Update on the WHO EUL for IVDs

Irena Prat, In vitro Diagnostics Assessment Team Lead

World Health Oragnization

WHO EUL: background

- Mechanism developed in response to the 2014 - 2016 Ebola outbreak
- 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
- Essential data requirements for IVD EUL:
  - Quality Management Systems Review and Plan for Post-Market Surveillance: review of the manufacturer's QMS documentation and specific manufacturing documents;
  - Product Dossier Review: assessment of the documentary evidence of safety and performance.

Manufacturers' response

SARS-CoV-2	NAT	Antibodies	Antigen
		- 18 months -	
Total EOI: 154	65	41	48
Under assessment: 77	17	30	30
EUL listed: 28	23	1	4
EUL not listed: 44	24	10	10
Ebola	**NAT**	**Antibodies**	**Antigen**
		- 10 months -	
Total EOI	----------	25	----------
EUL listed: 7	4	NA	3
Zika	**NAT**	**Antibodies**	**Antigen**
		- 10 months -	
Total EOI	----------	33	----------
EUL listed: 4	4	0	NA

> 300 contacts
> 200 calls

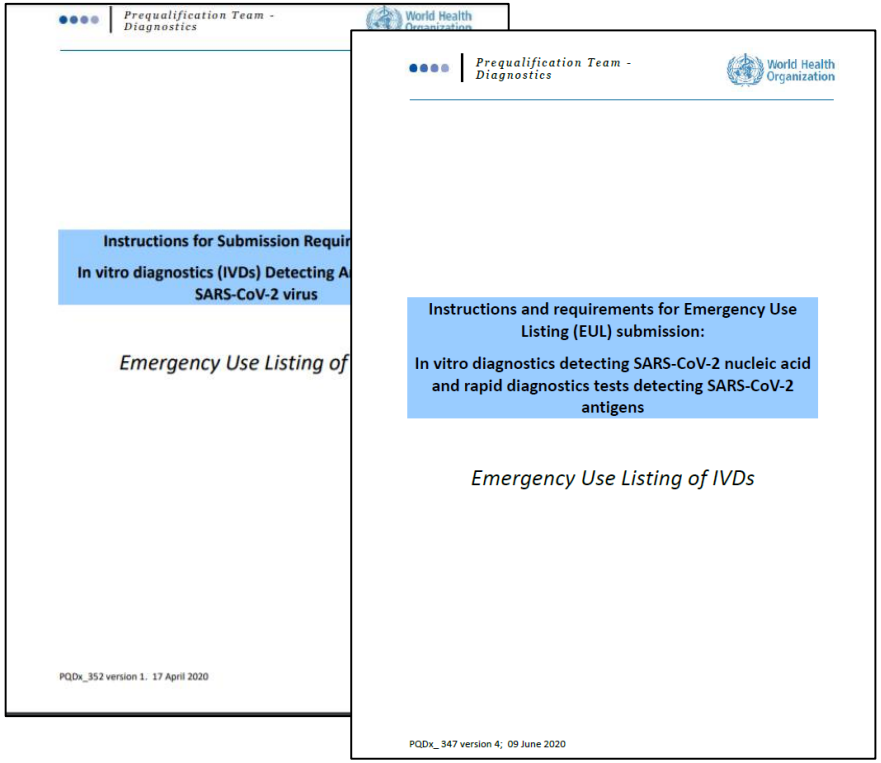
Illustration by David S. Goodsell, RCSB Protein Data Bank; doi: 10.2210/rcsb_pdb/goodsell-gallery-019, -015, -013

WHO SARS-CoV-2 EUL pipeline for IVDs

		Test types		
	Total	Nucleic acid	Antibodies	Antigen
Pre-submission interest	**>200**	*(split not available)*		
EOIs	**154**	65	41	48
Under assessment	**74**	17	30	30
EUL listed	**28**	23	1	4
EUL not accepted	**44**	24	10	10

Instructions for applicants

- In vitro diagnostics detecting SARS-CoV-2 **nucleic acid** and rapid diagnostics tests detecting SARS-CoV-2 **antigens (v5)**
- In vitro diagnostics (IVDs) detecting **antibodies** to SARS-CoV-2 (v2)



WHO experience with EUL reviews

Lack of alignment on requirements

- manufacturers struggling with divergent approaches and requirements
- transparence on requirements still to be improved

Little support to manufacturers for product validation

- despite agreement on the need to better support manufacturers (access to panels) after the Ebola and Zika outbreaks, such initiatives remain rare

Despite WHO instructions are published several manufacturers continue to use inappropriate comparator assays in their studies

Many manufacturers are new to regulatory requirements

- shift from research to full production is challenging

Many countries still require in-country clinical studies

- Limited interest for reliance in LMIC

Resources

Challenges: product dossier

High volume of applications to screen & review & 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

Challenges: 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)

Some solutions implemented

Transparent requirements published

Prioritization of critical technologies

Abridged assessments of USFDA listed NAT assays

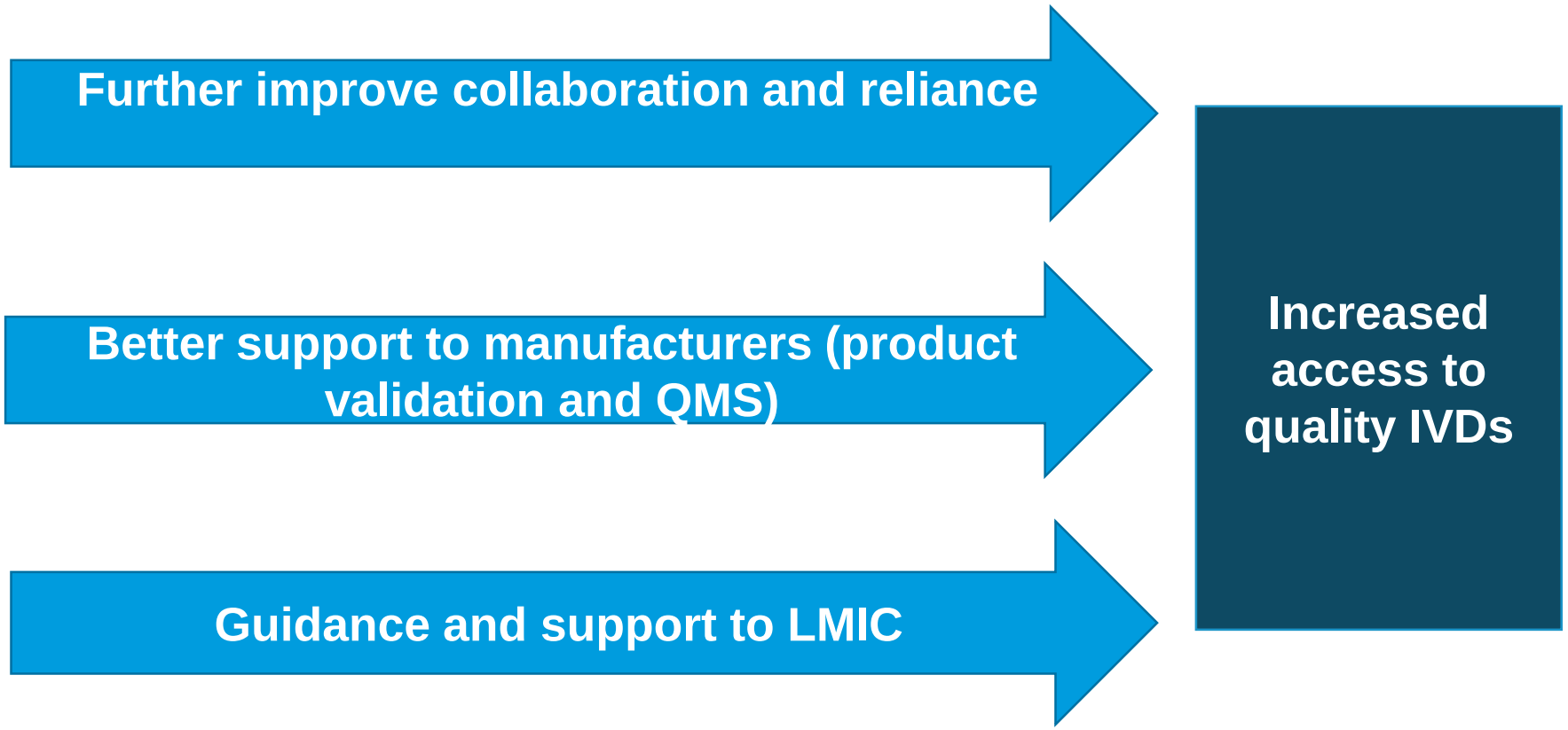
Desk audits of QMS documentation

No EUL performance evaluation required (pros and cons)

Collaboration with partner institutions supporting Mx validation studies

Facilitated procedure developed to support NRAs

Way forward


Further improve collaboration and reliance
Better support to manufacturers (product validation and QMS)
Guidance and support to LMIC
Increased access to quality IVDs

World Health Organization

Thank you