Emergency Use Diagnostics in a Pandemic: A Global Perspective

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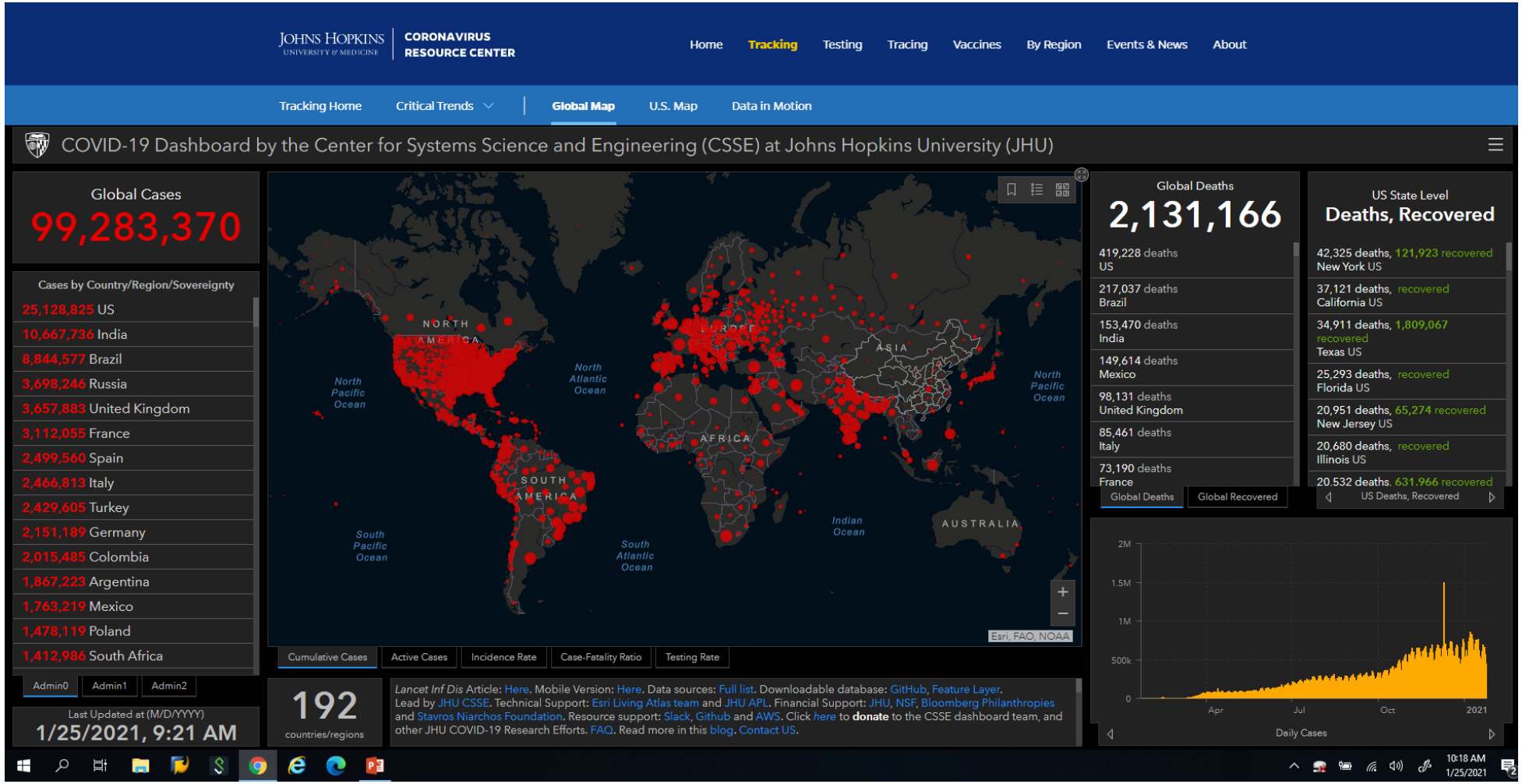
Unprecedented Global Pandemic Exposes Extreme Unmet Medical Needs
Challenges Regulatory Paradigms



As of January 2021:

COVID-19 cases and deaths continue to rise

Diagnostic testing continues to be a challenge

Regulators continue to be challenged in reviewing emergency use *in vitro* diagnostic tests, delaying access to many other life-saving IVDs

Source Johns Hopkins COVID-19 Dashboard *(accessed January 25, 2021)*

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It’s about people, not numbers

Eleanor Amelia Miller
August 1, 1928- January 6, 2021

Roche is Singularly Focused on Supporting the Global Response to COVID-19

Years of Development and Commercialization, Compressed into Months

Jan. 30
WHO declares Public Health Emergency of International Concern (PHEIC)

Roche announces availability of TIB-MOLBIOL LightMix Modular assay for RUO testing

Feb. 1
Initiation of wet-lab work in Pleasanton

Feb. 27
cobas® omni channel assay published

Mar. 11
EUA submission for cobas® SARS-CoV-2 Test

Mar. 12
EUA granted for cobas® SARS-CoV-2 Test

Mar. 13
First shipments of cobas® SARS-CoV-2 Test leave Indianapolis

May 2
EUA granted for Elecsys® Anti-SARS-CoV-2 assay

June 4
EUA granted for Elecsys® IL-6 assay

July 15
Surpassed 15 million tests shipped

Sept. 3
EUA granted for cobas® SARS-CoV-2 & Influenza A/B Test for 6800 / 8800 systems

Sept. 14
EUA for cobas® SARS-CoV-2 & Influenza A/B Nucleic Acid Test for use on the cobas Liat System

Nov. 25
EUA granted for Elecsys® Anti-SARS-CoV-2 S

TBD
Elecsys® Antigen Test*

SARS-CoV-2 Rapid Antigen test*

JAN 2020 | FEB 2020 | MAR 2020 | APR 2020 | MAY 2020 | JUN 2020 | JUL 2020 | AUG 2020 | SEPT 2020 | Q4 2020 | Q1 2021

*Product not available in the U.S.

SARS-CoV-2 Diagnostics Portfolio[1]

Comprehensive portfolio of tests and digital solutions

	Clinical Labs		Near Patient	
Molecular solutions	• TIB MOLBIOL LightMix® Modular SARS-CoV-2	*Launched*	• **cobas**® SARS-CoV-2 & Influenza A/B	*Launched*
	• **coba**s® SARS-CoV-2	*Launched*		
	• **cobas**® SARS-CoV-2 & Influenza A/B	*Launched*		
Immunology solutions	• Elecsys® Anti-SARS-CoV-2	*Launched*	• SARS-CoV-2 rapid antibody	*Launched*[3]
	• Elecsys® Anti-SARS-CoV-2 S[2],	*Launched*	• SARS-CoV-2 rapid antigen	*Launched*[3,4]
	• Elecsys® Anti-SARS-CoV-2 antigen	*Launched*	• SARS-CoV-2 rapid antigen (saliva/nasal)	*In-development*[3]
	• Elecsys® IL-6 Test to diagnose cytokine release syndrome	*Launched*	• SARS-CoV-2 & Influenza A/B rapid antigen	*In-development*[3]
Digital solutions	• Viewics LabOps COVID-19 for efficiency improvements	*Launched*	• NAVIFY Remote Monitor[4]	*Launched*
			• v-TAC[5] digital algorithm for blood-gas	*Launched*
			• iThemba Life COVID-19	*Launched*

[1] Not all products are available in all countries; [2] S=spike protein; [3] external distribution partnership; [4] US only; [5] v-TAC=venous to arterial conversion

Developer Challenges

- Clinical and Regulatory
  - **Access** to specimens/virus
  - Accuracy of, and access to, comparator (CDC test)
  - Changing templates and **moving targets** (swinging pendulum)
  - Lack of **clarity in regulation** (LDTs); disparities
- Scaling **production** in a short period of time
- **Capacity** of clinical labs
  - Dependent on installed base of analyzers on which tests will run
  - Availability of trained staff under CLIA
  - In some cases, can produce faster than labs can run the test
- Availability of **consumables** needed to collect specimens or run tests (e.g., swabs, PPE)
- Access to **Real World Data** on specific tests

Building Regulatory Agility During the COVID-19 Global Pandemic Has Been Critical

COVID-19 is draining regulatory resources worldwide

- **>7,600** entries of COVID-19 trials in WHO International Clinical Trials Registry Platform (ICTRP)*
- **1,031** test kits commercially available or in development for the diagnosis of COVID-19 listed in the FIND database*

Sheer volume of innovation

- About **75% of regulatory authorities** struggle to perform all core functions consistently well and depend often on better resourced authorities in other countries**
- Even well-resourced regulators are putting non-COVID-19 related product submissions on the back burner

Lack of regulatory capacity

- Ensuring access to new generations of products and cumulative innovation around the evolving science **of the novel virus** is critical

Evolving science of the new virus

**Source: Global regulatory agility during covid-19 and other health emergencies, https://www.bmj.com/content/bmj/369/bmj.m1575.full.pdf
*Site visited January 18, 2021

Most IMDRF Regulators Use Emergency Regulatory Pathways (1/3)

	Emergency Exemption or Approval	Emergency timeline*	Normal timeline*
Australia	1st Emergency exemption for COVID-19 Published in Jan 2020 to exempt COVID-19 test kits registration for PHLN members 2nd Emergency exemption for COVID-19 Published in March 2020 to repeal the first one; expanded the scope to all accredited pathology laboratories; ended in July Expedited assessment for COVID-19 All COVID-19 tests will be prioritized	1-2 weeks via expedited assessment	5-6 months for Class 3 products
Brazil	Emergency Registration for COVID-19 Open from March – September 2020	2-3 weeks	3-months for Class 3 products
Canada	Interim Order for COVID-19 To ensure quicker and more flexible approval of the importation and sale of medical devices	5 days to 3 months	1 year for Class 4 products

* Timelines reflect review timelines based on observations and estimations
** Average review timeline (excluding filing review and supplementary response time) according to CMDE data

Most IMDRF Regulators Use Emergency Regulatory Pathways (2/3)

	Emergency Exemption or Approval	Emergency timeline*	Normal timeline*
China	Emergency Approval Procedure Procedures established in 2009 and activated in Jan 2020 for COVID-19 Prioritized review for all COVID-19 products	1-3 days	6-8 months** for Class 3 products excluding clinical study timeline
EU	None	Self-declaration of conformity	Self-declaration of conformity

* Timelines reflect review timelines based on observations and estimations

** Average review timeline (excluding filing review and supplementary response time) according to CMDE data

Most IMDRF Regulators Use Emergency Regulatory Pathways (3/3)

	Emergency Exemption or Approval	Emergency timeline*	Normal timeline*
Russia	Emergency Registration for COVID-19 with a simplified procedure and reduced dossier; special import permission and local technical testing are waived	2 weeks	50 working days (official review) for Class 3 products, excl. clinical trials and supplement request
Singapore	Provisional authorization for COVID-19 as a risk-calibrated review process to help expand the number and variety of diagnostic tests	3 days to 3 weeks	8 and 11 months for Class C & D products via abridged pathway
US	Emergency Use Authorization for COVID-19 based on less data than in non-urgent circumstances via expedited review	1 day to 3 months	6-8 months for Class 2 De Novo

* Timelines in general are based on observations and estimation

Lifecycle Management of Emergency Authorizations/Approvals (1/2)

	Emergency review	Authorization Validity	Post Market Surveillance (PMS)
Australia	Full review	Full license/Conditional Approval No expiry date	Special PMS for Serology PoC tests
Brazil	Special Review	Conditional approval Valid for 1 year	Same as normal PMS requirements
Canada	Special Review	Authorization for Import Valid till the Interim Order is stopped	Same as normal PMS requirements
China	Special review/Full review	Emergency License (Condition Approval in the beginning of the outbreak) ; Valid for 1 year	Strengthened PMS requirements for COVID-19 products (additional focus was communicated within the authority)

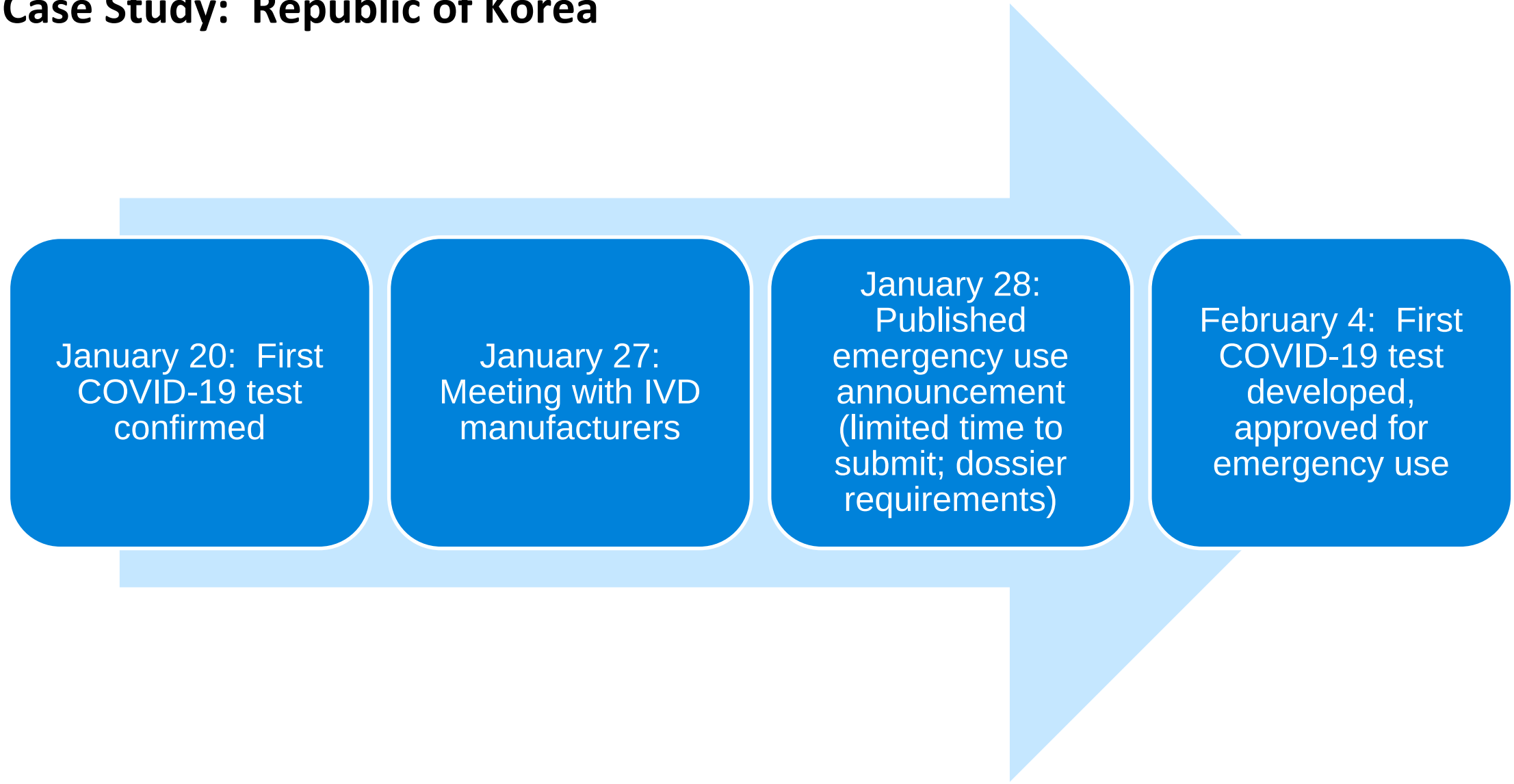
Lifecycle Management of Emergency Authorizations/Approvals (2/2)

	Emergency review	Authorization Validity	Post Market Surveillance (PMS)
Japan	Full review	Full license or Conditional approval No Expiry date	Same as normal PMS requirements
South Korea	Full review	Full license, Valid for 5 years	Same as normal PMS requirements
Russia	Special Review	Special Registration Certificate with batch number, valid till 01/01/2021	Same as normal PMS requirements
Singapore	Special Review	Provisional Authorization Valid till further notice	Periodic reports on specific data on the safety and/or performance
US	Special Review	Emergency Use Authorization Valid till the EUA declaration is terminated or the EUA is otherwise revised or revoked	Expanded reporting obligations required

Existing or Newly Created Reliance Model for COVID-19

	Existing Reliance model	Reliance model enabled during COVID-19
Australia	Comparable Overseas Regulators Accepting certificates issued by EU Notified Bodies, and decisions by US FDA, Health Canada, MHLW/PMDA, and MDSAP certificates	
Brazil	MDSAP	
Canada	MDSAP	Interim Order. Required information (partial) may be omitted if market approval obtained in a foreign regulatory authority (national level & state level) via pre-market evaluation (not exemption); MDSAP certificate can be replaced by ISO 13485:2016 or GMP
China		
EU		
Japan	MDSAP (Pilot)	
Korea		
Russia		
Singapore	Reference Regulatory Agency: TGA, Health Canada, US FDA, Japan MHLW, EU Notified Bodies	
US	MDSAP	

Case Study: Republic of Korea



Case Study: Lessons Learned

- Adapted approach **prior to COVID-19 pandemic** based on learnings from 2015 MERS crisis
- Close **monitoring** of the China situation enabled Korea to act quickly
  - Acquired genome sequencing from China on January 13
- Close **collaboration** with regulators, manufacturers/developers and health care providers
- **Quick review** by regulators
- **National approach** that included:
  - Center dedicated to handling laboratory control of infectious diseases
  - Social distancing
  - Contact tracing
  - Large number of collection centers (including drive-through) and testing institutions early
  - Good communication system with public health authorities

“This will not be the last pandemic. History teaches us that outbreaks and pandemics are a fact of life. But when the next pandemic comes, the world must be ready – more ready than it was this time.”

Dr. Tedros Adhanom Ghebreyesus,
Director General
The World Health Organization (WHO)

Key Takeaways

[Prioritization] To prioritize regulatory resources for COVID-19 products until the global pandemic is over

[Risk-calibration] To implement risk-calibrated pre-market approval with enhanced post authorization surveillance

[Accept] To accept overseas clinical evidence, leveraging real-world data , instead of duplicating all efforts locally

[Reliance] To leverage regulatory reliance and harmonization platforms, to share information for synchronized decisions

[Convergence] To develop IMDRF guidance for internationally harmonized emergency regulatory mechanism

[Resilience] To enable global supply resilience and improve access to a broad portfolio of testing technologies

[Agility] To practice regulatory agility elements during & beyond the pandemic

Doing now what patients need next