Development of new technical specifications for PQ (TSS): Blood glucose monitoring devices and HbA1c POC devices

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Outline

- Trigger for the new technical specification documents
- Current landscape of BGM and HbA1c POC IVDs
- TSS development process and Timelines
- Overview of technical specifications
- Challenges
- Next steps

Trigger action for a new TSS document

- needs assessment -

- Prequalification eligibility criteria expanded to a new IVD **(TSS documents)**;
- Absence or lack of existing published guidance (WHO, international or national guidance or standards) on similar or related topics;
- Consultation with disease programme within WHO HQ or regional offices;
- Anticipated new WHO recommendations which will impact WHO PQ – Diagnostic Assessment activities; and/or
- Key stakeholders' request for new or additional guidance documents.

Diabetes Resolution - Diabetes targets

Five new targets set the standard that, by 2030:

- **80%** of people living with diabetes are diagnosed
- **80%** have good control of glycaemia
- **80%** of people with diagnosed diabetes have good control of blood pressure
- **60%** of people with diabetes of 40 years or older receive statins
- **100%** of people with type 1 diabetes have access to affordable insulin and **blood glucose self-monitoring**

More info: www.who.int/news-room/feature-stories/detail/first-ever-global-coverage-targets-for-diabetes-adopted-at-the-75-th-world-health-assembly

Overview of workstreams

Workstream 1	Access to essential diabetes medicine and associated health technologies
Workstream 2	Technical products (e.g., global coverage targets, global price tag)
Workstream 3	Prevention, health promotion and health literacy
Workstream 4	Country support
Workstream 5	Research and innovation
Workstream 6	Governance, strategy and partnership (e.g., TAG-Diabetes, Global Diabetes Compact Forum)

Blood glucose monitoring device manufacturers….

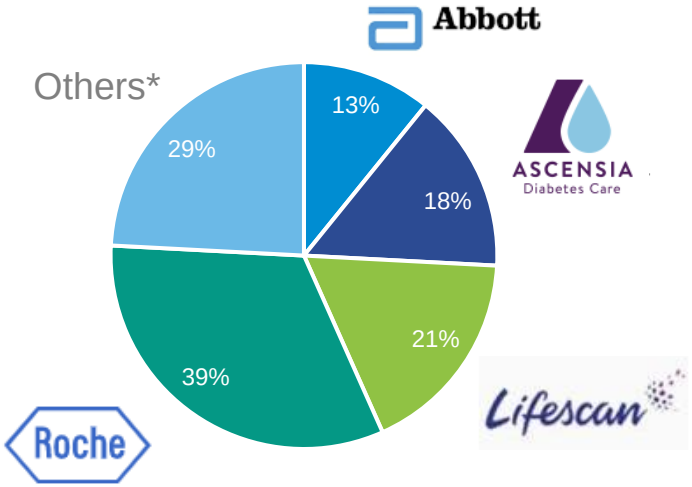
Market

The blood glucose monitoring market is estimated to be worth over **6.4 bn US$ globally** (2.4 bn in LMICs)[1]

Four companies hold **70%** of the LMIC market share

Test **strip sales** drive **97%** of the revenue

Market share distribution of BGM manufacturers in LMICs



Products

Globally, there are >80 companies on the market with BGMs

Many meters/strips are “original external manufacturer” (OEM) products → produced by company A, re-branded by company B and company C → sold in the same or different markets

>50% of companies are offering two or more meters

Company examples; Source: FIND landscape, data on file

1 Source: https://www.finddx.org/wp-content/uploads/2021/10/Market-Report_Self-monitoring-Devices-in-LMICs.pdf

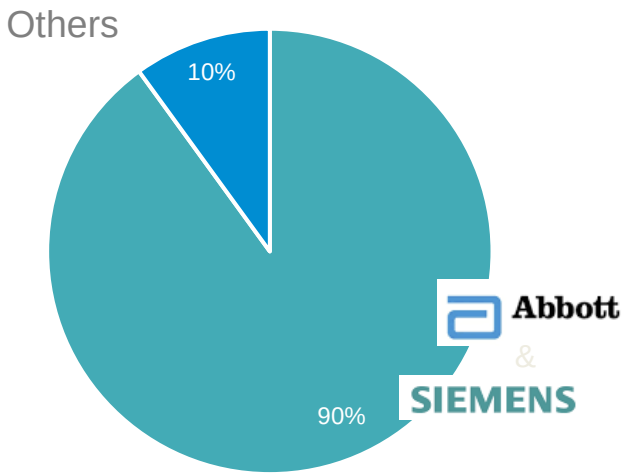
HbA1c POC device manufacturers….

Market

The **global POC HbA1C** testing market is estimated to be between US$ 0.7-1.5 billion

"**Africa** is expected to be the **fastest-growing region**"[1]

Two companies hold **90%** of the global POC HbA1c market[2]



Products

Globally, a recent FIND landscape identified 49 companies with HbA1c POC devices on the market, offering 76 devices[3]

HbA1c POC devices/cartridges can also be OEM products

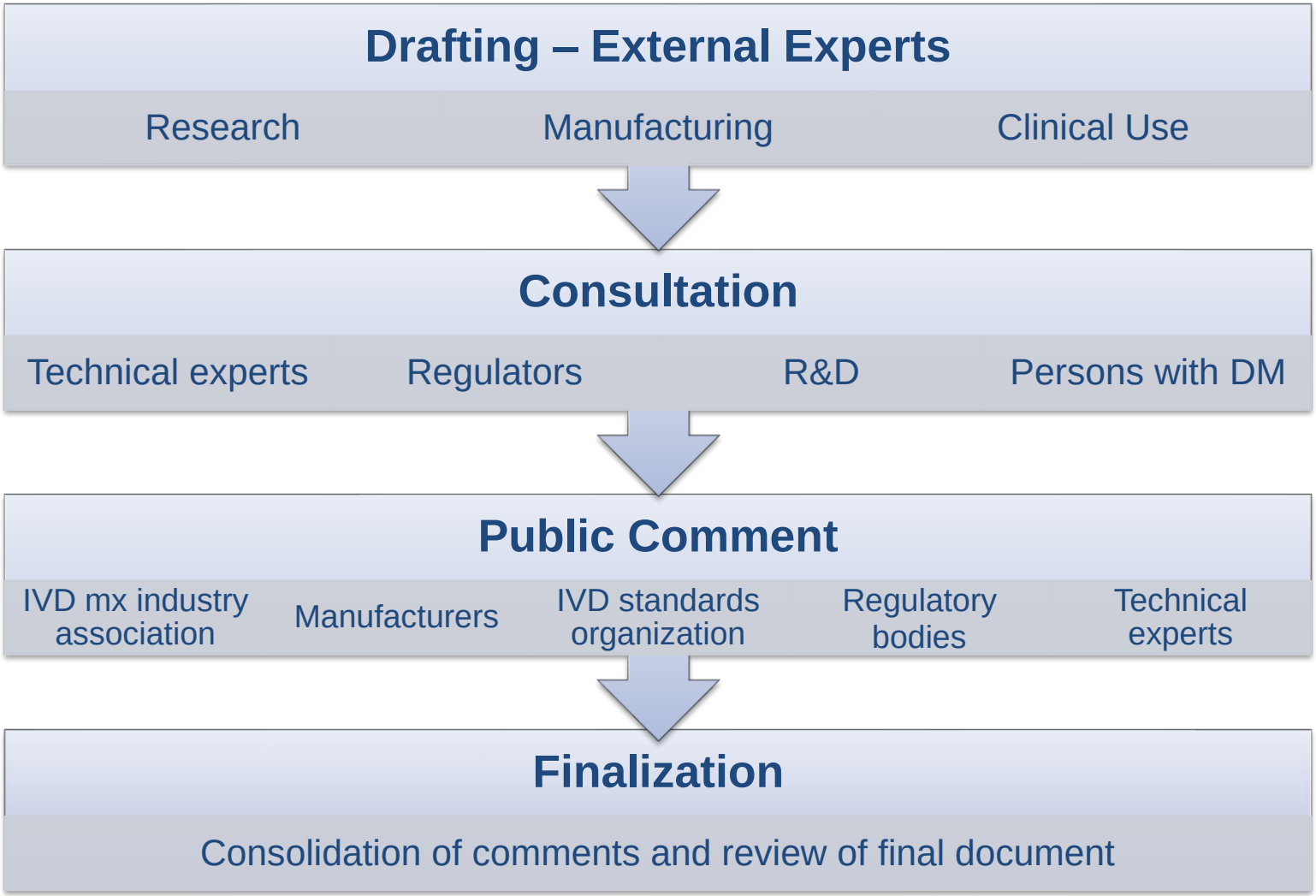
*some examples of others:

1 https://www.businesswire.com; https://www.thebusinessresearchcompany.com/report/poc-hba1c-testing-market

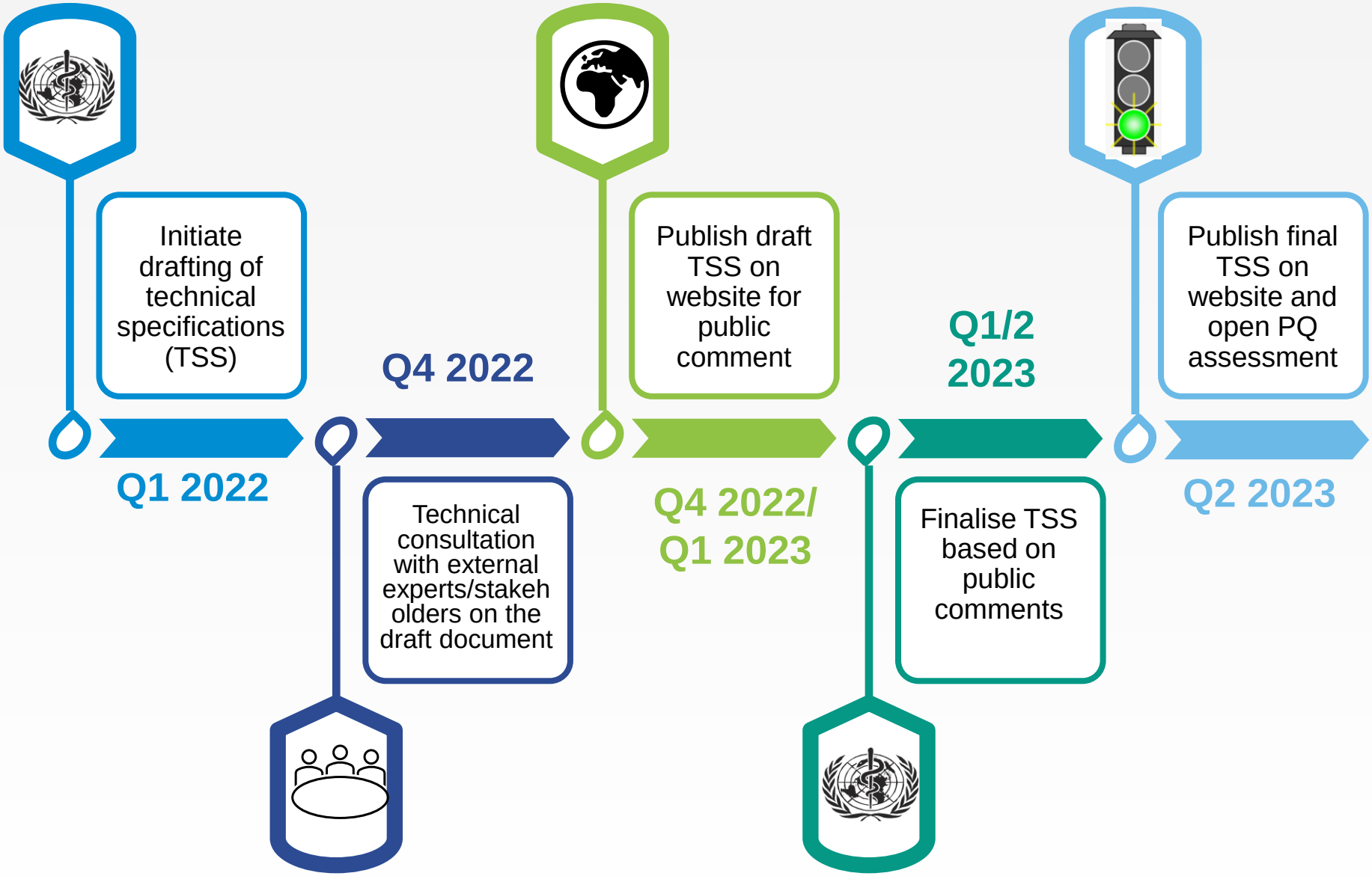
2 Lenters-Westra et al. Analysis: Investigating the quality of POCT devices for HbA1c, what are our next steps? Technology Report 2019

3 Company examples; Source: https://www.finddx.org/wp-content/uploads/2022/01/20220110_Landscape-POC-HbA1c_Final-2022.pdf

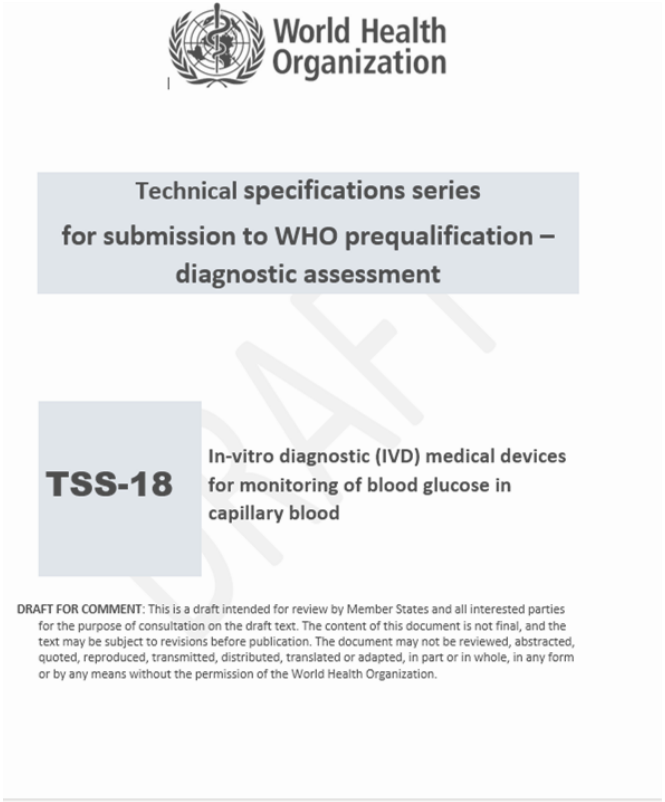
TSS development process



Timelines for BGM and HbA1c POC IVD TSS



Overview of the technical specifications document



World Health Organization

Technical specifications series
for submission to WHO prequalification – diagnostic assessment

TSS-18

In-vitro diagnostic (IVD) medical devices for monitoring of blood glucose in capillary blood

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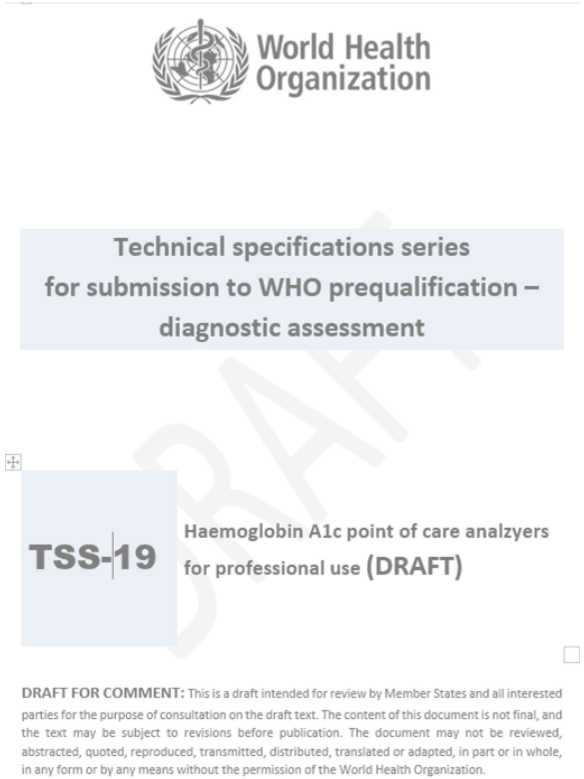

World Health Organization

Technical specifications series
for submission to WHO prequalification – diagnostic assessment

TSS-19

Haemoglobin A1c point of care analzyers for professional use (DRAFT)

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TSS - Overall Structure

- Introduction
- Other WHO guidance documents
- Performance principles for WHO PQ
  - Intended use
  - Diversity of specimen types, users and testing environments
  - Applicability of supporting evidence to the IVD under review (locked down design of IVD, IFU, lots, reference standard)
- Table of Requirements
  - Analytical performance
  - Clinical evidence
  - Qualification of usability
- Source documents

- "shall" indicates that the manufacturer is required to comply with the technical specifications;
- "should" indicates that the manufacturer is recommended to comply with the technical specifications, but it is not a requirement;
- "may" indicates that the technical specifications are a suggested method to undertake the testing, but it is not a requirement.

WHO guidance documentation

WHO NCD Diabetes publications guide PQ in drafting TSS (and inform the manufacturer on the IVD use)

PQ guidance documents exist to support manufacturers preparing their dossier

Performance principles for WHO prequalification

Diversity of specimen types, users and testing environments and impact on required studies

BGM:

- Variety of users: **self testers and lay users**– trained HC workers – professional lab users
- Critical specimen type: capillary blood
- Diverse environments: extremes of humidity, temperature and altitude
- Function: used for monitoring diabetes
- → specific requirements for analytical specificity studies, stability studies, validation of procedure and human factors/flex studies, for clinical and usability studies
- ISO 15197 +

Diversity of specimen types, users and testing environments and impact on required studies

HbA1c POC IVDs

- Scope of users more limited than BGM but still diverse: trained users at point of care (e.g mobile testing facilities) - professional use in labs
- Critical specimen type: Capillary blood (and venous blood accepted in addition)
- Diverse environments which have potential to affect performance of the IVD (humidity, temperature, dust, etc.)
- Diverse populations with different prevalence of variant Hb, haemoglobinopathies, synthesis disorders
- Function: monitoring of DM or aid to diagnosis of T2DM

Applicability of supporting evidence to IVD under review

BGM/HbA1c:

- Description of what is considered to be a final (locked-down) version of the IVD
- Explanation of the number of lots/critical components to be used
- How results should be reported
- What is considered an acceptable comparator reference method for analytical and clinical studies

Part 1) Analytical performance & other evidence

Stability of specimens Collection, processing, transport, storage of all specimen type(s) claimed in the IFU	**Validation of Assay Procedure** ▪ Validation of assay parameters ▪ Carry over
Validation of Specimens ▪ Validation of alternative site testing ▪ Demonstration of validity of all specimen types ▪ Demonstration of equivalence of claimed anticoagulants and/or frozen samples	**Usability and human factors**
Metrological traceability of calibrators and control material values	**Electromagnetic compatibility** **Software/firmware validation**
Accuracy of Measurement ▪ Trueness ▪ Trained operator accuracy ▪ Precision (repeatability, reproducibility)	**Cleaning and disinfection validation**
Analytical Specificity ▪ Potentially interfering substances and medical conditions	**IVD Stability** ▪ Shelf life (including transport stability) ▪ In-use stability
Measuring range of the assay ▪ Measuring range ▪ Linearity	

Part 2) Clinical evidence & Part 3) ….

Part 2) Clinical evidence

Diagnostic accuracy performance	
Variant interference (HbA1c)	

Part 3) Qualification of usability (self testing/ POC)

Label comprehension study	
Results interpretation study	
Observed untrained user study (BGM self test)	

Challenges with drafting TSS for BGM

- Due to lack of resources to diagnose diabetes - handheld BGMs are being used for diagnosis in resource limited settings
    - However 1st version of TSS will not include validation requirements for diagnosis claim
    - Manufacturers to contact WHO in advance if they have this claim as part of their intended use

Next steps

End of 2022 - Q1 2023
Draft TSS to be published on our website and disseminated for public comment

Aim to get substantial feedback as we enter this new area of work

Resources for manufacturers

- CLSI documents
- ISO 15197 and other ISO standards…
- HbA1c Secondary reference materials and Glucose reference materials are available
    - Info will be included in the TSS draft documents
- PQ Technical Guidance series documents
- Support for manufacturers from the WHO – Local Production & Assistance (LPA) Unit https://www.who.int/teams/regulation-prequalification/lpa

THANK YOU