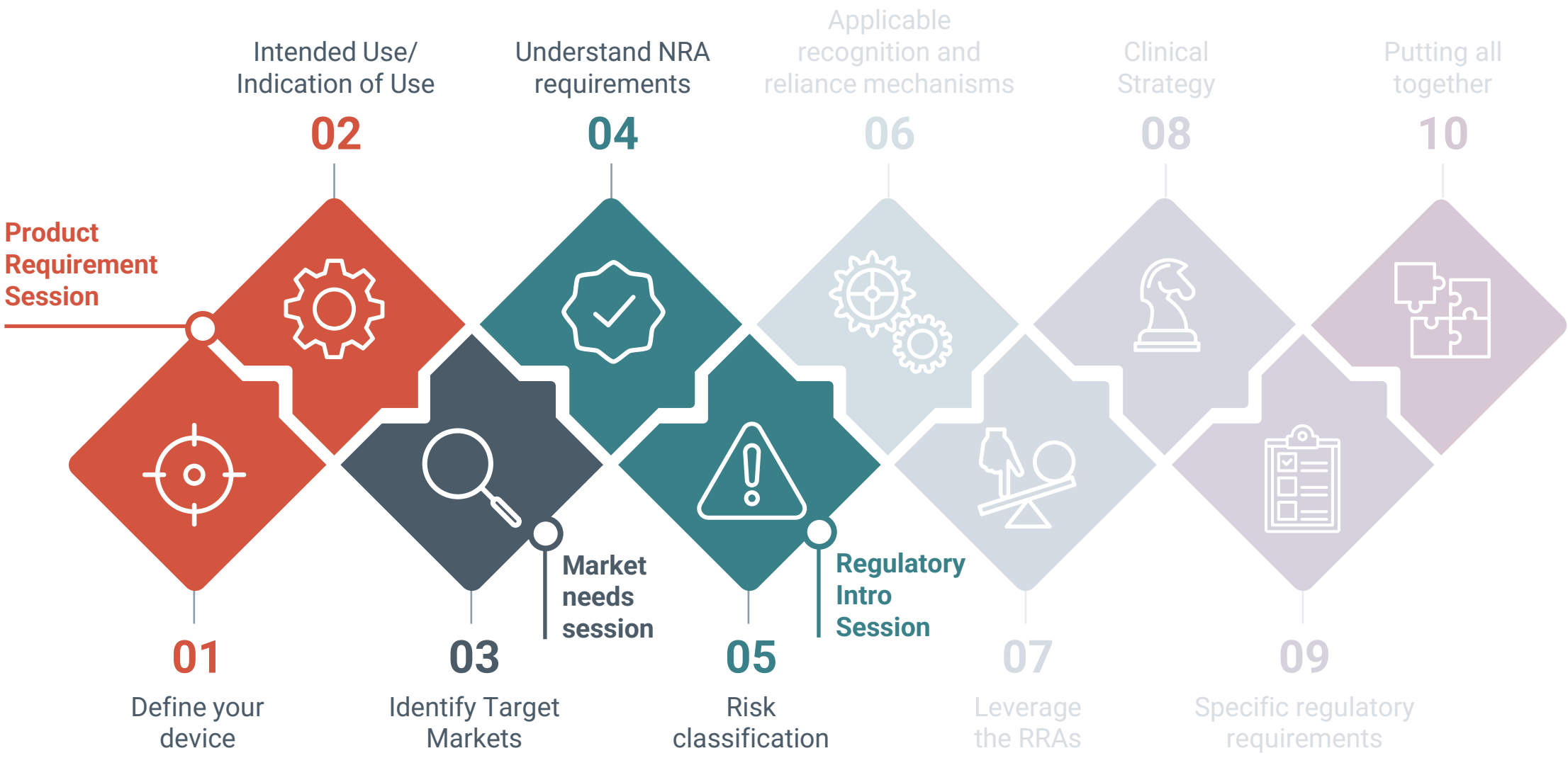
It involves assessing the classification and risk level of the IVD, choosing the appropriate regulatory submission route, and leveraging any available expedited programs or harmonized standards.

By planning for streamlined documentation, clinical trials, and post-market surveillance, the strategy minimizes delays and reduces costs while ensuring compliance and patient safety.

10 STEPS FOR CREATING A REGULATORY STRATEGY



10 STEPS FOR CREATING A REGULATORY STRATEGY



STEP 1:

DEFINE YOUR DEVICE

Have a clear understanding of your device and all its components and determine which (if any) components could be considered as separate, independent devices. Also consider if the device is re-usable, has an instrument that needs servicing, and any associated consumables. The regulatory definitions below can help guide this assessment.

Instrument:

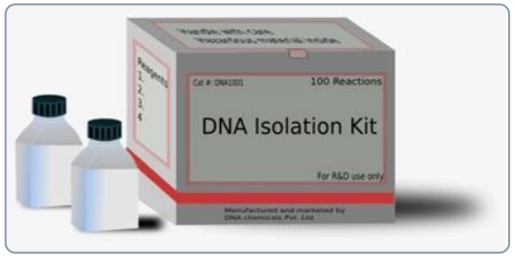
Equipment or apparatus intended by the manufacturer to be used as an IVD medical device.

(GHTF/SG1/N045:2008)

Kit:

A collection of medical products including medical devices, and other products that are packaged together to achieve a stated intended use, being distributed as a single medical device.

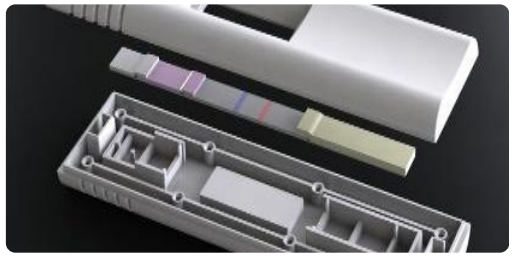
(GHTF/AHWG-UDI/N2R3:2011)



Ancillary Reagents:

Reagents that an assay manufacturer specifies in device labelling as “required but not provided” in order to carry out the assay as indicated in its instructions for use; specified by catalogue or product number or other specific designation.

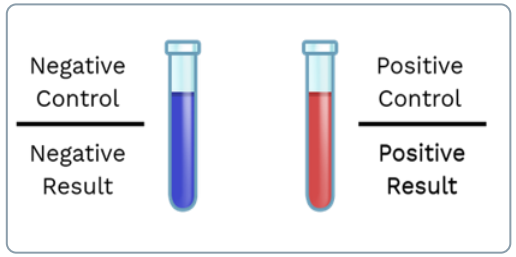
(FDA Class II Special Controls Guideline: MTB NAAT)



System:

A combination of products, either packaged together or not, which are intended to be inter-connected or combined to achieve a specific medical purpose.

(EU MDR Article 2)



STEP 2:

DEFINE THE INTENDED USE/INDICATIONS FOR USE

Intended Use
"About the device itself"

What analyte is detected/measured?
- Antibody/Antigen
- DNA/RNA
- Other chemical compound

Using what technology?
- Principle of operation (LFIA, molecular)
- Quantitative or qualitative
- Automated or manual
- Accessories or instruments

In what specimen?
- Swab
- Urine
- Venous or fingerstick whole blood

Indications for Use
"About the end user and patient"

What illness/condition is the device used for?
- Diagnosis
- Disease differentiation
- Screening
- Monitoring
- Patient Management

What is the target population?
- Symptomatic (infected)
- Asymptomatic (suspected of infection)
- Neonates, children adults
- Pregnant women
- Etc

Who is the intended user?
- Trained laboratorian
- Untrained operator
- Self-tester

What is the use setting?
- Laboratory/hospital
- Point of care
- Home use

STEP 3:

IDENTIFY YOUR TARGET MARKETS

- Selecting the right target markets is a critical step
- Factors including the following can help select a target market:
  - Market size (e.g. disease burden)
  - Growth potential
  - Competition
  - Reimbursement policies
- Consider conducting market research to identify countries and regions that meet your business objectives

STEP 4:

UNDERSTAND NRA REQUIREMENTS

- Identify the requirements for market entry into each target country by their respective **National Regulatory Authority (NRA)** by becoming familiar with their respective laws/acts, regulations and guidelines.

  If possible, engage with a local regulatory expert with experience in navigating the complexities of international markets.

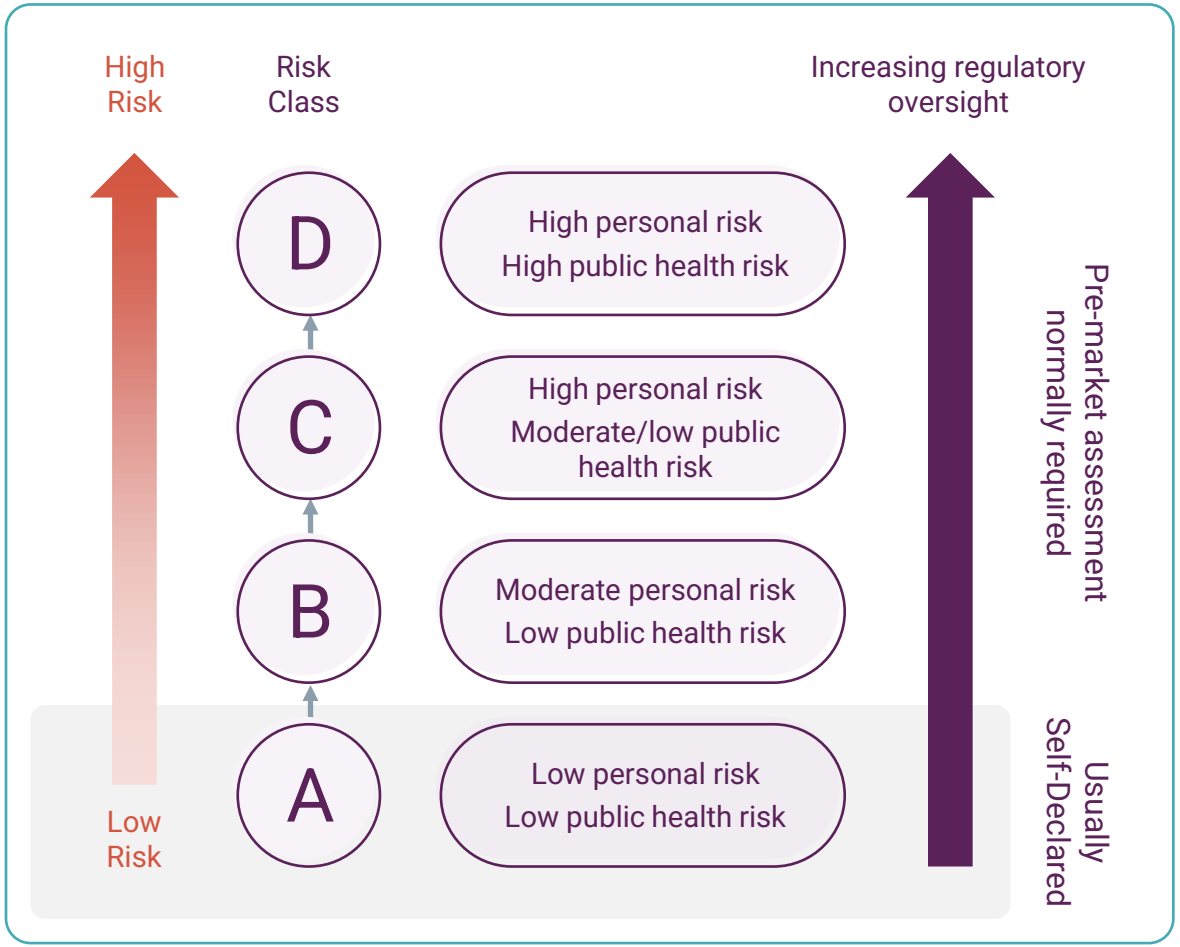
	India	South Africa	Kenya	Indonesia
	CDSCO	**SAHPRA**	**PPB**	**Ministy of Health**
Act	Drugs & Cosmetics Act, 1940	Medicines and Related Substances Act, 1965 (Act 101 of 1965) (amended 2017).	The Health Act 2017	No. 17 of 2023 on Health
Regulation	Medical Devices Rules 2017	Regulations Relating to Medical Devices and In Vitro Diagnostic Medical Devices (2016)	Health Products and Technologies Regulations (Gazette Notice 35 2014	Regulation 62/2017
Guidance/ Technical Standards	Guideline documents published on the CDSCO website	Guideline documents published on the SAHPRA website	Guideline documents published on the PPP website	As available on FARMALKES website

STEP 5:

DETERMINE THE RISK CLASSIFICATION OF THE DEVICE IN EACH TARGET MARKET

- Risk class determines the controls a regulator applies to a device, including the need for pre-market assessment and if certain standards should be complied with.
- The intended use drives the NRAs market authorization requirements given that the higher the risk of the device to a patient, user or the population, the greater the oversight (and requirements) in both premarket assessment and in the post-market setting that a regulator often applies.
- High risk submissions require an assessment of your QMS.

KEY TIP:
To avoid costly repeats of studies or re-write of technical documentation, identify and plan your documentation to meet the requirements for the highest risk classification the device is expected to be.



STEP 6:

DETERMINE APPLICABLE RECOGNITION AND RELIANCE MECHANISMS

- Often the National Regulatory Agency (NRA) of target countries has limited ability to undertake a premarket conformity assessment to assure safety and performance of higher risk IVDs, and as such, rely on either the conformity assessment or the regulatory authorisation of IVDs on the market in jurisdictions with mature regulatory authorities. These mature agencies are referred to as **Reference Regulatory Agencies (RRAs)**.

The most often cited RRAs are those of the “GHTF Big 5” (Canada, US, EU, Australia, Japan); these countries have well-established, mature regulations and regulatory processes for IVDs and medical devices.

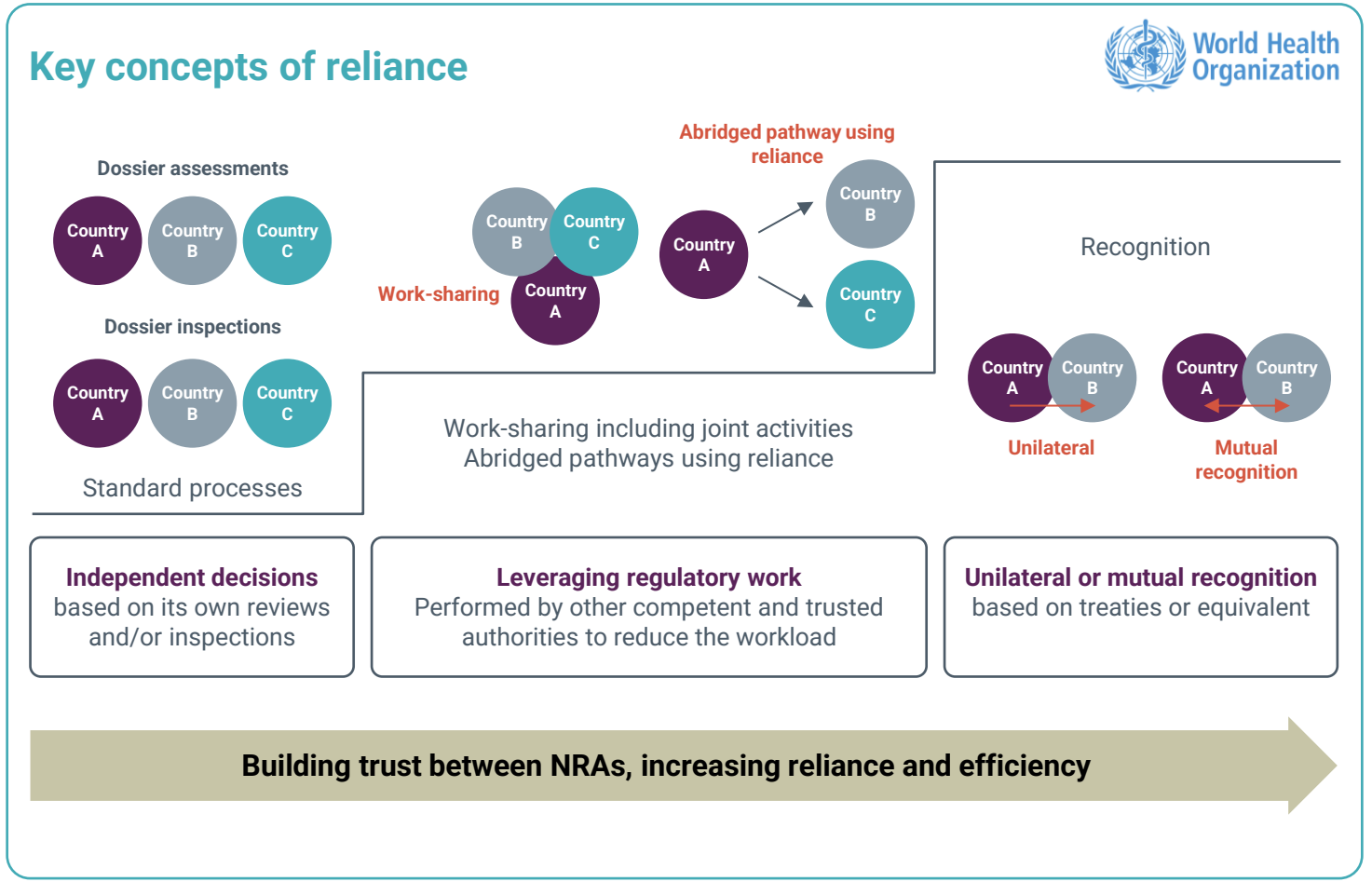
STEP 6:

DETERMINE APPLICABLE RECOGNITION AND RELIANCE MECHANISMS

Some country's regulations apply principles of recognition and reliance to give products access to their regional market.

Recognition: When a regulatory authority accepts the regulatory decision of another authority (also known as the Reference Regulatory Authority or RRA) "as its own" decision.

Reliance: When a regulatory authority takes into account the work products of another authority/RRA (e.g. inspection reports, scientific assessment reports) to inform their own decision. Their ultimate decision may be different than the initial authority.



STEP 6:

DETERMINE APPLICABLE RECOGNITION AND RELIANCE MECHANISMS

RRA	NRA			
	India CDSCO	**South Africa SAHPRA**	**Kenya PPB**	**Indonesia MoH**
Australia TGA	REC	REC	REC	REC
Health Canada	REC	REC	REC	REC
US FDA	REC	REC	REC	REC
EU	REC	REC	REC	REC
Japan PMDA/MHLW	REC	REC	REC	REC
WHO PQ		REC	REC	

REC = Recognition of RRA authorization
REL = Reliance on RRA conformity assessment

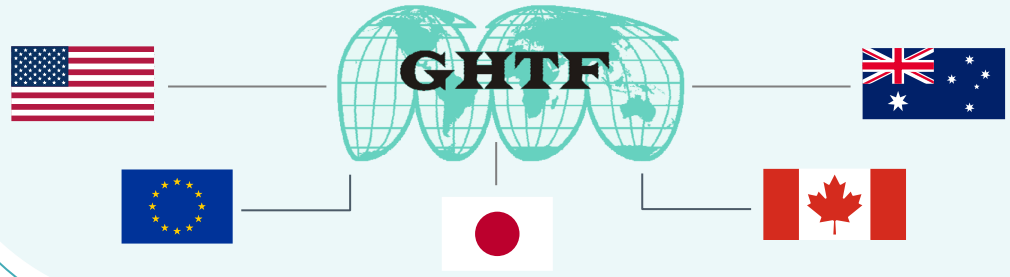
STEP 7:

LEVERAGE THE REFERENCE REGULATORY AGENCIES (RRAS)

TARGET MARKETS + RECOGNITION AND RELIANCE MECHANISMS

IDENTIFY THE RRA THAT COULD FAST-TRACK YOUR MARKET APPROVALS

Global Harmonization Task Force



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IDENTIFY THE RRA THAT COULD FAST-TRACK YOUR MARKET APPROVALS,
including their risk classification system and the resulting impact on conformity assessment and use the most stringent requirements as starting

STEP 7:

LEVERAGE THE REFERENCE REGULATORY AGENCIES (RRAS)

WHO PQ AND RECOGNITION AND RELIANCE

WHO PQ and Recognition and Reliance

In LMICs, many countries also refer to products listed on the WHO website following a WHO Quality Assurance (QA) procedure. The most comprehensive of these is WHO Prequalification (PQ). This can result in expedited processes and prioritization by that jurisdiction's regulatory agency

Procurement

Although regulatory authorisation by the target countries provides a legal basis for placing a product onto that single market, this authorisation may be insufficient to facilitate procurement by large donors.

RRA and WHO for Procurement

Authorization by a mature regulatory authority can lead to an abridged assessment by WHO and also by multiple LMIC NRAs. In addition, it is often a requirement of a donor's procurement policy. As such, authorization by these RRAs could have an indirect benefit on expediting both regulatory approvals and product procurement.

Organization

PEPFAR

PMI

USAID
FROM THE AMERICAN PEOPLE

UNFPA

Unitaid
SAVE LIVES FASTER

unicef

STEP 8:

DETERMINE THE CLINICAL STRATEGY

CLINICAL STUDY CAPACITY WILL DRIVE THE STRATEGY

- **Cost of clinical performance evaluations are often the major contributor determinator to the cost of any market access activities.**
  - A key input into the regulatory strategy is the clinical strategy (and budget) for the device and must be taken into account early in strategic development.
- Based on target markets and the relevant RRAs, identify clinical performance evaluation requirements in terms of where data needs to be generated, and size of data set required (also dependent on Intended Use).
- Keep the most extensive clinical performance evaluations as the ***goal***, and define how you can work towards that using smaller, national data sets which will be less expensive to obtain one by one.

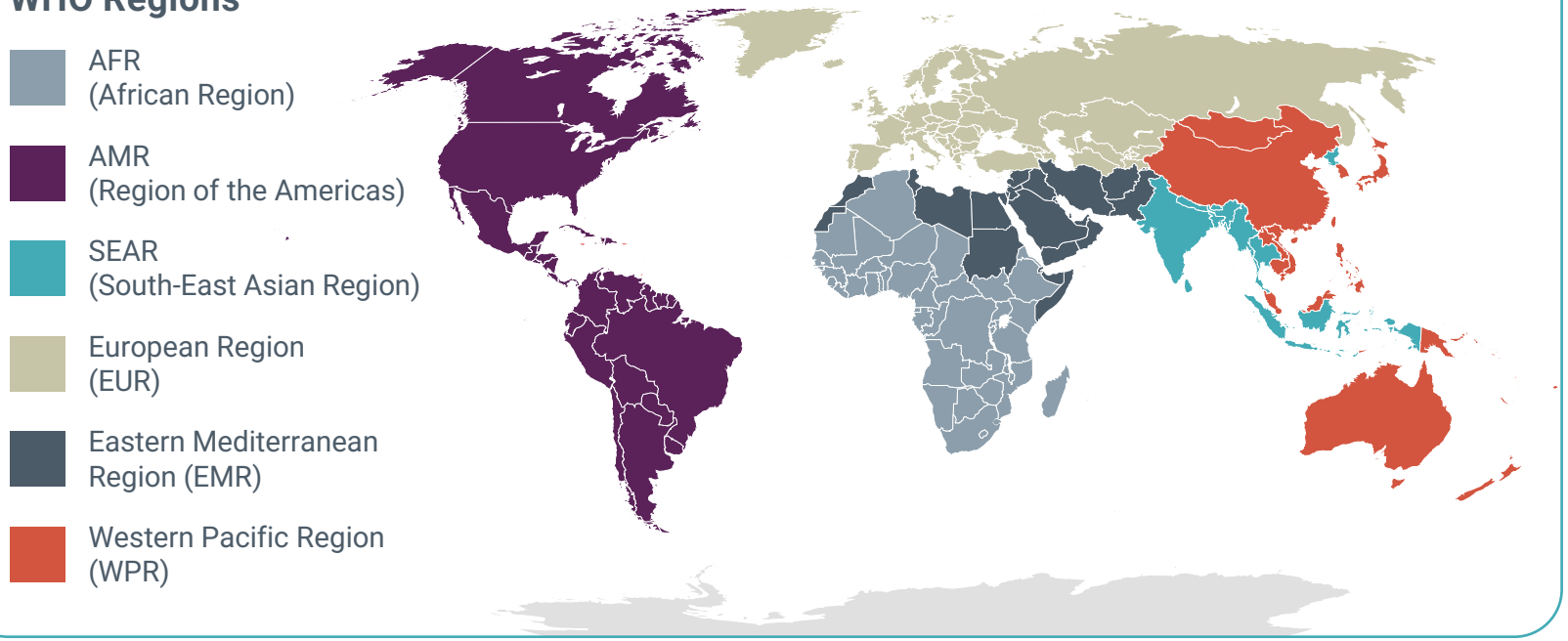
STEP 8:

DETERMINE THE CLINICAL STRATEGY

IMPORTANT:
RRAs will generally want to see clinical studies performed in multiple geographically different locations.

- Prepare a Post-Market Surveillance Plan
  - Both high and low prevalence populations
  - Countries where different strains/genetic variants exist
- Start local, but identify appropriate next study locations to help you achieve your target market goals

WHO Regions



STEP 8:

DETERMINE THE CLINICAL STRATEGY

INDICATIONS FOR USE AND CLINCAL STRATEGY

1. One way to minimize time to market is to evaluate if there are a “lower risk” Indications for Use that could be targeted first that would require less expensive/less extensive clinical performance studies, that would allow you to enter markets/generate revenue faster

2. Determine what level of QMS is required for each Indications for Use – may need to “upgrade” some facets of the QMS (e.g. risk management)

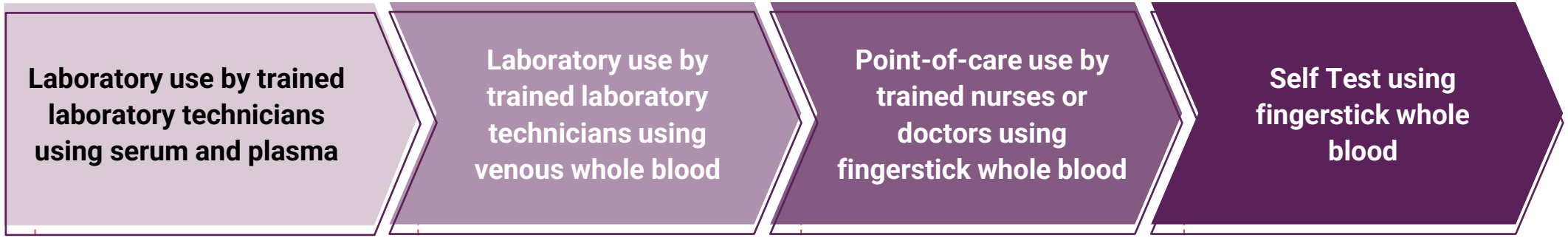
3. Create a plan of what product requirements/studies are needed for each Indication for Use

4. Execute on that plan as time and resources permit

STEP 8:

DETERMINE THE CLINICAL STRATEGY

EXAMPLE OF BUILDING ON INDICATIONS FOR USE



- Can use left-over samples from a hospital, or banked samples
- Need fresh blood samples, but could be left-over samples from a hospital or fresh prospective collections.
- Need prospective collections of fresh fingerstick whole blood Usability studies by non-technical personnel.
- Usability studies Performance studies on lay users using self-collected blood samples.

STEP 8:

DETERMINE THE CLINICAL STRATEGY

ALIGN YOUR STUDY DESIGNS WITH REGULATORY REQUIREMENTS

- Follow Good Clinical Practices (GCPs) and review Ethics requirements (ISO 20916)
- Use a hierarchy of standards to generate study designs (ISO, CLSI)
- Use good study design.
  - *MedTech Europe "Clinical Evidence Requirements under the EU IVDR" V3, 2023*
  - *EQUATOR Network (equator-network.org) - research reporting guidelines*
  - *Prepare a study protocol with pre-defined acceptance criteria*
- Use good reporting practices
  - *E.g. STARD 2015, OECD Good Laboratory Practices (GLP)*
  - *Generate verified line-listed data*
  - *Generate individual Study Reports*

STEP 9:

SPECIFIC REGULATORY REQUIREMENTS

In addition to the analytical and clinical data needed for the regulatory approval, other elements need to be considered **BEFORE SUBMISSION**

DEVICE STUDY REQUIREMENTS

- Studies on local populations
- Testing performed by local testing bodies (e.g. clinical performance studies, incoming lot release)
- Specific usability studies

QMS

- Manufacturing establishment requirements (e.g. ISO 13485, MDSAP, ANVISA)
- Cost to upgrading the QMS
- (Annual) Establishment Listing fees

REGISTRATION REQUIREMENTS

- Studies on local populations
- Testing performed by local testing bodies (e.g. clinical performance studies, incoming lot release)
- Specific usability studies

LABELLING

Includes box/pouch, bottles, Instructions for Use (IFU))

- Will be subject to revision by each jurisdiction
- Think ahead - use graphics instead of text where possible
- Use a certified translation service. Validate the translation by carrying out BOTH forward and reverse translation

LEGAL REQUIREMENTS

- Need for a country-specific representative vs distributor or importer

STEP 9:

SPECIFIC REGULATORY REQUIREMENTS

REGULATORY INTELLIGENCE AND COMPLIANCE MONITORING

KEEPING ON TOP OF CHANGING REQUIREMENTS

- Adherence with regulatory standards and country-specific requirements is key to a streamlined regulatory strategy. If one is missed, a submission may be delayed or rejected entirely.
  - Previously discussed utility of ISO 13485:2016 certification in the QMS Principals presentation
  - Also key is the compliance with ISO 14971 to demonstrate your commitment to risk mitigation and regulatory requirements
  - Be aware of other regulatory standards and associated regulations that may impact your device (e.g. the EU Data Privacy Act (GDPR); REACH/RoHAS, etc.
- Being aware and informed of these requirements helps you prepare for future impact on your device and product sales.
- Create a plan on how to address any updates or modifications to regulations.
- Understand reporting requirements for any changes to the device or to the QMS.
- Update the regulatory strategy as needed.

STEP 10:

PUTTING IT ALL TOGETHER

FIND

EXAMPLE – CREATE YOUR OWN

Using all the information gathered on target NRAs and their RRAs, QMS and clinical study requirements, strategize on how you can reach as many target jurisdictions in the most timely and affordable manner.

	CURRENT STATE	STEP 1: Expand to other countries in region	STEP 2: Expand to ASEAN countries. Target Singapore HSA as RRA	STEP 3: Use WHO PQ to expand outside of region
QMS	Locally certified QMS (not ISO 13485)	Target other NRAs that accept current QMS	QMS upgrades to achieve ISO 13485 certification	ISO 13485 certification
Intended use	Professional use on venous blood/serum/plasma	No change to intended use/ user	Add POC use (fingerstick whole blood)	Add POC use (fingerstick whole blood)
Analytical	Locally required analytical performance studies in one or more selected sample types	New analytical performance studies required – e.g. sample type equivalence study	New analytical performance studies required by HSA	New analytical performance studies required by WHO
Clinical	No clinical performance studies required	New clinical performance studies as required by region	Prospective clinical performance studies at POC	Prospective clinical performance studies at POC at 3 sites in >2 WHO regions
Usability	No usability studies required	No usability studies required	Usability studies as required by HSA	Usability studies as required by WHO

COST, EFFORT, TIME

STEP 10:

PUTTING IT ALL TOGETHER → TESTING THE STRATEGY

Communicate Communicate Communicate!

- Engage with regulators as early and as often as you can (pre-submission meetings)
- Ask the hard questions to get the answers you need
- Replies may alter the strategy, so prepare to be flexible!
- Strategies can take multiple years to complete – touch base on progress and if the strategy still makes sense regularly (e.g. Phase Gate or Design Review meetings)

AND THE WORK CONTINUES…

Once Regulatory Approval is obtained the Regulatory work continues

Prepare a Post-Market Surveillance Plan

- Regulatory compliance does not end with pre-market submission and device approval; post-market surveillance is crucial for insuring ongoing compliance and identifying potential issues or improvements.
- Prepare your PMS Plan BEFORE the device is approved
- Meet minimum requirements for ALL target jurisdictions
- Implement a vigilance system to report adverse events/take corrective action as needed

Look ahead (line extension/claim expansion)

- With Sales Team, anticipate future target markets or market needs/ indications for use
- Wherever possible, plan and design studies early to avoid repeating studies

Regulatory Intelligence and Compliance Monitoring

- Stay informed
- Create a plan on how to address any updates or modifications to regulations
- Understand reporting requirements for any changes to the device or to the QMS
- Update the regulatory strategy as needed

KEY TAKEAWAYS

1

Consider all target markets up front.

2

Prepare the strategy to include requirements for the highest risk device in terms of study design and documentation (to avoid repeats, having to re-create documentation to support a higher risk class), even if you will start with an “easier” claim to start market entry and then “upgrade” to claims that are more expensive/harder to obtain.

3

Consider least burdensome/ least expensive jurisdictions vs. ones that can open doors via Recognition and Reliance.

4

Take advantage of pre-submission discussions to test your strategy.

5

Plan ahead - Consider impact of multiple markets/languages on your labelling to “future proof” the strategy.

FIND

QUESTIONS & FEEDBACK