The Regulation Harmonization in Global COVID-19 Pandemic _ the perspective of A IVD manufacturer

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Intro_ experience of Manufacturer

To understand the context of Sugentech, which has offered variety of COVID-19 products from home-use to complex Lab, for more than 100 countries in the world

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Sugentech

COVID-19 Products

Point of Care Test

- IgM & IgG
- IgG

COVID-19 diagnosis and related immunity check

RDT
Serology test

ELISA
LAB
System

Lab, CLIA-certified Lab

- Total COVID-19 Ab
- Neutralization Assay-Ab efficacy test

Home-use

Kit+ Instrument +
App+ Dashboard

Mobile App integrated
Smart System

Virus Ag detection

Point of Care Test

- NanoGold based RDT
- TRF* based

Has been sold in more than 100 countries

TRF= Time Resolved Fluorescence,

Situation Overview of COVID-19

We have been all quite PANIC in global COVID-19 PANDEMIC, while all still being in LEARNING phase

Still-in-learning COVID -19 disease Characteristics

1) COVID-19 High ratio of **asymptomatic patients**: " Epidemiological investigations reveal approximately **40 percent** of all confirmed cases so far are asymptomatic,"

2) WHO's analysis on COVID-19 cases tells **"Latent period"** from 'contact' to 'actual release' of the virus is **1-12.5 days with median of 5-6 days**

3) Just before or soon after latent period, patients have high viral levels in upper respiratory tract, **which then fall over the course of approximately 10 days**

4) Prolonged Virus shedding **even several weeks even after symptom resolution**

5) Every COVID-19 patients produce Ab but Some shows **Rapid Loss of COVID-19 Abs**

Key Implication

- ✓ Not-yet established, **Clinical practice**
- ✓ Limited accessibility to Diagnosis **: EUA only in a few countries, No clear track**
- ✓ **Keep- Changing Registration Guidelines** in each regulation Scheme
- ✓ **Money source :** Fluctuating and Different from normal

COVID -19 diagnosis Considerations

Key Diagnosis Technology

Immunochemistry Ag
Immunochemistry Ab
Molecular, RT-PCR

Test Environment

Home-use
Point of Care (POC)
Lab

Regulatory Body

MoH & equivalent
FDA & Equivalent
EUA or EQUIVALENTS (IO)
Accelerated Normal Registration

Regulatory Scheme

Money Source

Insurance?
Gov. Fund?
Global Fund?

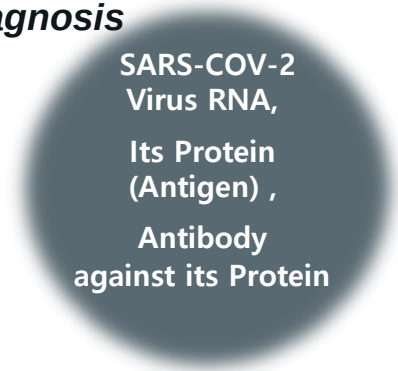
1) http://www.koreaherald.com/view.php?ud=20200915000999
2) https://www.coronaqna.com/en-virus#:~:text=With%20the%20result%20of%20the,days%20last%20February%5B1%5D.
3) J Infect. 2020 Sep; 81(3): 357–371. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7323671/
4) Humoral immune response and prolonged PCR positivity in a cohort of 1343 SARS-CoV 2 patients in the New York City region
5) https://www.the-scientist.com/news-opinion/studies-report-rapid-loss-of-covid-19-antibodies-67650

Not-defined Clinical pathway of COVID-19 Yet

Diagnosis has to be viewed in the holistic clinical process. The unprecedented COVID-19 is too embarrassing for everybody, for every stakeholders

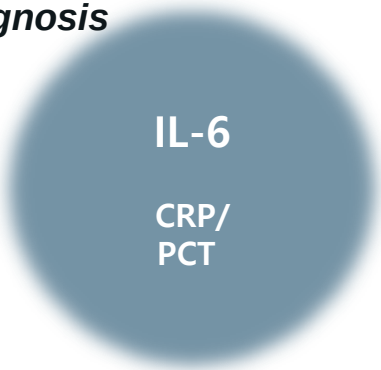
Even this is not the same and even not clearly described in most countries

Diagnosis



Clinical pathway for Screening

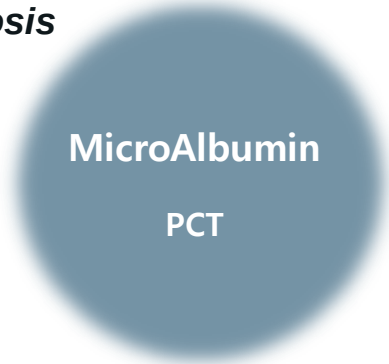
Diagnosis



Clinical pathway for Stratification of patients

for effective care using the limited resources, Tool to identify COVID-19 patients at risk of severe disease (check the prognosis)

Diagnosis



Clinical pathway for Care,

multi-disciplined care while considering the injuries of organ such as Lung and Kidney

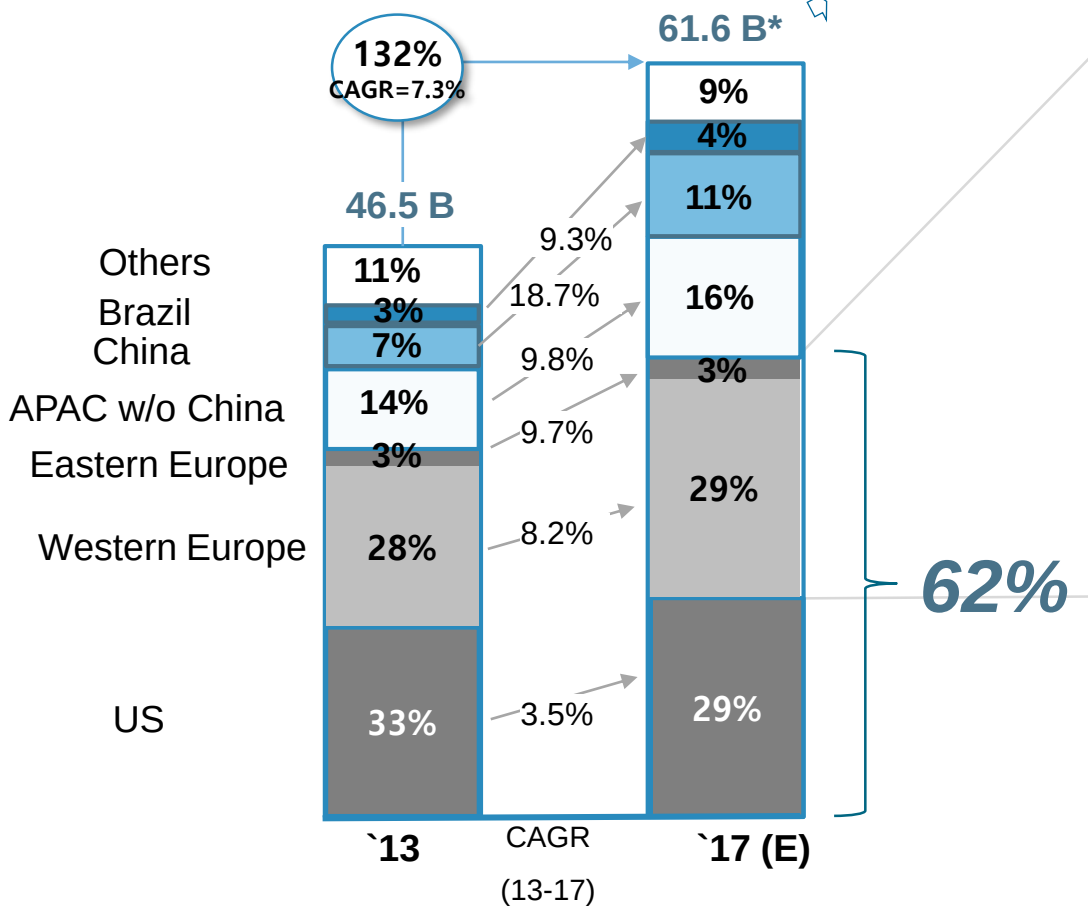
checking the sepsis and urgent care

deciding the plasma therapy

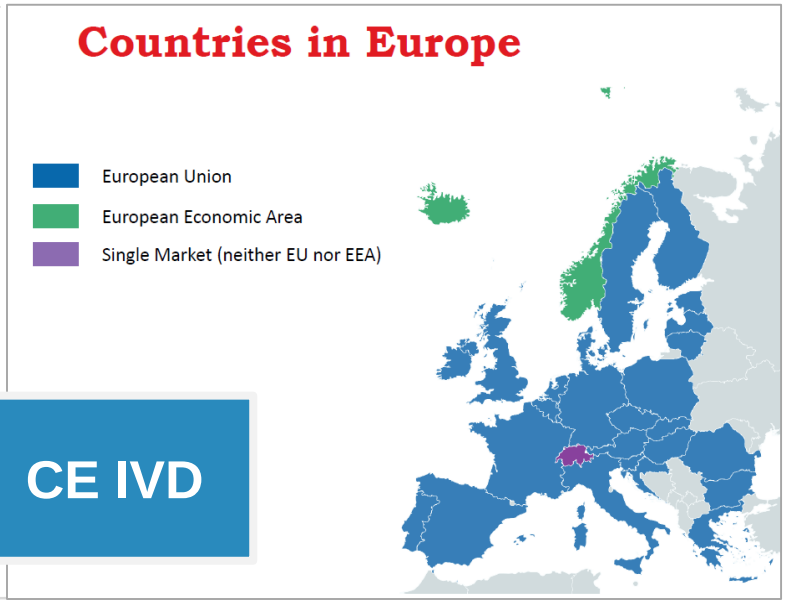
Global IVD Regulation Scheme Overview

IVD market has been grown while overachieving the expectation and the main regulatory bodies and scheme could be considered as CE, USFDA, etc.

IVD Market Size and Portion (%)



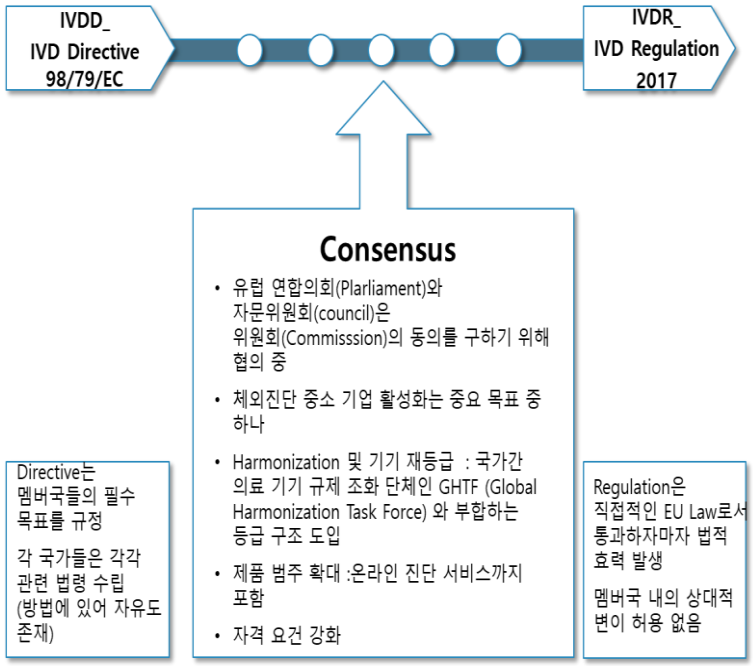
IVD Regulation Framework



Source: Frost & Sullivan *In many other report the sales of IVD in 2017 reached at about 75B.

CE, Regulatory Scheme of COVID-19

In COVID-19, CE has to go through the IVDR change management, which make the burden worse for NB…



Grace and Transitional period

- Notified Body (NB) has to be newly appointed
- Many requirements to prepare for IVDR
- New appointment of NB, limited resources
- So different situation and issue in each countries of Europe (COVID-19 Policy such as Shut-down controls and Travel controls), Healthcare resources, Culture, Level of incidents

- ***NB are in process of appointment***
- ***Workload to each NB***
- ***Different each country situation : for example the need of self-use***

Medical Device Regulations; A current perspective, J Young Pharm 2016 8:6-11: In-Vitro Diagnostic Medical Deivce , Briefing 2014 Nov: LJE analysis

EUA in US, , Regulatory Scheme of COVID-19

US EUA is leading the regulation scheme with EUA, but the CLIA regulation unique in US and changing clinical practice/implication add the complexity….

Legal Authority for EUAs

In the United States, EUAs are authorized by Section 564 of the Federal Food Drug and Cosmetic Act (FDCA) of 1938 (Public Law 75-717)

Subsequently amended by the Project BioShield Act of 2004 (S. 15, Public Law 108-276) for funding of the development and procurement of medical countermeasures against CBRN threats,

the Pandemic and All-Hazards Preparedness Reauthorization Act of 2013 (H.R. 307, Public Law 113-5),

the 21st Century Cures Act of 2016 (H.R. 34, Public Law 114-255) and Public Law 115-92 of 2017 (no short title)

EUAs may also only be implemented during the period of a public health emergency as defined by a declaration of the Secretary of Health and Human Services (HHS). Conditions determining the applicability of such declarations may be specified by federal statute. Code of Federal Regulations or an presidential executive order (Title 3 of the Code of Federal Regulations).

- ***CLIA regulation***
- ***US POC clinical study***
- ***NIH evaluation***
- ***Listing***

Examples of EUAs

In response to requests from the U.S. Centers for Disease Control and Prevention (CDC), on April 27, 2009 the FDA issued Emergency Use Authorizations to make available diagnostic and therapeutic tools to identify and respond to the **2009 swine flu pandemic** under certain circumstances. The agency issued these EUAs for the use of certain powerful antiviral drugs, and for the quantitative PCR Swine Flu test.

On April 22, 2013, the FDA issued an EUA for the CDC Human Influenza Virus quantitative PCR Diagnostic Panel-Influenza A/H7 (Eurasian Lineage) Assay. This test is for the presumptive detection of **novel influenza A (H7N9) virus**.

On June 5, 2013, the FDA issued an emergency use authorization for the CDC Novel Coronavirus 2012 quantitative PCR Assay. This test is for the presumptive detection of **Middle East Respiratory Syndrome Coronavirus (MERS-CoV)**, formerly known as Novel Coronavirus 2012 or NCV-2012.

On February 4, 2020 the Secretary of HHS has declared the public health emergency, that involves the **novel SARS-CoV-2 virus**, which causes the disease COVID-19, as justification for the deployment of the FDA Emergency Use Authorization (EUA) for certain medical devices involved in the diagnosis of COVID-19. In February 2020, The FDA issued an EUA for COVID-19 testing CDC test kits for COVID-19. In May 2020, the FDA issued an EUA for remdesivir, also for COVID-19.

Accessibility / Public Health Risk / Load of FDA

WHO with limited source of fund cannot lead the sourcing leadership for under and being developed countries….

Emergency use listing

The WHO Emergency Use Listing Procedure (EUL) **risk-based procedure** for **assessing and listing** unlicensed vaccines, therapeutics and in vitro diagnostics with **the ultimate aim of expediting the availability of these products to people affected by a public health emergency**. This will assist interested UN procurement agencies and Member States in determining the acceptability of using specific products, based on an essential set of available quality, safety, and efficacy and performance data. The procedure is a key tool for companies wishing to submit their products for use during health emergencies.

Eligibility of candidate products : vaccines, therapeutics and in vitro diagnostics

The common criteria for each could be summarized as

- Desperate need : serious or immediately life threatening (outbreak, epidemic or pandemic)
- The product is manufactured in compliance with current Good Manufacturing Practices (GMP) in the case of medicines and vaccines and under a functional Quality Management System (QMS) in the case of IVDs
- The applicant undertakes to complete the development of the product (validation and verification of the product in the case of IVDs) and apply for **WHO prequalification** once the product is licensed.

Fund?

EUA in Korea, Regulatory Scheme of COVID-19

Korea Gov. has shown strong leadership to control domestic COVID-19, but for its unique HC system, its practice cannot be transferred in other countries as it is …

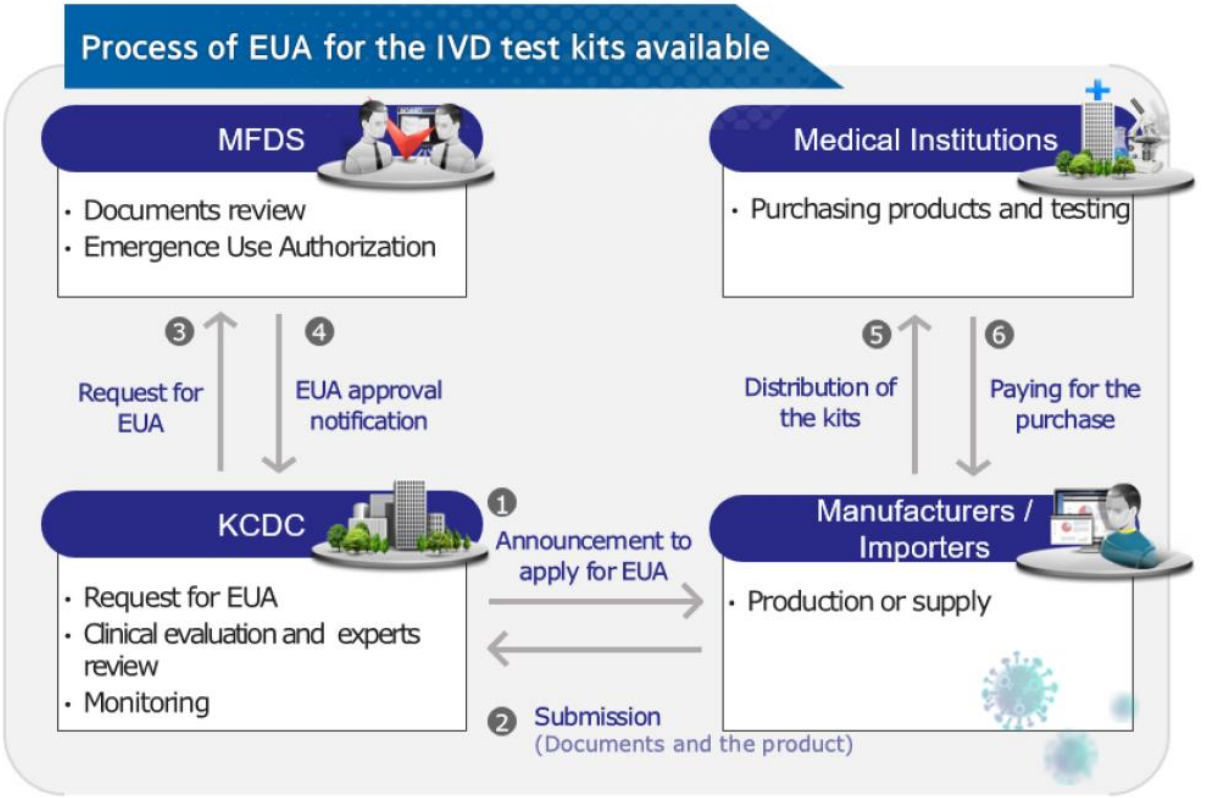
IVD test kits for COVID-19

The EUA program expeditiously allows prompt diagnosis of COVID-19 in collaboration with the concerned government agencies to prevent COVID-19 from being spread domestically

Emergency Use Authorization (EUA)

Article 46-2 of the MDA

Applied to medical devices in an urgent need to be used in order to adequately respond to the outbreak or pandemic of infectious diseases



EUA Item?

Key Consideration (1/2)

The global leadership is needed to get expedited availability in acceptable quality not to harm the global public health ….

The main issue : Expedited availability

- Accelerated Availability is the main purpose of EUA and critical need of market
- But in COVID-19 the EMERGENCY of each country in specific time CANNOT be same at all

The main issue : Clinical Resources

- The clinical asset and resource cannot be the same in each countries : In Korea RT PCT can serve mainly for screening up to some level of incidents
- Domestically sourced diagnosis
- COVID-19 disease understanding/knowledge

The main issue : Unprecedented Change Mgmt. Need

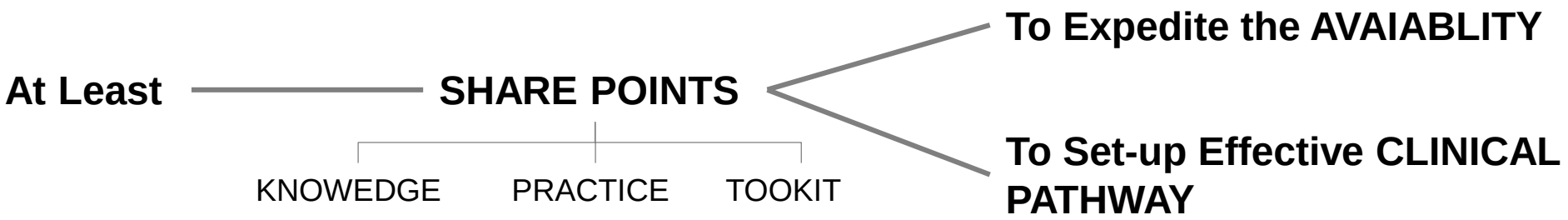
- Chaining situation and its velocity vs level of being Predictable
- FLEXIBILITY vs ROBUSTNESS
- SYSTEM & PROCESS could sometimes interfere with FLEXIBILITY
- Product registration and Quality management system (Mfg.)
- Political and Economical turmoil

The main issue : Not-Yet established Regulatory Scheme for Harmonization

- In many countries there is no clear track for IVD registration while IVD specific GMP and ISO for Mfg. being the similar situation
- EUA has to reflect each country situation specifically to expedite the availability

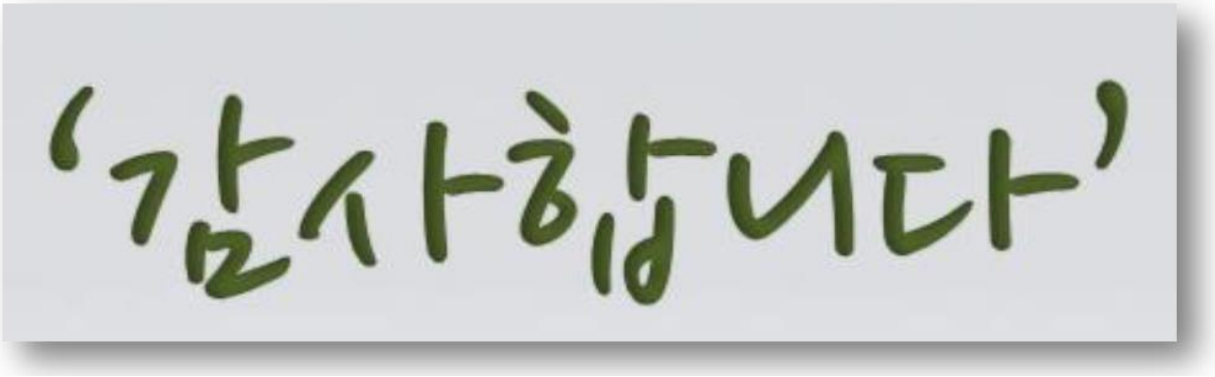
Key Consideration (2/2)

… IMDRF could be functioning as the share point for every stakeholders, while all members commit that together



FOR FIGHTING COVID-19 TOGETHER

IMDRF as one of major stakeholder of major market could announce the passion to start that SHARE POINT together?



‘Thank You’