



World Health
Organization

REGIONAL OFFICE FOR **Africa**

REGIONAL FRAMEWORKS FOR MEDICAL PRODUCT REGULATION

24 March 2021
WHO EUL for IVDs

Stanislav KNIAZKOV,
TO Regulatory Systems
MIM/ULC/ WHO AFRO



HEALTHY LIVES AND WELLBEING FOR ALL AT ALL AGES

The Actions Framework Targets

OUTCOMES
Essential services
utilization



HEALTH SECURITY

UNIVERSAL HEALTH COVERAGE

- Essential services availability
- Essential services coverage
- Financial risk protection

OTHER SDGS HEALTH INTERVENTIONS

- | | |
|----------------|-------------------|
| 1. Poverty | 8. Econ growth |
| 2. Nutrition | 10. Inequalities |
| 4. Education | 13. Climate |
| 5. Equality | 16. Inclusiveness |
| 6. Clean water | 17. Partnerships |

SERVICE SATISFACTION

By 2030:
at least 80% of Member States will have health systems that are performing optimally* for effective delivery of essential package of health and related services.

OUTPUTS
Health system
performance



ACCESS TO
ESSENTIAL
SERVICES

QUALITY OF
ESSENTIAL
SERVICES

DEMAND FOR
ESSENTIAL
SERVICES

RESILIENCE IN
ESSENTIAL
SERVICES
PROVISION

all Member States will have at least 80% of their populations utilising the identified essential package of health and related services

INPUTS /
PROCESSES
Health system
building block
investments



HEALTH FINANCING

NATIONAL AND SUB NATIONAL SERVICE DELIVERY SYSTEMS

HEALTH
INFRASTRUCTURE

MEDICINES, PRODUCTS
& SUPPLIES

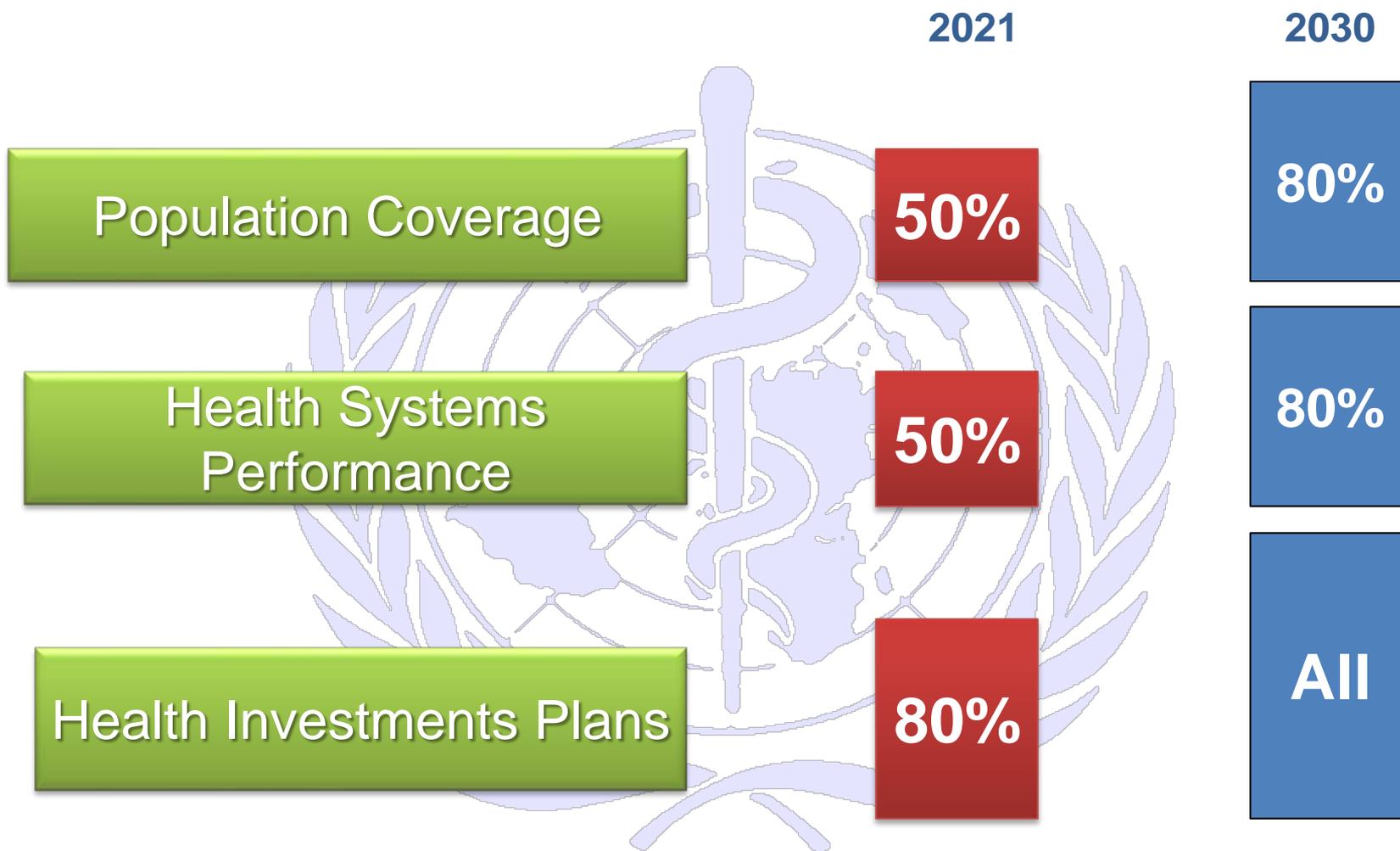
HEALTH WORKFORCE

HEALTH GOVERNANCE

HEALTH INFORMATION

all Member States will have in place and be implementing the investments plans needed to align their health systems to the SDGs

AF Interim Targets



Regional Strategy for Medical Product Regulation, 2016-2025

Adopted at the 66th Session of the Regional Committee for Africa in August 2016 in Addis-Ababa



AIM: to support NMRAs in fulfilling their functions for improving access to medical products which meet international standards of quality, safety and efficacy

Regional Strategy Target Areas

- ◆ Governance
- ◆ Expand regulatory functionality
- ◆ Strengthen regulatory capacity
- ◆ Counteract proliferation of S&F medical products
- ◆ Harmonization and convergence



Governance

- Functional NMRAs with
 - governing bodies
 - quality management systems

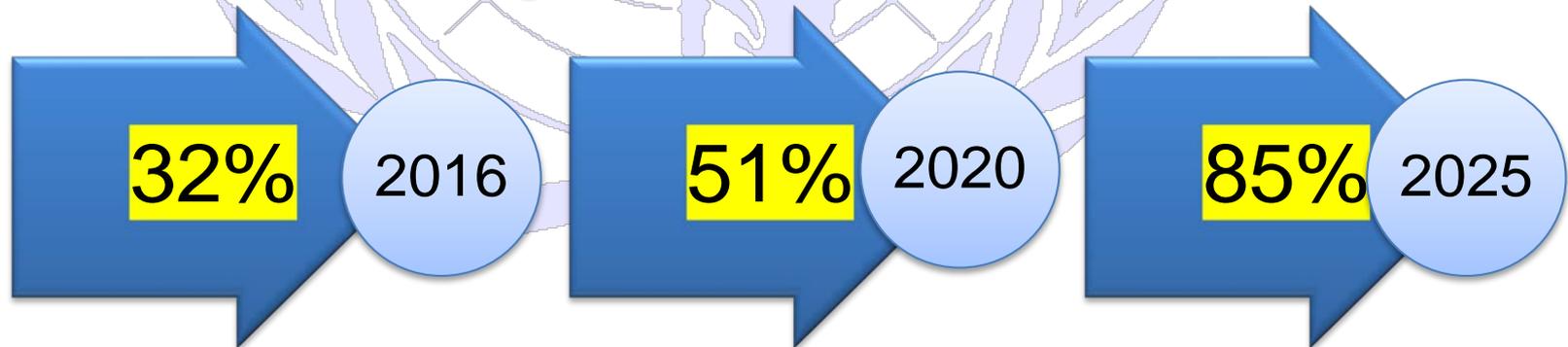


NMRAs Capacity

- Assessment of quality and preclinical data of medical products



- Medical device regulation

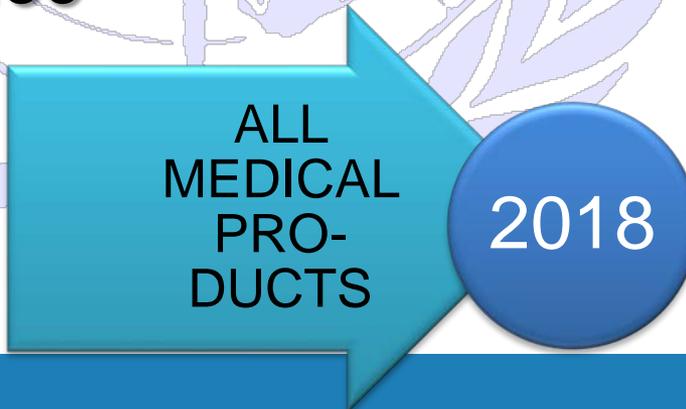


Implementation of Regulatory Functions

- Clinical trial application or marketing authorization



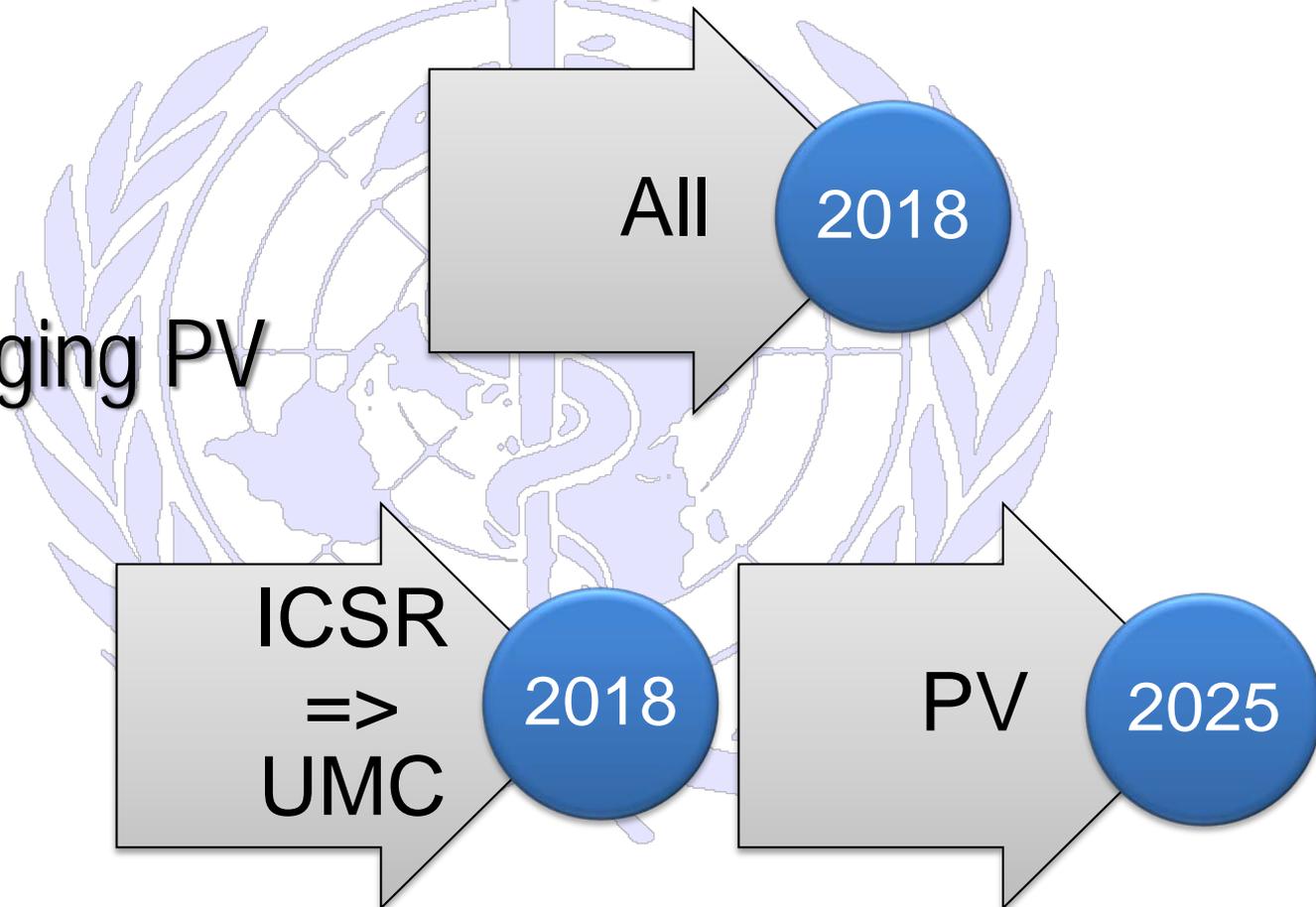
- Market surveillance



Combating SF

- Access to certified or prequalified QC laboratories

- Leveraging PV



Harmonization and Convergence

- Joint reviews of clinical trial applications

AVAREF
x 3-10
per year

2020

- Mutual recognition of regulatory decisions in RECs

29%

2016

100%

2018

- Establishment of AMA



World Health
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Thank you

Overview of Emergency Use Listing procedure



Ute Ströher, PhD

In Vitro Diagnostics assessment, WHO Prequalification



WHO EUAL/EUL background

- WHO Emergency Use Assessment and Listing (EUAL) mechanism developed in response to the 2014 - 2016 Ebola outbreak
- since Jan 2020: Emergency Use Listing (EUL) procedure
- It is intended to assist interested procurement agencies and Member States on the suitability for use of a specific IVD, based on a minimum set of available **quality, safety, and performance** data
- Risk-based approach to expedite the availability of IVDs needed in public health emergency situations



EUL in context of the COVID-19 pandemic

- 30 Jan 2020: the WHO DG declared that the outbreak of 2019-nCoV constitutes a PHEIC
- 28 Feb 2020: manufacturers of IVDs for the detection of **SARS-CoV-2 nucleic acid** are invited to submit an EOI for assessment of candidate IVDs under the EUL procedure
- 17 Apr 2020: WHO extended the invitation to manufacturers of IVDs intended for **antibody detection**
- 09 Jun 2020: WHO extended the invitation to manufacturers of RDTs intended for **antigen detection**
- March 2021: WHO extends the invitation to manufacturers of IDTs intended for **antigen detection**

WHO PREQUALIFICATION TEAM:
DIAGNOSTICS



Invitation to manufacturers of in vitro diagnostics for SARS-CoV-2 to submit an application for emergency use listing by WHO (updated 9 June 2020).

1 Introduction

The global spread of COVID-19 has dramatically increased the number of suspected cases and the geographic area where COVID-19 testing is needed to identify infected individuals. In order to do this, in vitro diagnostics (IVDs) of assured quality, safety and performance are required.

On 30 January 2020, the Director-General declared that the outbreak of COVID-19 caused by SARS-CoV-2 constitutes a PHEIC. IVDs of assured quality, safety and performance are needed for e.g., screening suspect cases, diagnosis, case cluster finding or serosurveillance. Because this is a new strain of coronavirus that has not been previously identified in humans, there are several assays to detect SARS-CoV-2 now under development.

The World Health Organization (WHO) revised the Emergency Use Listing (EUL) Procedure (previously referred to as the Emergency Use Assessment and Listing Procedure (EUAL)) on 8 January 2020, to be used primarily during a Public Health Emergency of International Concern (PHEIC). The EUL process is based on an essential set of available quality, safety and performance data. The EUL procedure for IVDs to detect SARS-CoV-2 was established 28 February 2020, is intended to expedite the availability of IVDs needed in PHEIC situations and, in that context, to assist interested UN procurement agencies and Member States in determining the acceptability of using specific products for time limited procurement

2 Purpose of this invitation for EOI

The purpose of this Expression of Interest (EOI) is to invite manufacturers to submit IVDs for SARS-CoV-2 for review by WHO through an emergency assessment mechanism.

3 Product categories included in this EOI

- IVDs for the detection of SARS-CoV-2 nucleic acid
- Immunochromatographic (lateral flow) or Immunofiltration (flow through) rapid diagnostic test (RDT) to detect antibodies against SARS-CoV-2.
- Immunochromatographic (lateral flow) or Immunofiltration (flow through) rapid diagnostic test (RDT) to detect SARS-CoV-2 antigens. (Other platforms to detect SARS-CoV-2 antigen will be considered on a case by case basis. Contact diagnostis@who.int for further information).

4 Submission of applications

Applicants are strongly encouraged to contact WHO as early as possible to discuss specifics of the

Interest of manufacturers in WHO EU(A)L

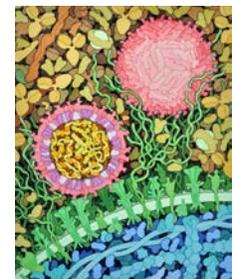


> 300 contacts
> 200 calls

SARS-CoV-2	NAT	Antibodies	Antigen
- 13 months -			
Total EOI	60	41	32
Under assessment	13	28	19
EUL listed	23	1	4
EUL not listed	22	6	3

Ebola	NAT	Antibodies	Antigen
- 10 months -			
Total EOI	-----	25	-----
EUL listed	4	NA	3

Zika	NAT	Antibodies	Antigen
- 10 months -			
Total EOI	-----	33	-----
EUL listed	4	0	NA



COVID-19 EUL Process

pre-submission call

application letter

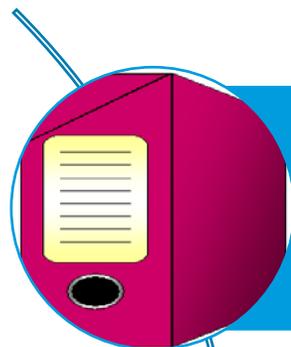
letter of agreement

product dossier
will be requested

QMS & dossier will be
reviewed

*Applications won't be
accepted without prior
consultation with WHO PQ!*

IVD assessment



- Technical documentation relating to safety and performance
- Product information
 - Product performance specifications
 - Labelling

EUAL/EUL:
minimal requirements



- Review of the documentation relating to the manufacture of the product and the manufacturer's QMS
- On-site inspection based on ISO 13485
 - Evidence of the implementation of a QMS

EUAL/EUL:
desktop review



- An independent laboratory evaluation coordinated by WHO
- Assesses the performance and operational characteristics

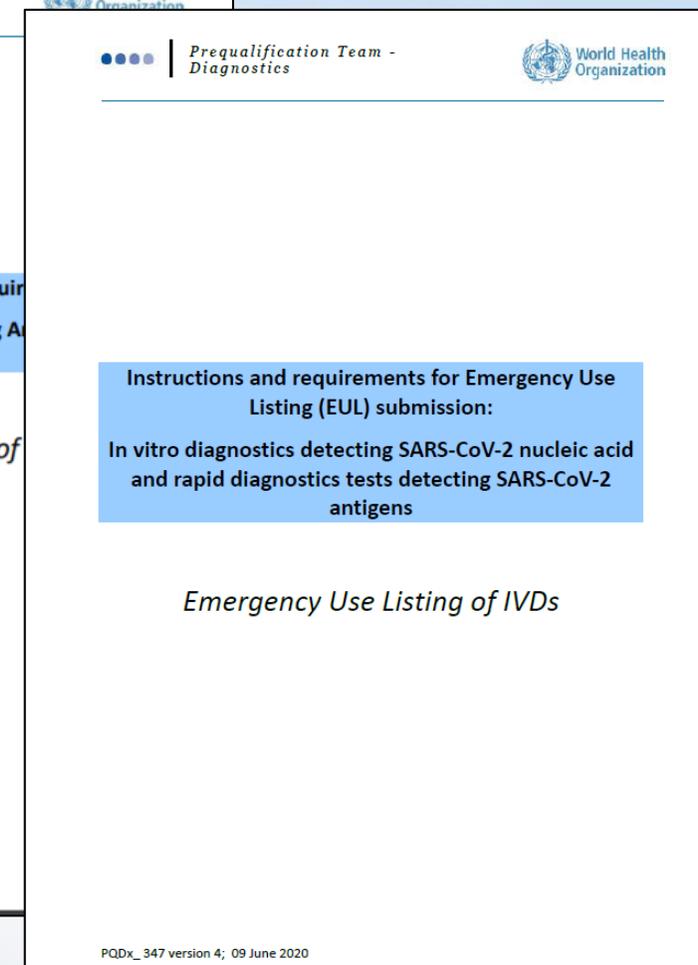
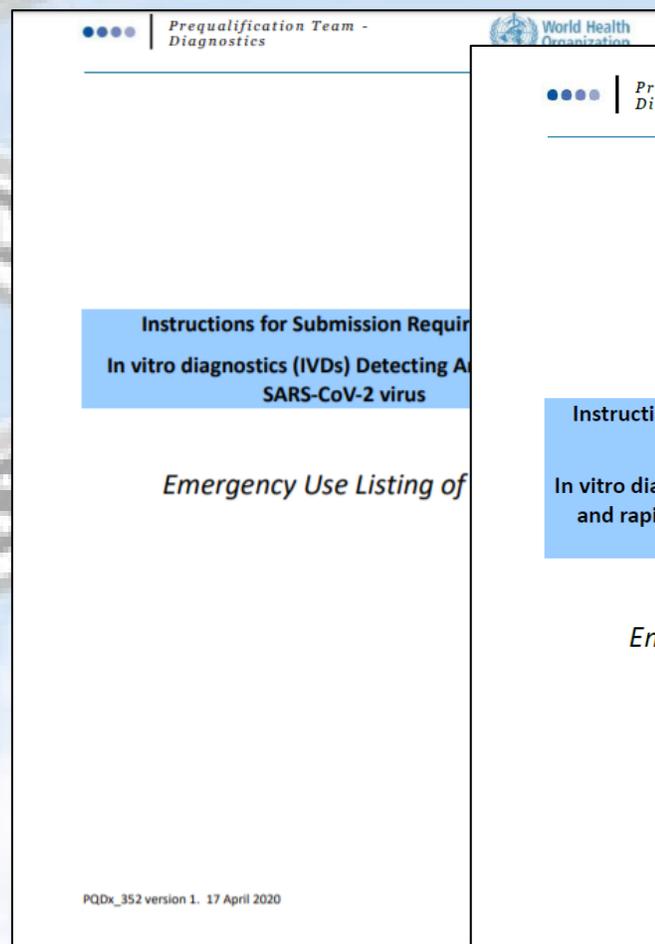
**EUAL: limited scope –
verify critical performance
characteristics**

Instructions for Submission Requirements:

- In vitro diagnostics detecting SARS-CoV-2 nucleic acid and rapid diagnostics tests detecting SARS-CoV-2 antigens (v4)

v5: March 2021

- In vitro diagnostics (IVDs) detecting antibodies to SARS-CoV-2 (v2)



Product dossier content

- **Product description and regulatory version**
- **Risk analysis**
 - Risk to patients/community arising from false positive or false negative results
 - Product associated hazards, such as instability leading to erroneous results
 - User-related hazards
- **Product design (formulation/composition/sequences & biosafety/biohazard)**
- **Product performance specifications (analytical & clinical)**
- **Labelling**
 - Instructions for use
 - Labels
 - User manuals etc.

Challenges associated with COVID-19 EUL

Dossier

High volume of applications to screen & review (23 EOIs in Jan & Feb 2021)
& change requests and commitments-follow up

Many of the dossier are of poor quality or incomplete → reviews require a lot of clarifications with the manufacturer (manufacturers have no or limited experience with WHO PQ/EUL, highly summarized, 'lost' in translation, data validity/integrity concerns)

Manufacturers are submitting products that are not in final lock down design → difficult to be sure that data assessed are applicable to the product version available for procurement

As the pandemic evolves and new evidence becomes available, technical requirements are being adjusted, some are applicable to already listed products

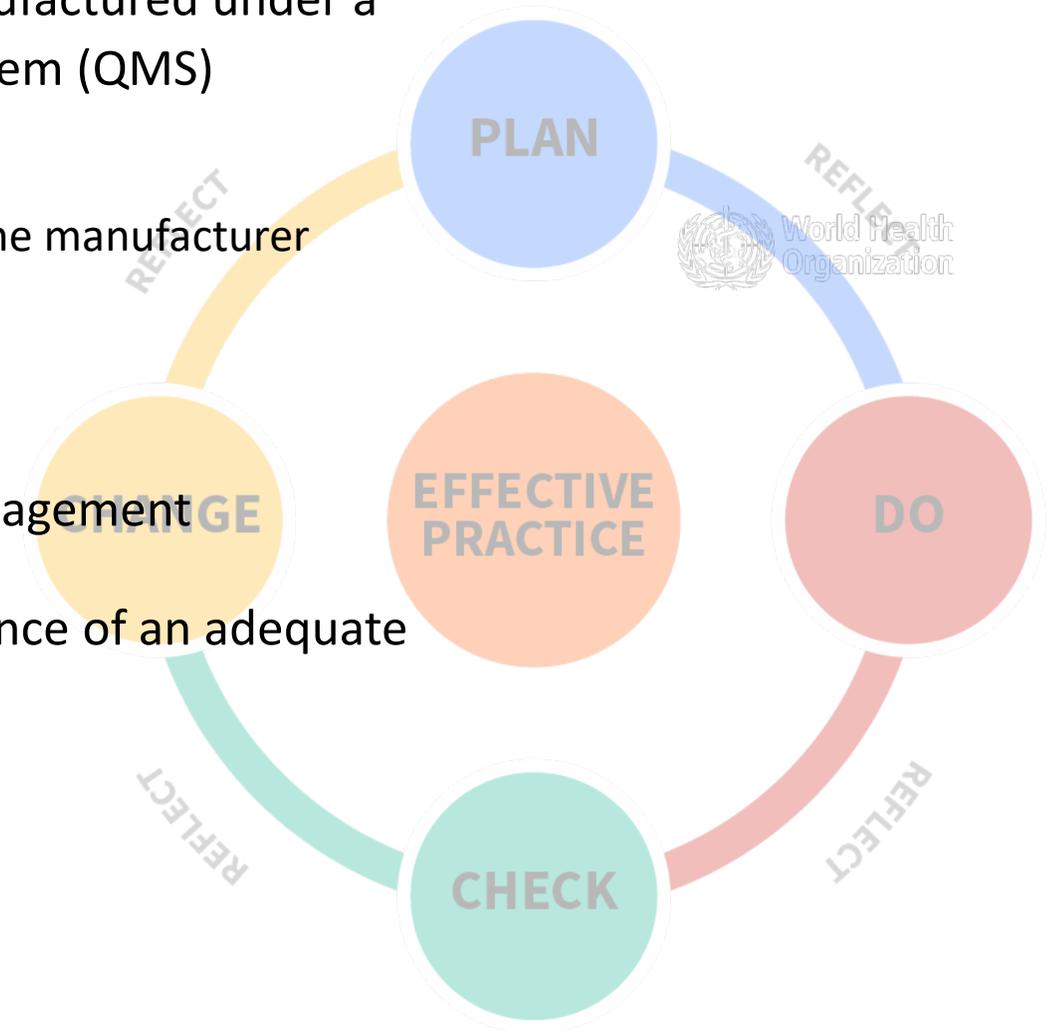
No site inspection or independent laboratory evaluation to verify documentation or performance

Quality management system

- IVDs submitted for the WHO EUL procedure must be manufactured under a suitable, adequate and effective quality management system (QMS)

WHO verifies that:

- there is sufficient objective evidence that the applicant is the manufacturer
 - there is evidence of an adequate QMS in place and
 - that the required manufacturing capacity exists
- ISO 13485:2016 is considered a benchmark in quality management
- WHO assesses evidence of implementation and maintenance of an adequate QMS including:
 - Quality control (QC) and batch release procedures
 - Production workflow
 - List of key suppliers
 - Manufacturing capacity



Challenges associated with COVID-19 EUL

QMS

A number of new manufacturers that have overnight grown out of research/university/laboratory facilities into fully operational manufacturing sites

Lacking understanding of important QMS principles and continuing to treat manufacturing as research

Lack of evidence of process controls (relying on individuals to control the process rather than the system)

Inadequately documented in-process and finished product QC

Reliance on suppliers without any mechanisms for their control

Lack of understanding of WHO reporting and feedback requirements

Certification issues (lack of certification, unacceptable scope, expired)

'Abridged' assessment pathway - COVID-19 EUL -



- For IVDs, some submissions for WHO EUL may have undergone a previous assessment through other emergency mechanisms, for example, the US FDA Emergency Use Authorization (EUA) process
- Avoiding duplicative work, if the review of the other emergency mechanism is deemed to be of a satisfactory standard

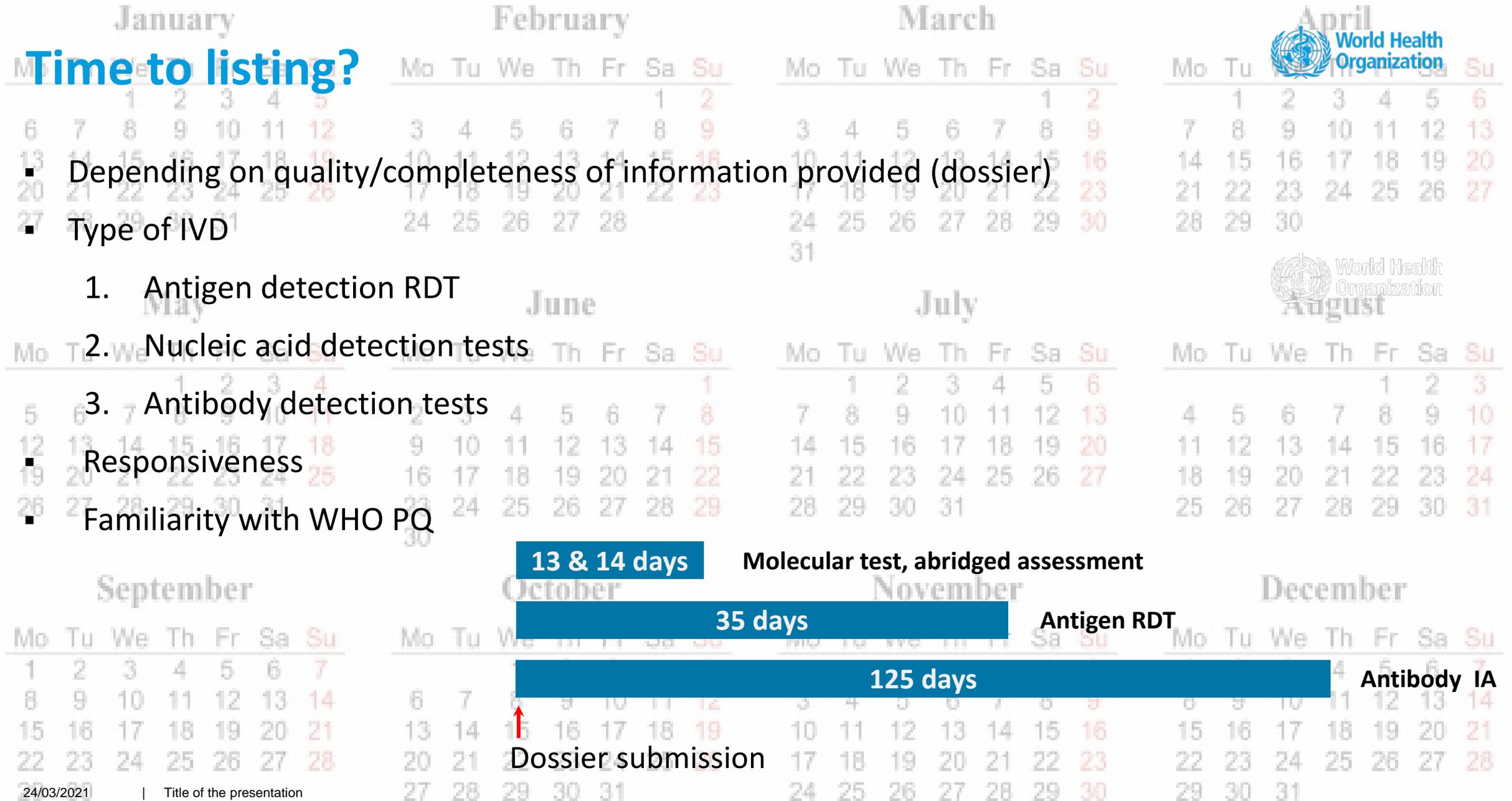


Only applicable to FDA EUA NAT assays

- FDA dossier + additional studies (precision, robustness, clinical)
- **no screening for completeness** -
- Desk review of the QMS (as per regular EUL assessment)

Time to listing?

- Depending on quality/completeness of information provided (dossier)
- Type of IVD
 1. Antigen detection RDT
 2. Nucleic acid detection tests
 3. Antibody detection tests
- Responsiveness
- Familiarity with WHO PQ



EUL listed – and then?

- Any reportable changes to the product (as defined in the WHO guidance document PQDx_121 “Reportable Changes to a WHO Prequalified In Vitro Diagnostic Medical Device”) must be communicated to WHO

(<https://apps.who.int/iris/bitstream/handle/10665/251915/WHO-EMP-RHT-PQT-2016.01-eng.pdf;jsessionid=830C82950055325AF37A0A8302BE4623?sequence=1>)

- Product design, labeling, IFU, specimen types, manufacturing site

- After a product has been listed, the manufacturer is required to also take into consideration the post-market surveillance activities (as defined by WHO guidance “Post-market surveillance and market surveillance of medical devices, including in vitro diagnostics”

(<https://www.who.int/publications/i/item/guidance-for-post-market-surveillance-and-market-surveillance-of-medical-devices-including-in-vitro-diagnostics>)

- Variants of concern (VOC) resulting in single target failure



EUL listing - renewal

Validity of EUL listing is for the duration of the emergency with a maximum of 12 months, but can be extended when deemed necessary.

COVID EUL:

1. Manufacturers will be asked by email to confirm they interest in extending the EUL status
2. Extension of EUL status will be granted if
 - the manufacturer has addressed/is addressing the commitments that are listed in their public report (e.g., international standard)
 - Manufacturer must have reported all changes (including labelling & IFU, manufacturing site) for assessment (product that was listed is the same product that is available for procurement)
 - Products may be taken off the EUL list if new data become available that change the benefit-risk balance of the product or upon termination of the PHE.

Priority categorization

March 2021

<https://extranet.who.int/pqweb/vitro-diagnostics/coronavirus-disease-covid-19-pandemic-%E2%80%94-emergency-use-listing-procedure-eul-open>

High priority:

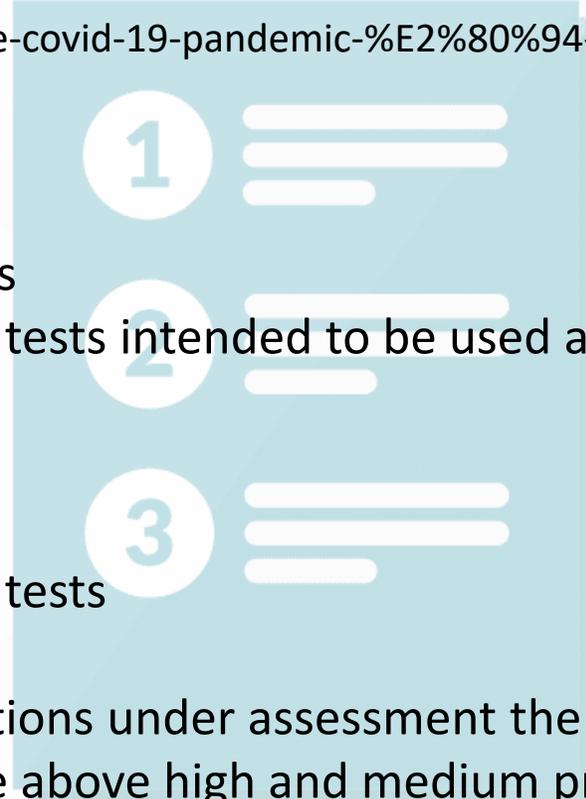
- EUL applications for SARS-CoV-2 antigen detection tests
- EUL applications for SARS-CoV-2 nucleic acid detection tests intended to be used at a point-of-care

Medium priority:

- PQ applications
- EUL applications for SARS-CoV-2 nucleic acid detection tests

Please also note that due to the current peak in applications under assessment the PQ team is only accepting EUL pre-submission calls and new EOIs for the above high and medium priority:

No SARS-CoV-2 antibody tests are accepted for EUL



COVID-19 EUL Eligibility

We do not accept applications for:

- Multipathogen tests (e.g. SARS-CoV-2 & Flu A/B)
- IVDs to determine correlate of immunity (e.g., neutralizing antibodies)
- IVDs detecting IgA, IgM only
- Sequencing reagents
- Extraction free RT-PCRs with inadequate internal control design

We do not accept applications for, but might be in future:

- RT-PCR tests to monitor occurrence of deletions/mutations associated with VOCs
- PoC tests intended for Self-testing

SARS CoV-2 variants of concerns (VOCs)

Distribution of 20I/501Y.V1 per country

Compare

- **Monitoring emerging variants and ...**
- **Review of all EUL listed RT-PCR tests**
 - 4 products detect the spike gene
 - In silico analysis revealed that 2 of those are potentially impacted by deletions associated with VOC-202012/01 (UK).
 - Risk for false negative results is assessed as low, as both products detect 2 additional viral targets
 - Manufacturers are amending the IFU and or publishing information for users

WHO Incidents and Substandard/Falsified Medical Products Team

- **Manufacturers**
 - Reminded of PMS obligations
- **Information notice with advice on action by IVD users** (<https://www.who.int/news/item/19-01-2021-who-information-notice-for-ivd-users-2021-01>)

IVD users should notify the IVD manufacturer in the following circumstances:

 - Increased discrepancies in cycle threshold (Ct) values between different gene targets.
 - Failure to detect specific gene targets, including those containing gene sequences that coincide with documented mutations.

Gracias
Merci
Obrigada
Thank you



Questions?
diagnostics@who.int

Emergency Use Listing Dossier Review



Susie Braniff

In vitro Diagnostics Assessment Team

March 2021

Product dossier for EUL

Instructions and Requirements for EUL submissions

Product Dossier

- Product information
- Product design & manufacture
- Product performance evidence
 - *Analytical studies*
 - *Clinical studies*
- Post market surveillance
- Commitments to EUL



Prequalification Team - Diagnostics

World Health Organization

Instructions and requirements for Emergency Use Listing (EUL) submission:
In vitro diagnostics detecting SARS-CoV-2 nucleic acid and rapid diagnostics tests detecting SARS-CoV-2 antigens

Emergency Use Listing of IVDs

PQDx_347 version 4; 09 June 2020

Prequalification Team - Diagnostics

World Health Organization

Instructions and requirements for Emergency Use Listing (EUL) Submission:
In vitro diagnostics detecting antibodies to SARS-CoV-2 virus

Emergency Use Listing of IVDs

PQDx_352 version 2; 03 July 2020

Product information

Product identification, design and function

- Identify all regulatory versions of the product
 - Clearly state which version is submitted for EUL
- Legal manufacturer
- Product name and product code/s
- The intended use
 - What the product detects, the format and the function
 - Validated specimen types
- Control materials
- Specimen collection & transport materials
- Associated accessories, reagents, instruments & software (if applicable)
- A complete list of kit configurations that will be made available



Product information

Product identification, design and function

Testing capabilities

- Specimen throughput capacity
- Time to result

Risk analysis

- Identify and quantify all foreseeable hazards
- Risk mitigation measures
- Information for users on residual risks
- A risk benefit statement
- Evidence that the risk analysis is part of the manufacturer's risk management plan



Product design & manufacture

How the product works and how it is made

Product design

- Formulation and composition
 - *Full list of ingredients*
 - NAT: *sequences for primers & probes, design of IC*
 - Ag RDTs: *antibody details, including epitope target*

Biosafety & biohazard

- Evidence to demonstrate correct use of the product is safe, must consider:
 - *Specimen type, specimen collection & processing, inactivation of specimen and safe disposal*

Design changes

- Records of any design change/s associated with the product



Product performance specification

Establishing product performance

Evidence of relevant investigations to support the intended use

- Each study submitted must contain:
 - Study description, study identifier, product identifier (e.g. lot numbers), IFU version used, beginning and end date
 - Clearly defined acceptance criteria
 - Summary findings and a conclusion
 - The study protocol and full report
- For studies planned or in progress:
 - Study protocol and plan
 - Expected completion date and when report will be submitted to WHO



Analytical performance

Evidence that the test works as intended

Stability of specimens

- Storage and transport conditions

Matrix equivalence

- For IVDs that claim more than 1 specimen type
- *If matrix equivalency is demonstrated only one representative specimen type (or matrix) needs to be used in precision, analytical specificity, robustness & IVD stability studies.*

Metrological traceability

- Calibrator and control material values



Precision

- Repeatability and reproducibility

Analytical specificity

- Interfering substances
- Cross reactivity
- Microbial interference studies

Analytical sensitivity

- Limit of Detection (LOD) determined using the entire test system

Specimen preparation → detection

Analytical performance

Specific requirements for different test formats

Nucleic Acid Tests

- Validation of primer and probe choice
- Ct range for procedural control

Flex studies

- Variation in specimen & reagent volume
- Handling contamination
- Operating temperature
- Ruggedness of instrument/s

Rapid Diagnostic Tests & EIAs

- High dose hook effect
- Validation of cut-off value (with a reader)

Flex studies

- Variation in specimen & reagent volume
- Handling contamination
- Operating temperature
- Reading times
- Illumination effects

Refer to the relevant EUL Instructions document for guidance

Stability of the IVD

Demonstrate shelf-life, shipping stability and in-use stability

Shelf-life stability

- Include shipping stability
 - Extremes of temperature, humidity and pressure during transport
 - Reflect environmental conditions in countries of supply
- Accelerated studies may be submitted for initial shelf-life claim but must be followed-up with real time studies
- For on-going studies provide protocol & plan
- Minimum requirements for the sample panel tested

In-use stability

- Operating temperature & humidity range
- Freeze/thaw cycles of reagents / controls
- On-board stability must be considered for an IVD used with an instrument
- Study must include all labile components
 - Buffer vials, sealed cartridges, etc.
- Results must support handling claims made in the IFU



Clinical evidence

Data generated from the clinical intended use of the IVD

Specimens

- From the intended use population
- For each claimed specimen type
- Ideally prospectively collected specimens should be used

*Specimen information should be reported:
i.e. collection date, presence / absence of symptoms, other test results, clinical diagnosis, etc.*



Comparator method

- Same set of clinical specimens tested on a second assay
 - IVD with WHO EUL or US-FDA EUA
 - NAT must use different primer/probes
 - Provide results (*i.e. Ct values*) for each specimen on both tests
- Percent agreement should be calculated
- Resolution of discrepant results

NAT IVDs
100 positive
100 negative

Ag IVDs
100 positive
400 negative

Ab IVDs
200 positive
800* negative

Plan for post-market surveillance

Tracking performance in the field

Evidence of a procedure for:

- Monitoring customer feedback
- Detecting and acting on adverse events
- Managing product problems
- Non-conforming goods and processes

Activities are expected to be in accordance with WHO guidance



Labelling

Information provided to the user

Where possible a complete set of labelling should be provided

Packaging Labels

- Outer labels (secondary packaging)
- Component labels
- Instrument label (if appropriate)



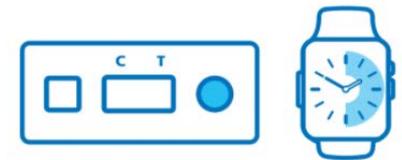
Instructions for Use (IFU)

- Reviewed for clarity, correctness and suitability



Other instructional material provided

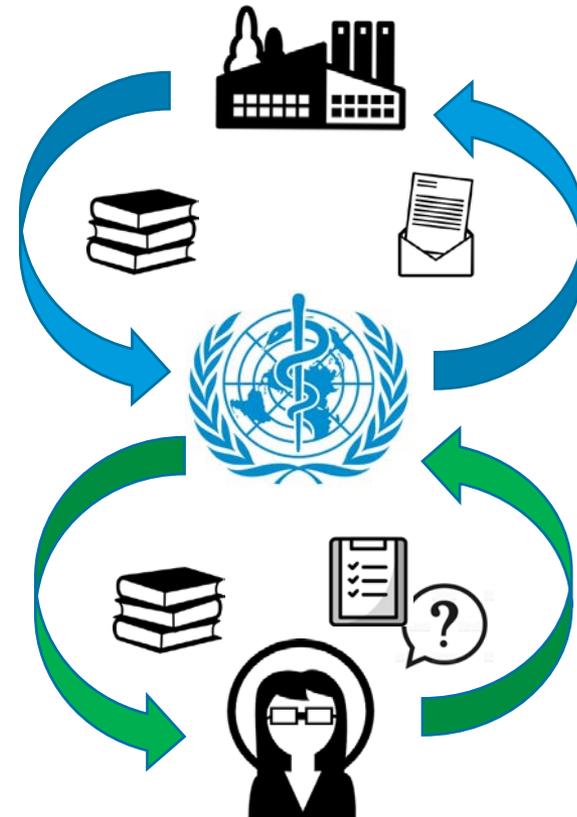
- Instrument manuals
- Job aides



Dossier review process

Coordinated by WHO

- Manufacturer submits dossier to WHO
 - Dossier screened for completeness
 - Dossier sent to subject matter expert for technical review
 - Expert provides completed dossier review checklist and notes any deficiencies in the dossier
 - WHO prepares dossier review letter for manufacturer requesting additional information or clarifications
- Process repeated with manufacturer's response to the dossier review letter



Commitments to EUL

Additional information required to be submitted for review

WHO acknowledges that not all studies may be complete when an IVD is submitted to EUL

For required studies that are in progress the manufacturer must provide:

- A full study protocol
- A study plan with dates, including expected date of completion

For stability studies

- Accelerated studies may be accepted for an initial shelf-life claim
- Must be followed-up with a real time study
 - The protocol and study plan must be provided to WHO

Commitments to EUL will be stated in the Public Report

Thank you



World Health
Organization

WHO
20, Avenue Appia
1211 Geneva
Switzerland

Quality Management Review as part of the EUL procedure

Philippe Boeuf – Lead Inspector – Prequalification Unit - Geneva

An atypical review process

QMS compliance typically assessed during an onsite inspection

COVID-19 EUL specific circumstances:

- Onsite inspections paused
- More rapid decision needed

WHO PQ mandate:

- QMS compliance must be assessed
- No waiver on QMS requirements



A solution: desk assessment

What: Review of data without real-time communication with the site

How:

- Objective evidence of QMS compliance sent by the manufacturer
- Assigned inspector reviews documents
- If required, requests additional information
- Decision on QMS compliance



Stringent compliance criteria

Some jurisdictions can waive certain QMS requirements

Example: Section III of EUA by FDA

III. Waiver of Certain Requirements

I am waiving the following requirements for your product during the duration of this EUA:

- Current good manufacturing practice requirements, including the quality system requirements under 21 CFR Part 820 with respect to the design, manufacture, packaging, labeling, storage, and distribution of your product, but excluding Subpart H (Acceptance Activities, 21 CFR 820.80 and 21 CFR 820.86), Subpart I (Nonconforming Product, 21 CFR 820.90), and Subpart O (Statistical Techniques, 21 CFR 820.250).

WHO PQ applies stringent QMS compliance criteria:

- All applicable ISO 13485 clauses: entire life cycle of the product
- WHO requirements: post-market surveillance,...
- EUL-specifics: production capacity,...

QMS compliance documentation for all sites

- Evidence of **implementation and maintenance of an adequate QMS** (e.g. current ISO 13485 certificate or equivalent)
- Most recent regulatory (or certification body) **inspection report**.
- A copy of the **quality manual**.
- A list of current **quality management** documentation.
- The most recent **management review** report.

- Flow chart of the **entire manufacturing process**.
- Details of the **production workflow** including QC points (in process and final release activities).
- **Quality control (QC)** and batch release procedures.
- List of **critical supplier(s)** including supplied products (components/raw materials/accessories) and services.
- Procedure(s) for the **control of design and development changes**.
- Procedure(s) relevant to the identification and the control of **non-conforming goods, corrective and preventive action, recalls, field safety notices, etc.**

- When was the product developed and when was it first placed on the market or the planned timeline for placing on the market.
- List of all **countries in which the product under assessment is intended to be marketed**.
- **Manufacturer's experience with the product** (including research-use-only products), especially (but not limited to) number of products distributed, number of customer complaints, if any, type(s) of complaint(s) and customer feedback.

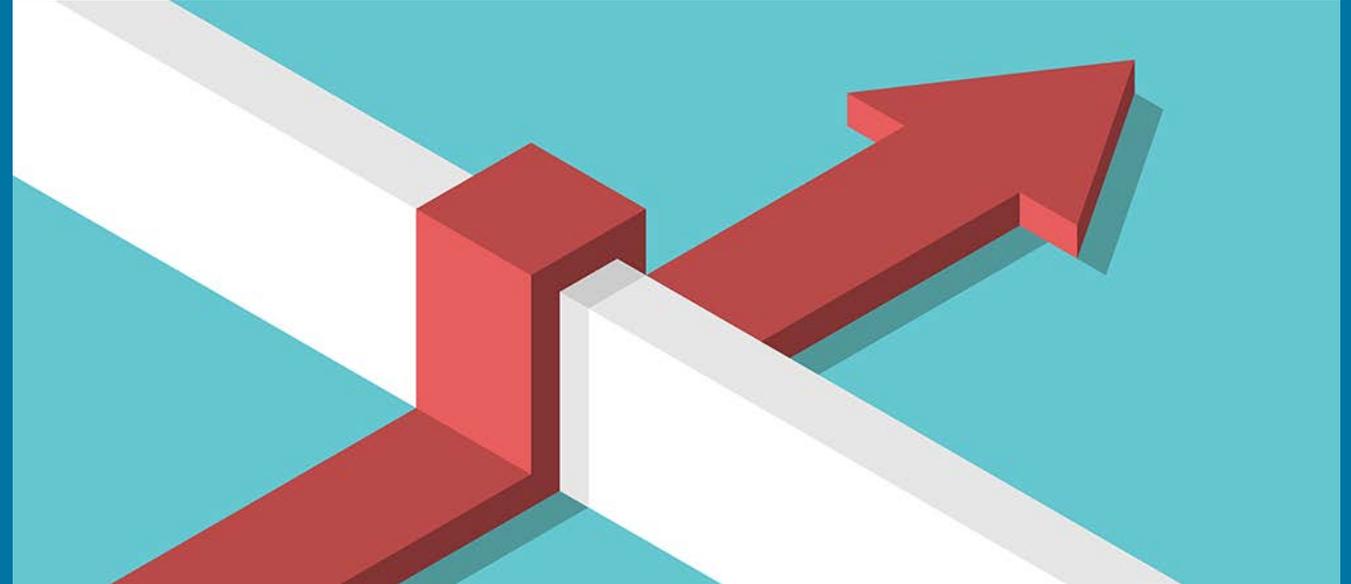
Challenges and limitations of desk assessments

Challenges:

- Documents not in searchable format
- Poor quality of scanned documents
- Translation of documents

Limitations:

- No analytical raw data supplied – only summarized data
- Some key requirements impossible to assess (e.g. data integrity)
- Lack of experience with the site or manufacturer



Challenges and limitations of desk assessments

- Do not, cannot and will not replace onsite inspections
- Site compliance in the context of EUL generally valid for 12 months
- Onsite inspection as soon as possible
- Remote/hybrid inspections being discussed
- Post-listing requirements
 - Report changes
 - Post-market surveillance



Conclusions

- Desk Assessments are **atypical** but are used and supported by regulators across the globe
- WHO PQ EUL is a **stringent process** considering the entire life cycle of the products
- Desk assessments have **limitations and challenges**
- Desk assessments are a **temporary measure** to assess site compliance. They do not, cannot and will not replace onsite inspections

THANK YOU



World Health
Organization



Accessing public WHO EUL information: Charles Chiku

March 2021

Accessing public WHO EUL information



Overview and priority categorization

- ❑ access an overview of the EUL and how it has evolved over the period of the pandemic.
- ❑ Eligibility criteria for IVDs and requests for manufacturers with IVDs that meets the eligibility criteria to submit their Expression of Interest (EoI) to EUL procedure.
- ❑ Priority Categorization of applications for Prequalification (PQ) and Emergency Use Listing (EUL) assessments of in vitro diagnostics.
- ❑ WHO EUL procedure
- ❑ <https://extranet.who.int/pqweb/vitro-diagnostics/coronavirus-disease-covid-19-pandemic-%E2%80%94-emergency-use-listing-procedure-eul-open>

Accessing public WHO EUL information



**INVITATION TO SUBMIT,
SUBMISSION REQUIREMENTS &
INSTRUCTIONS, Q&A**

**PUBLIC REPORTS AND IFUS FOR
PRODUCTS ELIGIBLE FOR
PROCUREMENT**

**PUBLIC REPORTS FOR
PRODUCTS NOT ELIGIBLE
FOR PROCUREMENT**

FURTHER INFORMATION

Status of ongoing applications

- ❑ The list of SARS-CoV-2 IVDS currently under assessment is updated every week.
- ❑ The information shows at which of the assessment an application is at in the assessment process.
- ❑ Key identifiers for a product are,
 - Manufacturer name,
 - Product name
 - Product code(s)
 - Regulatory version
 - EUL application number

Status of ongoing applications

SARS-CoV-2 Nucleic Acid Tests: progress of the active applications in the emergency use listing assessment pipeline

Manufacturer name	Product name	Product code(s)	Dossier review	QMS Desk Assessment	EUL application number
Guangzhou Supbio Bio-technology and Science Co., Ltd	SARS-CoV-2 (ORF1ab/N) Nucleic Acid Detection Kit (PCR-Fluorescent Probe)	SUPI-2501		◆	EUL 0520-207-00
Wuhan EasyDiagnosis Biomedicine Co., Ltd.	COVID-19 (SARS-CoV-2) Nucleic Acid Test Kit	nCOV-PCR-02-100B		R	EUL 0523-209-00
Diagnostics for the Real World Ltd	SAMBA II SARS-CoV-2 Test	8500-12	awaiting submission	awaiting submission	EUL 0530-072-00

R information requested from manufacturer	 in process	◆ stage complete	F follow-up amendments
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Please note: these tables are updated regularly; while every attempt is made to provide current data, the most recent information might not be reflected. This table is intended only as an update on progress and does not reflect a final decision on EUL. This table should not be used to inform procurement. Information may not yet be reflected here.

Last update: 16 March 2021

Accepted IVDs for SARS-CoV-2

- ❑ Products that were accepted under EUL procedure are listed on a table accessible on the following link,

<https://extranet.who.int/pqweb/sites/default/files/documents/>



World Health Organization

WHO Emergency Use Listing for In vitro diagnostics (IVDs) Detecting SARS-CoV-2

RoW: Rest of the world. Regulatory version applied to products not approved by stringent/mature NRAs or not regulated
Last updated: 17 February 2021

Rapid Antigen Detection Tests

Date Listed	EUL number	Product name	Regulatory version	Product code(s)	Manufacturer	Packaging
19 November 2020	EUL-0587-032-00	Panbio COVID-19 Ag Rapid Test Device (NASAL)	CE-mark	41FK11, 41FK21	Abbott Rapid Diagnostics Jena GmbH	25 T/kit
02 October 2020	EUL-0564-032-00	Panbio COVID-19 Ag Rapid Test Device (NASOPHARYNGEAL)	CE-mark	41FK10, 41FK20	Abbott Rapid Diagnostics Jena GmbH	25 T/kit
22 September 2020	EUL-0563-117-00	STANDARD Q COVID-19 Ag Test	CE-mark	09COV30D	SD Biosensor, Inc	25 T/kit

<https://extranet.who.int/pqweb/sites/default/files/documents/>

WHO Public Reports for accepted products under EUL



- ❑ Product identifiers (Product name, product codes, manufacturer, regulatory version and EUL application number)
- ❑ Date accepted for EUL and duration of eligibility for procurement under EUL.
- ❑ Intended Use.
- ❑ Specimens validated to be used with the product
- ❑ Product configurations (Number of tests/kit variations)
- ❑ Items required but not provided
- ❑ Outcome of QMS and Dossier assessment, including commitments if applicable.
- ❑ Scope of listing and manufacturers obligations to maintain the listing (reportable changes and Post Market Surveillance reporting)

<https://extranet.who.int/pqweb/sites/default/files/documents/>

Thank you



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Collaboration with NRAs for EUL IVDs

24 March 2021

Best practices in regulation of IVDs

- ✓ **Premarket** - Market Authorization of in vitro diagnostic, risk-based decision based upon thorough review of scientific data which include:
 - Review of the product technical file (Dossier) based on EPSP.
 - Manufacturing site inspection - verify existence and compliance to **Quality Management System** (ISO13485) including physical verification of data (Analytical and clinical performance)
 - Performance evaluation
- ✓ **Post-market surveillance and market surveillance** – FSN, FSCA and vigilance reporting.

The class of the IVD determines what regulatory controls will be implemented at both premarket and post market phases.



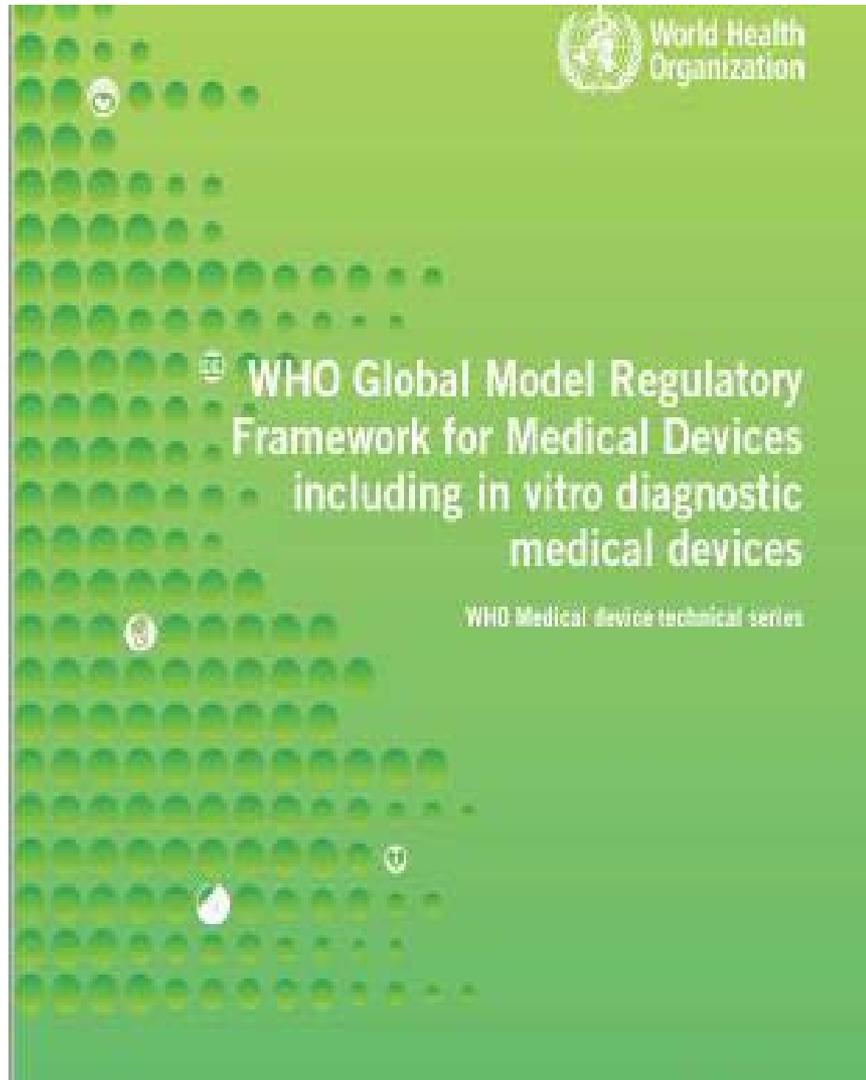
COVID-19 pandemic

Unprecedented times:

- ✓ Very few available diagnostics with limited performance data and yet there is an urgent demand for IVDs;
- ✓ There are no readily available regulatory-approved, mass-produced in vitro diagnostics (IVDs) – safety and performance
- ✓ There is a need for fast, efficient regulatory procedures to bring new diagnostics to the affected communities
- ✓ High demand for PPEs (gowns etc) and medical devices ventilators, masks.
- ✓ Unknown manufacturers such as vehicle manufacturers developing ventilators with limited evidence of safety and performance.
- ✓ Donations from unknown manufacturers/sources, political pressure to approve such products



WHO Global Model Regulatory Framework



4.2.2.6 Establish provisions for exceptional premarket situations

In situations such as public health emergencies, exemptions from some regulatory requirements may be needed. Such exemptions should, however, be applied in such a way as to allow the regulatory authority to evaluate the risks and benefits of the specific situation and authorize the proposed deviation. Such exemptions should be clearly stipulated and explained.

The law should establish defined exemptions from, and provide enforcement discretion for, compliance with certain requirements, for example, medical devices for humanitarian use, public health emergencies, clinical investigations, exhibition use and medical devices donated to the country by charities or the manufacturer. Regulators should issue clear guidance on such exemptions (see section 5).

Approaches during emergencies

- ✓ Reliance/recognition - WHO EUL (Survey in February 2021: 80% of NRAS rely on listing/authorization by trusted institutions such as WHO and other matured NRA for COVID 19 assays; 94% of countries aware of the WHO EUL and its utilization (68%) to facilitate in country authorization.
- ✓ Regulatory flexibilities (import control, market authorization, conditional approvals etc). Marketing Approval – registration (12 - 24 months) to listing/authorization through expedited review (up to 3 months).
- ✓ Collaboration through establishment of task force/special team with key stakeholders such as NRA, NRL, research institutes, academia to identify, review and authorize assays for use in the country.
- ✓ Sharing of information among regulators through the Regional Harmonization Initiatives and on NRAs websites.
- ✓ Post market and market surveillance.



31 January 2021 COVID 19 Serology Listed Tests



List of assays for detection of COVID 19 antibodies or antigen authorized for Emergency Use.
Recently added tests (1-31 January 2021) are indicated by Green fonts

2	Jurisdiction/ Country	Date Listed	Product name	Type of the assay	Product code(s)	Manufacturer	Link to IFU
3	WHO	2 October 2020.	Panbio COVID-19 Ag Rapid Test Device	Point of care rapid antigen assay	41FK19	Abbott Rapid Diagnostics Jena GmbH	https://extranet.who.int/pqweb/vitro-diagnostics/coronavirus-disease-covid-19-pandemic---emergency-use-listing-procedure-eul-open
4	WHO	2-Oct-20	Panbio COVID-19 Ag Rapid Test Device (NASOPHARYNGEAL)	Point of care rapid antigen assay	41FK10	Abbott Rapid Diagnostics Jena GmbH	https://www.who.int/diagnostics_laboratory/eual/eul_0564_032_00_panbi_covid19_ag_rapid_test_device.pdf?ua=1
5	WHO	22-Sep-20	STANDARD Q COVID-19 Ag Test (NASAL)	Point of care rapid antigen assay	09COV30D	SD Biosensor, Inc	https://www.who.int/diagnostics_laboratory/eual/eul_0563_117_00_standard_q_covid19_ag_ifu.pdf?ua=1
6	Link	https://extranet.who.int/pqweb/sites/default/files/documents/201120_EUL_SARS-CoV-2_product_list.pdf				Updated 31 January 2021	

Conclusion



- ✓ Response to emergencies require extraordinary collaboration between actors: WHO, NRAs, NRLs, CDC, professional association, academia, research institutes etc.
- ✓ Today's reality and demand: to generate quality national decisions regulators globally **MUST** collaborate and **MUST** take into consideration the information available from other regulatory authorities;

Not using the outputs and outcomes from other regulatory authorities means lost opportunity, duplication of efforts, increased regulatory burden and waste of scarce resources.
- ✓ **Reliance/Recognition** are critical in facilitating regulatory decision and accelerating access to quality assured tests.



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