FIND

DEFINING PRODUCT NEEDS: REGULATORY REQUIREMENTS

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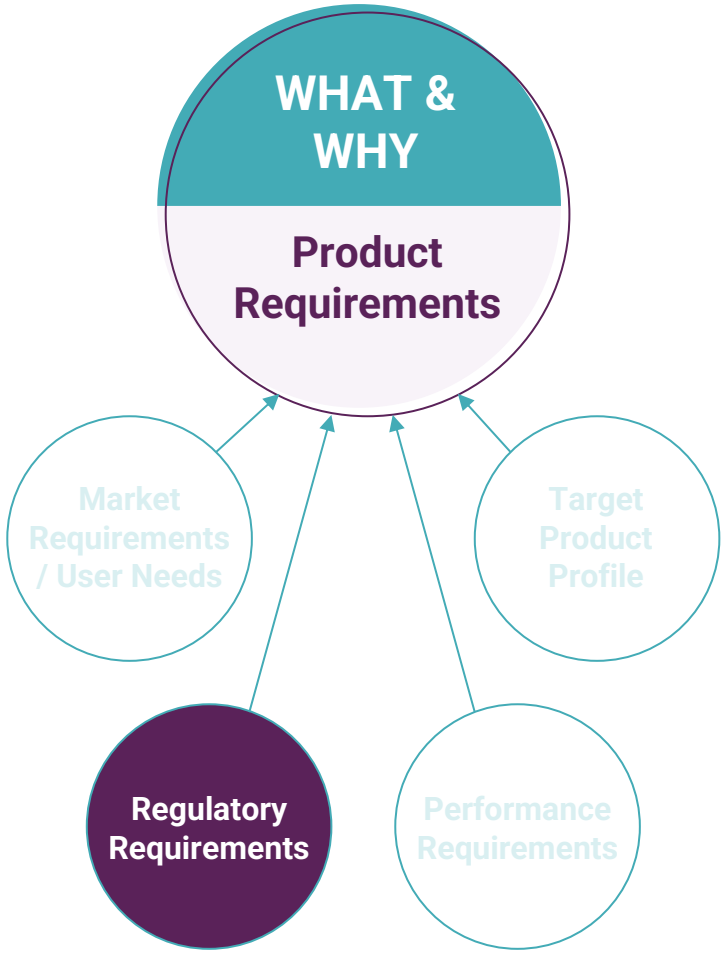
PRODUCT REQUIREMENTS



Examples of relevant categories/aspects for product requirements consideration:

Market Need Why is the product needed?	**Intended Use** Purpose of your device What the test does / how it works	**Indications for Use** Circumstances under which the test will be used
Target Markets Where is the test going to be sold?	**Procurement** Who will buy the product?	**Target Settings** Where the test will be used?
Target Analyte Which analyte to test?	**Specimen Type** (e.g. swap, urine, blood…)	**Analytical & Clinical Performance** (e.g. LoD, sen., spe.)
Operational Characteristics (e.g. shelf life, stability)	**Test Format** (e.g. LFT, strip, ELISA)	**Target COGs** What is the target cost?
Device Classification Based on Risk associated with Intended Use of test	**Waste Management** Test disposal after use	**Digital / Connectivity** Data storage, sharing…

TOPICS

Will review key elements that define regulatory requirements for product design including:

1. How **device type and target market(s)** guide where to look for requirements in general
2. How **Stringent Regulatory Authorities (SRAs) classify devices** based on the Intended **Use/Indications for Use** and how this impacts product requirements
3. Use/utility of **Standards and device specific searches** to get more insight into current thinking of an SRA on product requirements

GOAL:
Efficient and structured approach to product design that avoids costly delays and re-dos

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:

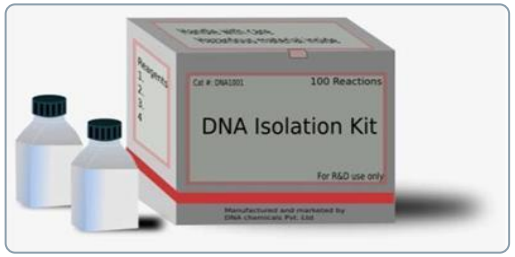
Equipment or apparatus intended by the manufacturer to be used as an IVD medical device.

(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:

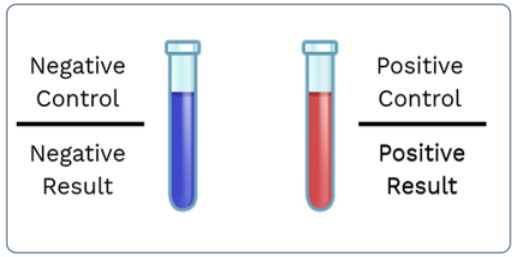
Reagents that an assay manufacturer specifies in device labelling as “required but not provided” in order to carry out the assay as indicated in its instructions for use; specified by catalogue or product number or other specific designation.

(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.

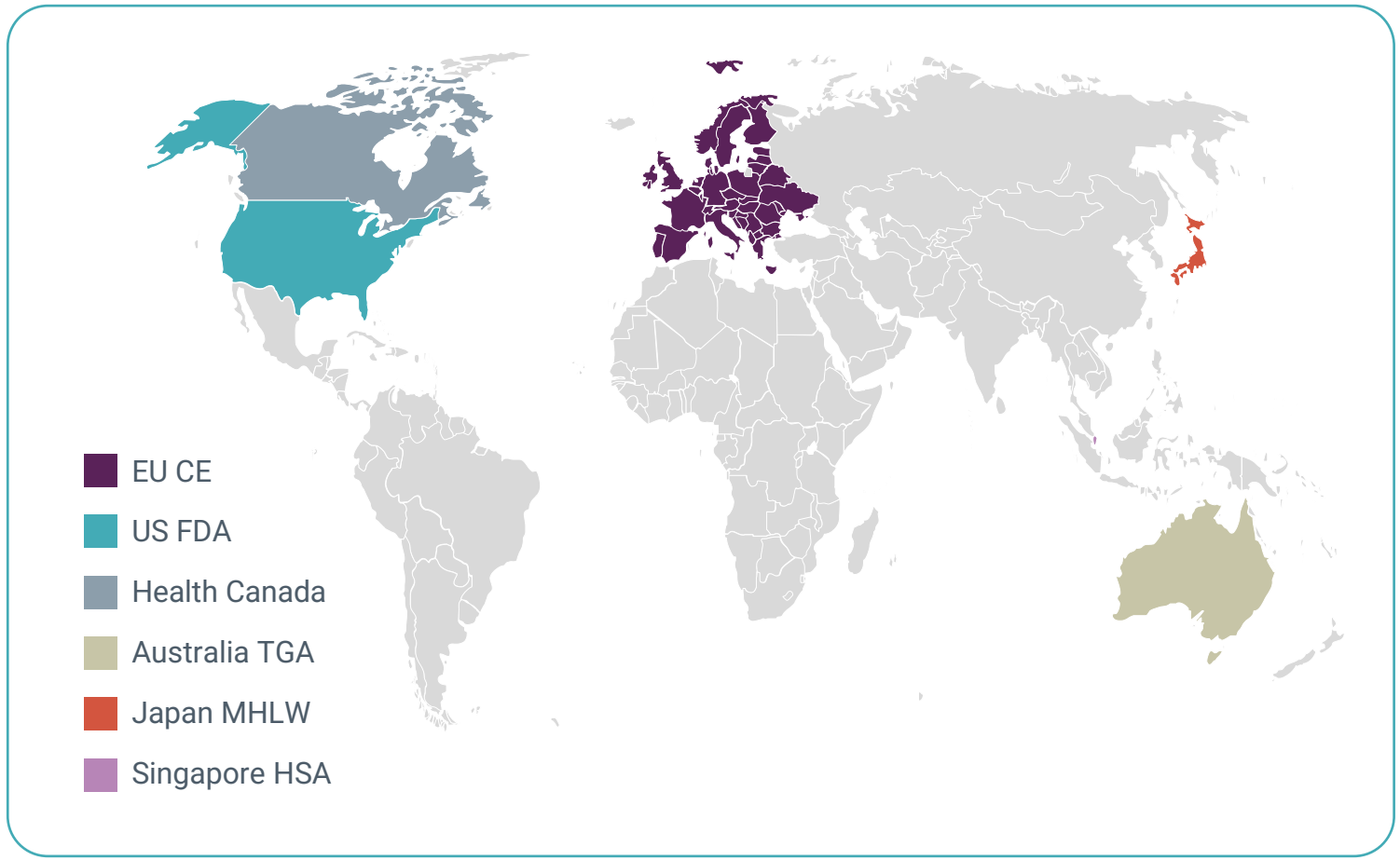
(EU MDR Article 2)



DEVICE TYPE AND MARKETS

IDENTIFY RELEVANT TARGET JURISDICTIONS

- Your company's location (local requirements)
- All countries in which you intend to sell your products and the *governing regulatory agency*
- **Refines the appropriate/ applicable regulations** to review/apply for your company/device



DEFINE 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

INDICATIONS FOR USE INCLUDES USABILITY

Pay attention to the impact of the intended user and use setting on risk classification!

Note: this is of high importance for many regulators but if **of key focus for the WHO**

Specific guidances for usability to be considered and separate risk assessments required

Additional performance validation studies required in hands of the intended users

e.g. human factors, flex studies, results interpretation, observed vs unobserved performance studies for critical tasks, clinical performance in hands of intended users

RISK BASED CLASSIFICATION

Level of risk	USA FDA	Australia TGA	Canada Health Canada	Japan PMDA/MHLW	EU Notified Body	IMDRF/ WHO
Low or no public health risk and/or low individual risk	Class I (low)	Class 1 IVD	Class I	Class I (low risk)	Class A	Class A
Low public health risk and/or moderate individual risk	Class II (moderate)	Class 2 IVD	Class II	Class II (low risk)	Class B	Class B
Moderate public health risk and/or high individual risk		Class 3 IVD	Class III	Class III (high risk)	Class C	Class C
High public health risk and/or high individual risk	Class III (high)	Class 4 IVD	Class IV		Class D	Class D

Data and Documentation Requirements

RISK CLASSIFICATION EXAMPLE – MOLECULAR TB DIAGNOSTIC TEST

INTENDED USE:

MOLDXTB test is a visually read Loop-Mediated Isothermal Amplification (LAMP) test intended for the rapid, in vitro qualitative detection of Mycobacterium tuberculosis complex (MTBC) DNA. The primers provided with this product are designed in the IS6110 region of the MTBC genome DNA. The test uses health care provider-collected tongue swab specimens from individuals (children and adults) with signs or symptoms compatible with TB. This test is intended to be performed by health care workers with minimal or moderate competency in general laboratory practice, at the point of care (POC).

RISK CLASSIFICATION EXAMPLE – MOLECULAR TB DIAGNOSTIC TEST

Level of risk	Canada (Health Canada)	EU IVDR (Notified Body)
Low or no public health risk and/or low individual risk	Class I	Class A
Low public health risk and/or moderate individual risk	Class II	Class B
Moderate public health risk and/or high individual risk	Class III	Class C
High public health risk and/or high individual risk	Class IV	Class D

RISK CLASSIFICATION EXAMPLE – MOLECULAR TB DIAGNOSTIC TEST

Level of risk	Canada (Health Canada)	EU IVDR (Notified Body)	Singapore (HSA)	South Africa (SAHPRA)	GHANA (FDA)
Low or no public health risk and/or low individual risk	Class I	Class A	Class A	Class A	Class I
Low public health risk and/or moderate individual risk	Class II	Class B	Class B	Class B	Class II
Moderate public health risk and/or high individual risk	Class III	Class C	Class C	Class C	Class III
High public health risk and/or high individual risk	Class IV	Class D	Class D	Class D	Class IV

INTENDED USE AND DEVICE CLASSIFICATION

RISK CLASSIFICATION EXAMPLE – MOLECULAR TB DIAGNOSTIC TEST

SRA	Risk Classification
Health Canada	▪ Class III (Rule 2 subrule b(i) - IVDD used to detect the presence of, or exposure to, a transmissible reagent that causes a serious disease where there is a risk of propagation in the Canadian population. ▪ Near-patient IVDD are automatically Class III https://www.canada.ca/en/health-canada/services/drugs-health-products/medical-devices/application-information/guidance-documents/guidance-document-guidance-risk-based-classification-system-vitro.html
EU CE IVDR	▪ Class C rule 3 c for detecting the presence of an infectious agent, if there is a significant risk that an erroneous result would cause death or severe disability to the individual, foetus or embryo being tested, or to the individual's offspring. ▪ Devices for near patient testing are classified in their own right https://health.ec.europa.eu/latest-updates/update-mdcg-2020-16-rev2-guidance-classification-rules-vitro-diagnostic-medical-devices-under-2023-02-10_en
Singapore HSA	▪ Class C (Rule 3a) - IVD medical devices intended for use in detecting the presence of, or exposure to, an agent that presents a moderate public health risk. ▪ Rule 4 – IVD medical devices intended for near patient testing are classified as Class C https://www.hsa.gov.sg/docs/default-source/hprg-mdb/guidance-documents-for-medical-devices/gn-14-r3-guidance-on-the-risk-classification-of-in-vitro-diagnostic-md-(2023-jul)-pub.pdf?sfvrsn=58f33d7a_2
South Africa (SAHPRA)	▪ **Class D** (Rule 1) - an IVD medical device intended to be used to detect the presence of, or exposure to, a transmissible reagent that causes a serious disease with a high risk of propagation. ▪ Rule 4 – An IVD for self-testing is classified as Class C unless a) the result of the examination is not determining a serious condition, ailment or defect, or b) the examination is preliminary and additional follow-up testing is required. https://www.sahpra.org.za/document/guideline-for-classification-of-medical-devices-and-ivds/
Ghana (FDA)	▪ **Class IV** (Rule 2a) - an IVDD that is intended to be used to detect the presence of, or exposure to, a transmissible agent is classified as Class II, unless it is intended to detect the presence of, or exposure to, a transmissible agent that causes a life-threatening disease if there is a risk of propagation I the Ghanaian population, in which case is it classified as Class IV. ▪ A near patient IVDD is classified as Class III. https://www.moh.gov.gh/wp-content/uploads/2016/02/Public-Health-Act-851.pdf

HOW RISK CLASSIFICATION IMPACTS REGULATORY REQUIREMENTS

CLASS	RISK LEVEL	EXAMPLES	SELECTED REGULATORY REQUIREMENTS (WHO Global Model Regulatory Framework for Medical Devices including IVDs)
A	Low individual risk and low public health risk	General use buffer	▪ Basic QMS Requirements ▪ Technical documentation requirements – none; no technical assessment
B	Moderate individual risk and/or low public health risk *-includes IVDs for self-testing with less risk to the patient than those in Class C*	Fertility testing	▪ ISO 13485-conforming QMS ▪ Technical documentation requirements – summary of studies may be submitted; analytical performance studies and limited clinical performance studies required.
C	High individual risk and/or moderate public health risk *-includes IVDs that are intended to be used for detecting an infectious agent without a high risk of propagation, or for detecting the presence of an infectious agent with the potential to cause death or severe disability in the case of an erroneous result*	Blood glucose self testing	▪ ISO 13485-conforming QMS ▪ Technical documentation requirements - Full Technical Dossier submitted for review; includes protocols, line listed data and final reports for all clinical performance studies. Analytical and clinical performance studies required. May require in country assessments and acceptance testing by a defined body/independent organization selected by the regulator.
D	High individual risk and high public health risk *- includes IVDs that detect or are exposed to life-threatening transmissible agents or transmissible agents and infectious diseases with a high risk of propagation*	HIV blood donor screening, HIV self testing	

RISK CLASSIFICATION AND INTENDED USE - RECAP

- Risk classification of device is a function of its **intended use** and may vary by jurisdiction

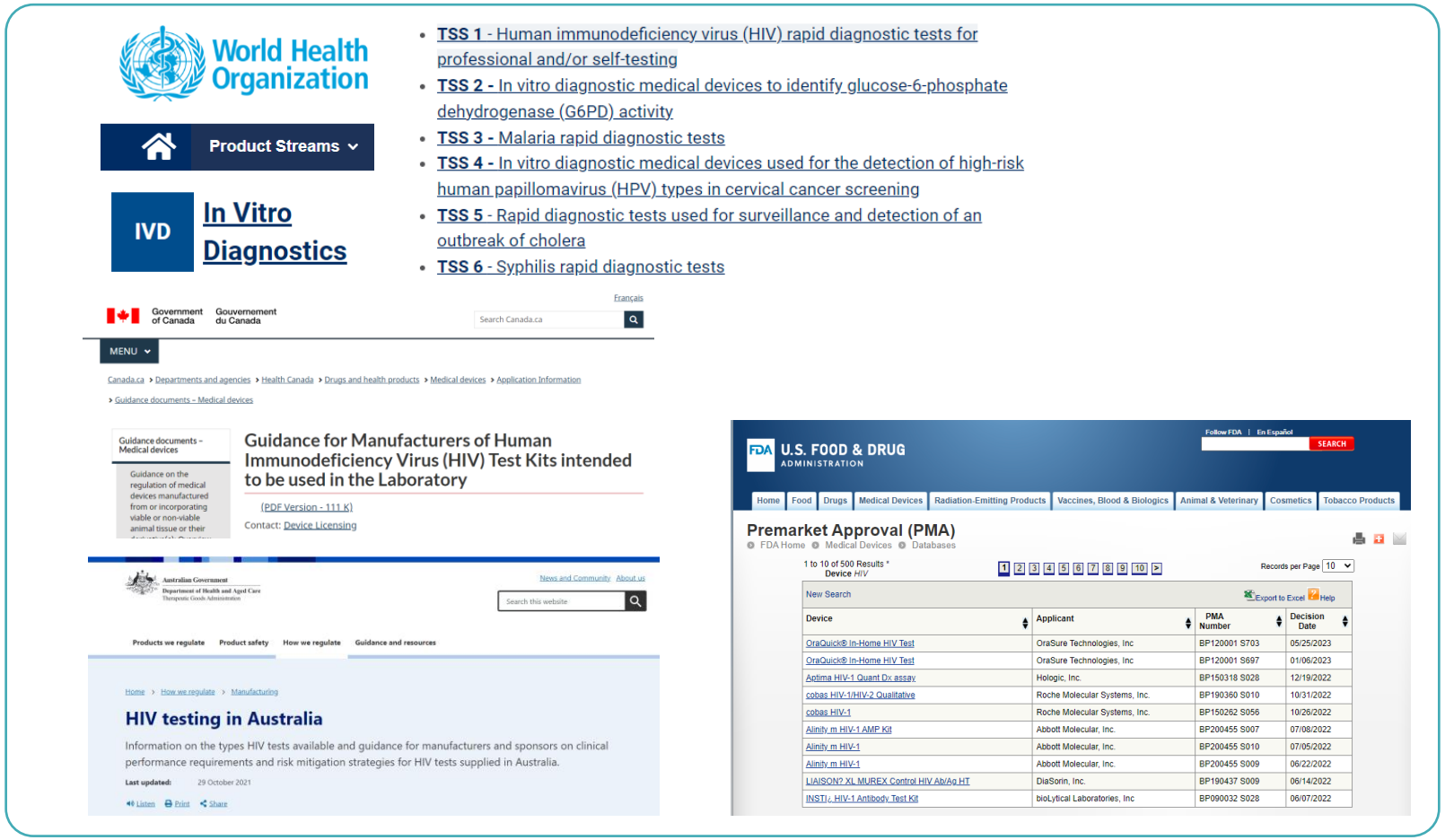
Indications for Use changes:

- design controls,
- risk management requirements,
- quality requirements,
- number and size of studies (including in-country evaluations),
- amount of associated documentation that needs to be submitted to an SRA,
- regulatory pathway of a device

TOP TIPS:
If there is any uncertainty, generate a plan to meet the requirements for the highest risk class/most "demanding" SRA to avoid repeating analytical or clinical performance evaluations or having to create documentation retrospectively

DEVICE SPECIFIC SEARCH

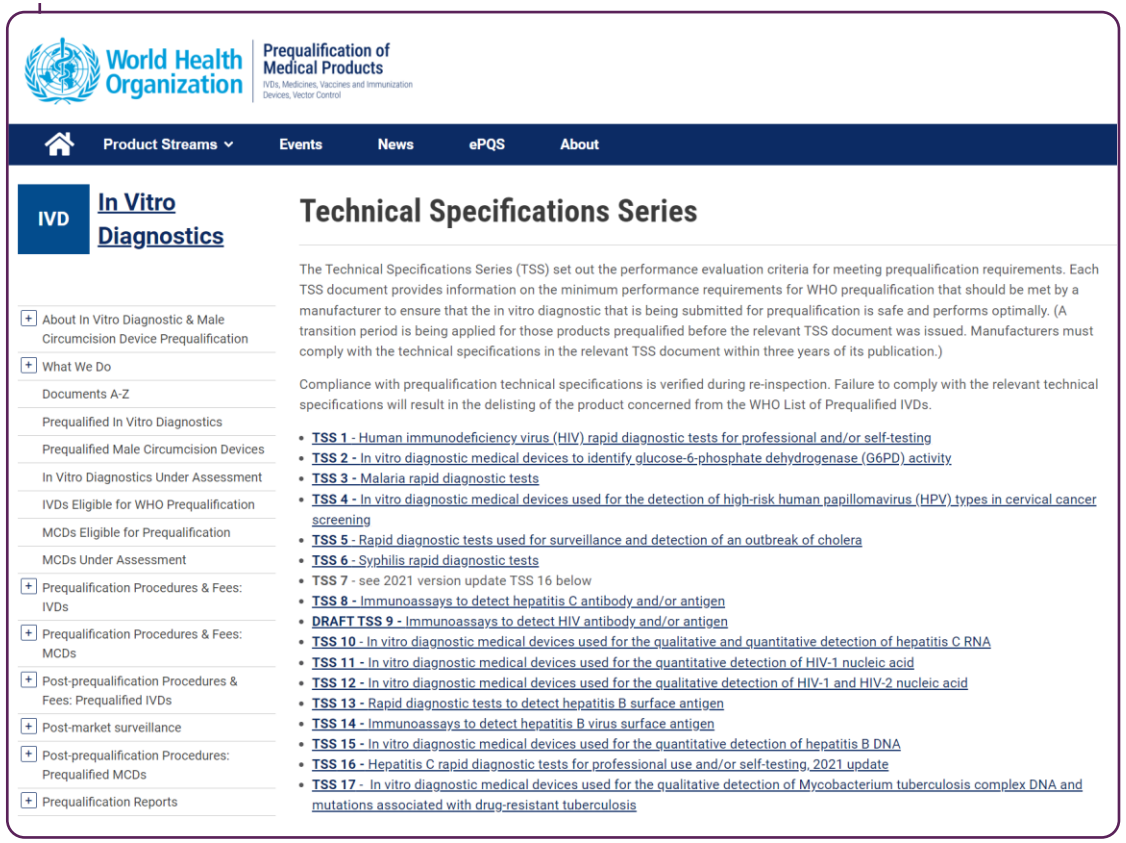
- Look globally for specific regulations or guidance for your device
  - Good start are Global Harmonization Task Force (GHTF) founding members* List of Approved Standards
- Identify similar devices on the market and research how they got to market/what studies they needed
  - Shows “current thinking” of an SRA on what is needed to get a specific type of device on the market



*GHTF Founding Members: Australia, Canada, EU, Japan, USA

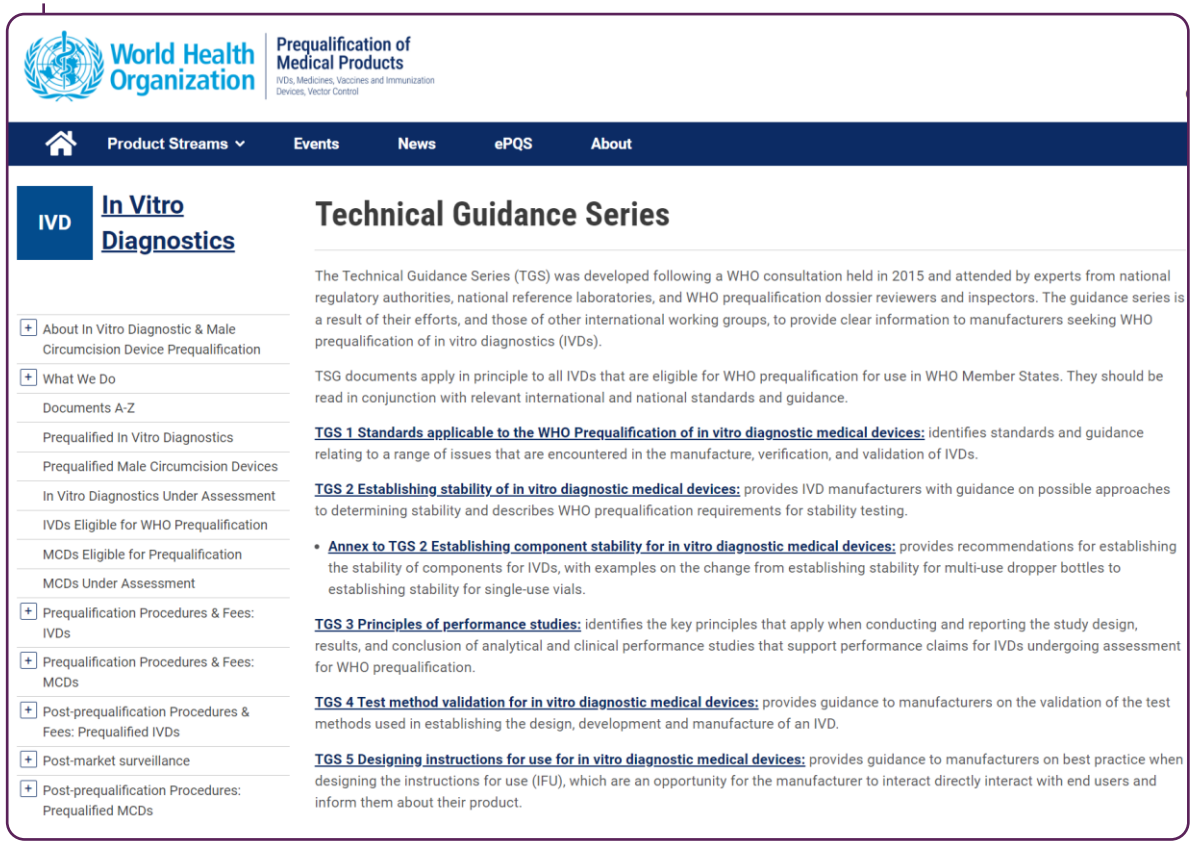
OTHER RESOURCES

- **Technical Specification Series (TSS)** describe WHO's interpretation of the minimum validation and verification studies to be undertaken by the manufacturer in support of in vitro diagnostic (IVD) performance claims



https://extranet.who.int/prequal/vitro-diagnostics/technical-specifications-series

- **Technical Guidance Series (TGS)** contain valuable information on a range of issues that are encountered in the manufacture, verification, and validation of specific categories of IVD. TGS apply in to all IVDs that are eligible for WHO PQ.



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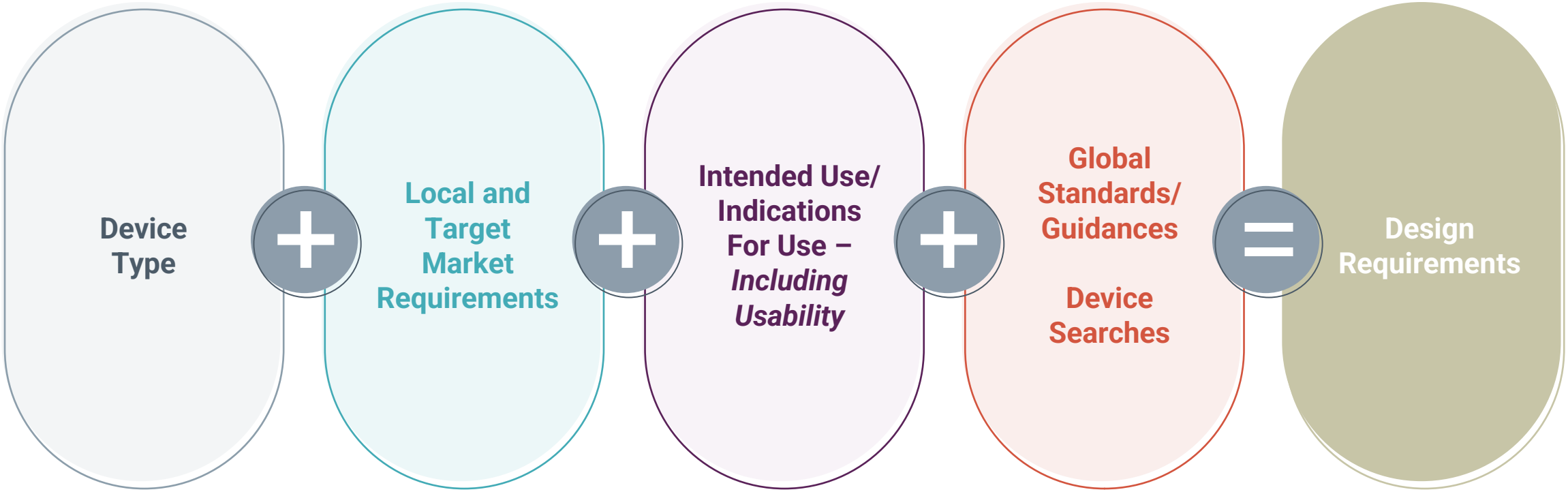
SUMMARY


Device Type
+
Local and Target Market Requirements
+
Intended Use/ Indications For Use – *Including Usability*
+
Global Standards/ Guidances
Device Searches
=
Design Requirements

KEY TAKEAWAYS

To minimize risk of having to repeat work to enter a new market:

1. Plan for all potential target markets.
2. Clearly define your Intended Use and Indications for Use.
3. Identify the most stringent risk classification for the device.
4. Search globally for guidance and standards.
5. Once this exercise is complete, identify product requirements.

FIND

QUESTIONS & FEEDBACK