Webinar Series: The Role of Vaccination in Maintaining Health and the Economy During Pandemics

Building the Right Regulatory Environment for COVID-19 Response & Long-Term Health Resilience

8 July 2021 21:00 (Washington, DC)

9 July 2021 9:00 (Singapore)

13:00 (Auckland)

Yi-Chu (Judy) Lin
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Regulatory Agility and Expedited Approach in Emergency Use

Experience Sharing from TFDA

9 July, 2021

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食 品 藥 物 管 理 署
Taiwan Food and Drug Administration

Outline

- Current Status of COVID-19 Pandemic
- Actions Against COVID-19
- Challenges of Emergency Use
- Lessons Learned from the Crisis

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FDA Taiwan Food and Drug Administration

Current Status of COVID-19 Pandemic

(updated 30th June 2021)

Global Status

Cumulative Cases

181,681,318
cases confirmed

3,947,880
deaths

2.17%
case fatality rate (CFR)

Status Here

Cumulative Cases

14,804
cases confirmed

648
deaths

10,196
recovered

Data from https://www.cdc.gov.tw/

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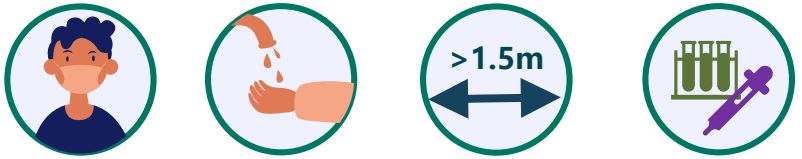
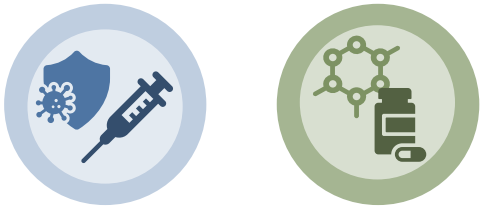
Public Health Management of COVID-19

Non-Pharmaceutical Interventions:



- Public masking
- Wash hands
- Social distancing
- Early and active identification, isolation, and contact tracking and tracing

Pharmaceutical interventions:



- Vaccine
- Therapeutic drugs

Response to COVID-19 Pandemic

DRUG SUPPLY

- ✓ Drug Supply Database Platform
- ✓ Guidelines

SANITIZER PRODUCTS

- ✓ Maximize Production
- ✓ Restrict Exportation

CLINICAL TRIALS

- ✓ Protect Right and Safety of Participants
- ✓ Recruitment Plateform

DRUG DEVELOPMENT

- ✓ EUA
- ✓ Consultation
- ✓ Rolling Review
- ✓ Technical and Financial Supports

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Domestic Pharmaceutical Development

Medigen Vaccine Biologics Corp.

MVC-COV1901 Vaccine

- **Protein subunit vaccine**
- Phase 1 initiated on Aug. 28, 2020
- Phase 2 initiated on Dec. 29, 2020

United Biomedical, Inc. Asia.

UB-612 Vaccine

- **Protein subunit vaccine**
- Phase 1 initiated on Aug. 30, 2020
- Phase 2 initiated on Jan. 29, 2021

Active Ingredient	Company	Approval Date by TFDA	Review Time (calendar day)
Remdesivir	**Gilead**	**June 2, 2020 (EUA)**	**< 10 days**
COVID-19 Vaccine	**AstraZeneca**	**Feb. 20, 2021 (EUA)**	**~ 30-45 days**
COVID-19 Vaccine	**Moderna**	**Apr. 22, 2021 (EUA)**	**~ 30 days**

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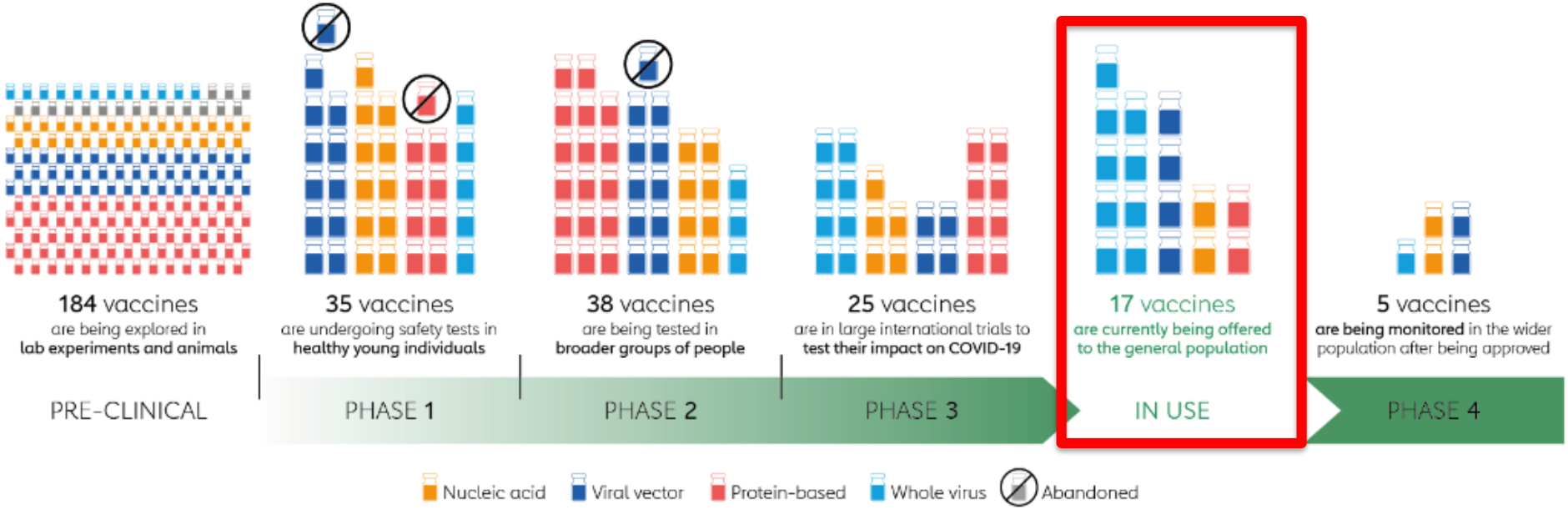
Global Race for COVID-19 Vaccines

- There are now **17** vaccines been developed and **available in use within 1.5 years** since the outbreak of COVID-19 in the late 2019.
- Around the world, there are now 103 COVID-19 vaccine candidates undergoing clinical trials and 184 candidates in pre-clinical development.

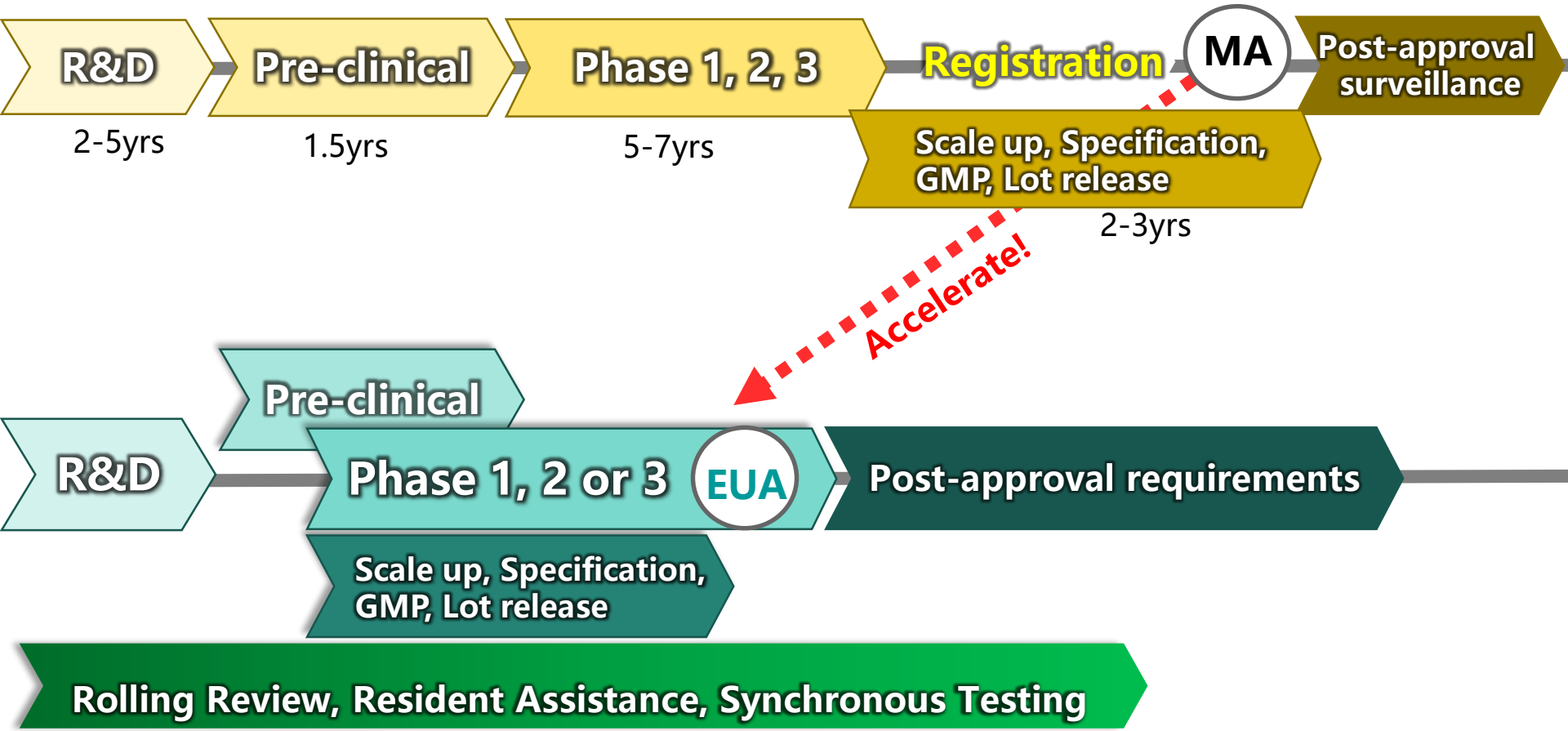


https://www.gavi.org/vaccineswork/covid-19-vaccine-race

Last updated on June 30th, 2021

Accelerating COVID-19 Vaccines Development

◆ **Typical timeline for vaccine development(>10 yrs)**



◆ **Acceleration for COVID-19 vaccine development**

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Regulatory Framework for Emergency

01 Pharmaceutical Affairs Act

02 Communicable Disease Control Act

03 Regulations for Approval of Specific Medical Products

04 Checklist for Application and Review

Law for Authorization and Procurement

- **Implementation of EUA approach**
  - **Article 48-2 of the Pharmaceutical Affairs Act**
    - The central competent health authority may **approve to manufacture and import** the specific drugs as special case:
      - For the purpose of prevention, diagnosed as life-threatening, severely disability diseases, and there is no domestic appropriate drug or alternative treatment.
      - **In responding to the necessity of emergency public health circumstances**
  - **Article 51 of the Communicable Disease Control Act**
    - When communicable disease occur or are expected to occur, the central competent authority **for the reason of emergency**, may **procure** pharmaceuticals and equipment, provided that the relevant documents shall be filled within six months and complete the test.

Documents Required for EUA Application

- **Article 3 of the Regulations for Approval of Specific Medical Products' Manufacturing or Importing :**
  - A complete prevention or therapy protocol and related references; The contents of the protocol shall include the application purpose of responding **the emergency public health circumstances** and documents to show **the benefits will greater than the risks**.
  - **The amounts** of the drug and the calculation basis.
  - Instructions of the drug (or the **package insert**)
  - The **certificates of the market approval** in regulatory authorities of the reference pharmacopeia or the drug’s
    - manufacturing and quality control documents,
    - the animal study reports,
    - the clinical data,
    - risk-benefit assessment report

Checklist for Application and Review (Clinical)

Technical documents of Phase II application on clinical trials

Objectives: Immunogenicity and safety

Phase I clinical study report：**Interim Report is acceptable**

- ☐ The results of **immunogenicity** for each vaccination in all dose groups.
- ☐ The results of **neutralizing antibody titers** for each vaccination in all dose groups. (including: methods for detection and quantification of neutralizing antibodies, seroconversion rate in each dose group. **Seroconversion rate**, defined as a **4-fold increased** in antibody titer from baseline.)
- ☐ The safety reports of the 21-28 day follow-up for each vaccination.
- ☐ The rationale of dose selection in Phase II clinical trials.

Technical Documents of Emergency Use Authorization (EUA)

- ☐ Clinical Data: All clinical trial reports, including un-published paper or literature
- ☐ Efficacy: Vaccine efficacy or preliminary efficacy data that might **predict protection against COVID-19, Immunogenicity in adult and elderly populations**
- ☐ Safety: Assess the whole population (at least **3000 participants**, and **track down at least 1 month** after the last dose) and the special ethnic group (including the elderly over 65 yr.). In addition, need to accumulate the safety data of different clinical phases, the safety assessment of specific ethnic group, major adverse effect assessment and vaccine-enhancement reports.
- ☐ Lot-to-lot clinical consistency trial results: using **3 batches** (in principle)

Minimal Requirement for EUA- CMC 1

Chemistry, Manufacturing, and Control

EMERGENCY

- ✓ **Drug Substance**
  Manufacture, characterization and elucidation of structure, control of drug substance, reference standards or material, container closure system, stability data, etc. should be provided

- ✓ **Intermediate**
  Composition, manufacture, controls of intermediate, container closure system, stability data, etc. should be provided

- ✓ **Drug Product**
  Description and composition of the drug product, pharmaceutical development, manufacture, control of excipients, control of drug product, reference standards or material, container closure system, stability data, etc. should be provided

Minimal Requirement for EUA- CMC 2

Quality Control and Specifications

EMERGENCY

◆**Manufacturing Process Controls and Development**

1. Manufacturing process controls and development of commercial batches for drug substance and drug product and process validation
2. Specifications of batch release, validation of analytical methods
3. Stability protocol and report
4. Comparability test (clinical trial batch and commercial batches)

◆ **Test items of quality specifications, such as:**

- ☐ Appearance
- ☐ pH
- ☐ Identification
- ☐ Content of Antigen
- ☐ Content of Adjuvant
- ☐ Bacterial Endotoxin
- ☐ Sterility
- ☐ Potency test
- ☐ Abnormal toxicity test
- ☐ Other parameters depend on characteristics

Minimal Requirement for EUA- Pharm/Tox

Pharmacology and Toxicology

- ✓ **Vaccine-induced Disease Enhancement :** evaluation of vaccine-associated enhanced disease through animal challenge studies (including immunopathology, viral load or titer, BW, etc.)
- ✓ **Safety Pharmacology :** Including assessment of effects on cardiovascular, central nervous and respiratory systems
- ✓ **Single (Repeated) Dose Toxicity :** complete study report
- ✓ **Genotoxicity :** complete study report
- ✓ **Reproductive and Development Toxicity :** complete report
- ✓ **Local Tolerance :** Draize Scoring (or other suitable test method)

Minimal Requirement for EUA- Clinical

Clinical

EMERGENCY

- ✓ **Clinical data :** All clinical trial reports and literatures of the vaccine
- ✓ **Assessment report of the risks and benefits :** should include over 3,000 vaccine recipients with at least one month safety follow-up data after completion of the full vaccination regimen and a median follow-up duration of at least two months
  - ➢ **Efficacy :** vaccine efficacy or or preliminary efficacy data that might predict protection against COVID-19; Immunogenicity of ≧65yr population
  - ➢ **Safety :** safety population and specific subgroups for safety assessment, all safety data accumulated from all Phase studies, adverse events of special interest, vaccine-induced disease enhancement assessment
  - ➢ **Manufacturing consistency:** lot-to-lot consistency trial

Current Consideration on Safety and Efficacy

Safety

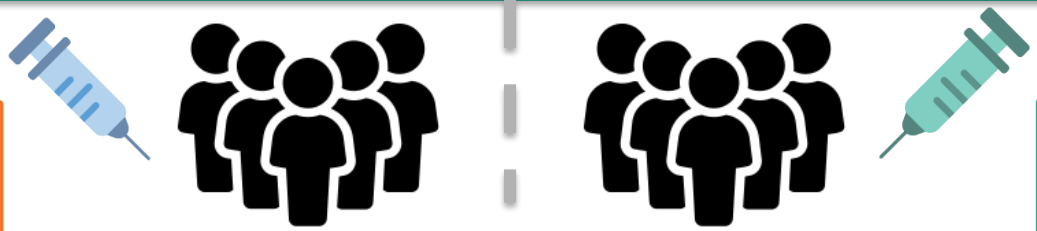
- **Over 3,000 vaccine recipients** with **at least 1 month** of safety follow-up data after the completion of the full vaccine regimen.
- **All vaccine recipients** with the **median** follow-up duration of **at least 2 months** after the completion of the full vaccine regimen.

Efficacy

- As the emergency situation, it might be considering to utilize the immuno-bridging method and adopt immunogenicity (neutralizing antibody) as surrogate endpoint to evaluate whether the vaccine has **triggered the same immunogenicity as the vaccine that has been used in emergency.**

Immuno-bridging Method

EUA granted vaccine



Vaccine under development

Review Process of EUA for COVID-19 Vaccines

COVID-19 vaccines manufacturers

Weekly meeting with vaccine developers, On-site audit for GMP compliance, Rolling review, Synchronous testing

Submit an EUA application to TFDA under emergency public health circumstances

Article 48-2 of the PAA;
Regulations for Approval of Specific Medical Products' Manufacturing or Importing

TFDA/CDE review, Advisory Committee

TFDA issue an EUA after ensuring the quality, safety and efficacy of the COVID-19 vaccine

Documents required for EUA application

- ✓ A complete prevention or therapy protocol and related references
- ✓ The amounts of the drug and the calculation basis
- ✓ Instructions of the drug
- ✓ The CMC, Pharm/Tox, Clinical technical documents of the drug#

Manufacture the COVID-19 Vaccine based on the granted EUA

Apply for lot release by manufacturers

Article 74 of the PAA;
Regulations of the Lot Release Procedures

TFDA issue the Lot Release Certificate. The vaccines can be sold and supplied after receiving a Drug Approval Seal.

Vaccines used in accordance with the policy

Accelerate Review Approaches

Taiwan Food and Drug Administration

- Division of Medicinal Products
- Division of Research and Analysis
- Division of Quality Compliance and Management

Center for Drug Evaluation

- Technical reviewers with strong background in medicine, pharmacology, chemistry, biology, statistics and other life science-related fields

Advisory Committee

- External experts from medical centers and academia, etc.

Review Optimizing Measures

1. Priority Review

- Accelerated approval approach
- Rolling submission and rolling review
- Technical advice from advisory committee

2. Review Considerations and Flexibilities

- Develop checklists of clinical trials and EUA applications for COVID-19 vaccines
- Adopt international Guidelines

3. On-site audit for GMP compliance

- GMP inspectors on-site checking for the quality of production during R&D stage

4. Develop analytical methods

- Develop validated analytical methods for vaccine development
- Set up reference standard for the analysis of vaccine potency

Project Team Consultation

- **Timely communication on regulatory, manufacturing process development, clinical and Pharm/Tox issues**
- **Weekly meeting with progress checking and assistance**

CDE Can Help

Regulatory guidance program for the development of domestic COVID-19 medicinal products

- **Project team** set up for each selected application
- **Provide free and active consultation**
- **Quick response** (initial response in 3~7 days) for inquiries
- **Aim for shortening the time required for the development** of COVID-19 medicinal products, including drugs, vaccines and medical devices.

Expert Meeting to Formulate Guidelines

In order to accelerate the development of COVID-19 Vaccine, TFDA has convened several expert meetings.

Expert Meetings

- Strategies of accelerating COVID-19 vaccines clinical trials
- Enhancement of vaccine-induced studies and animal challenging studies mode
- Analytical methods of neutralizing antibodies
- COVID-19 clinical trial reports review standards
- Emergency use authorization of COVID-19 vaccine

Clinical Trial Recruitment Platform

What

TFDA has established a platform to collect the basic and contact information of those who have expressed intentions to join the clinical trials. This database could provide vaccine developers or clinical trial sites information and **help them instantly contact people who are willing to participate in the trial**.

Who

- **Adults aged 20 and above** with the intention to take part in clinical trials
- **Minors aged 12 to 20** with intention to take part in clinical trials; they may sign up by themselves but consent from their legally statutory agents shall be obtained prior to the actual participation in the clinical trial.

When

2020.11.11-2020.11.30

Where

For more information, please refer to：**twcvt.fda.gov.tw**

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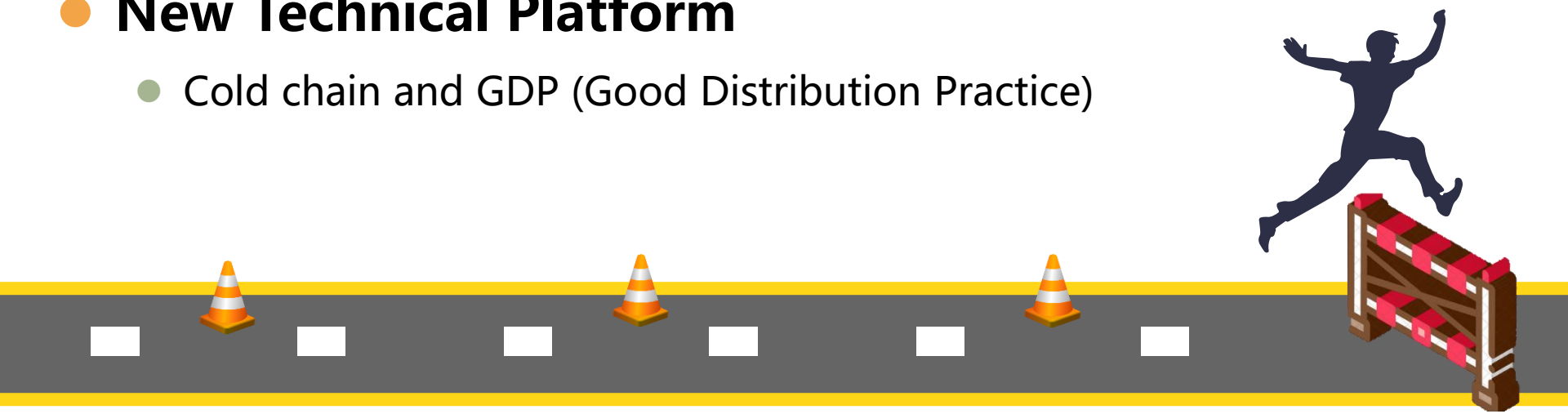
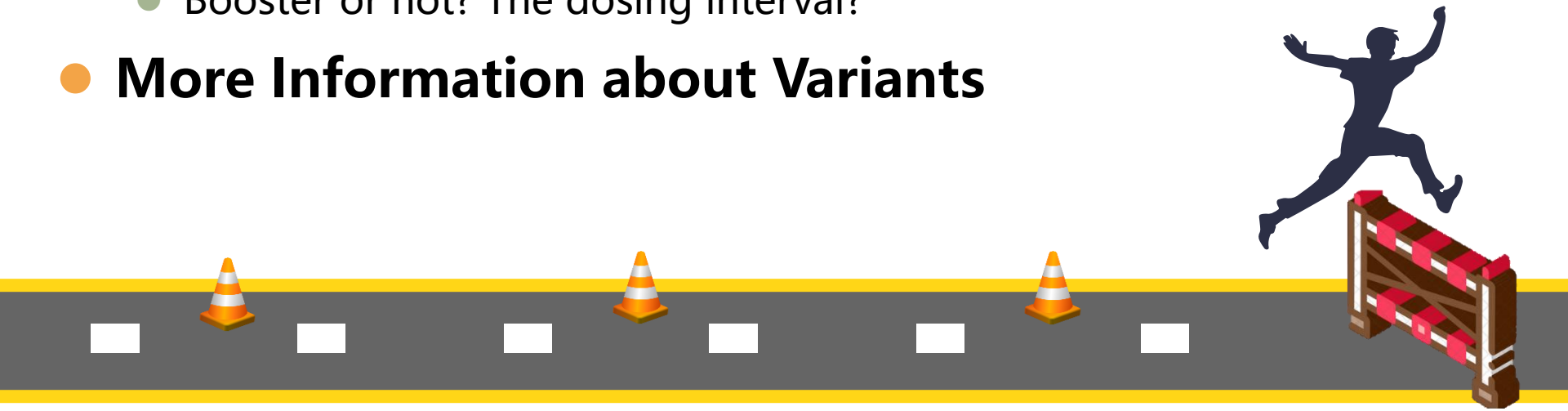
Challenges for Decision-Making

- **Maximize the Benefit and Minimize the Risk**
  - No vaccine is 100% effective and safe
- **Standard Parameter for Vaccine Protection**
  - Criteria for issuing an EUA
- **Number of Subjects Required for Vaccine Safety**
- **New Technical Platform**
  - Cold chain and GDP (Good Distribution Practice)



Challenges for Vaccine Confidence

- **Vaccine Safety Monitoring**
  - Post-vaccination surveillance and vaccine injury relief
- **Vaccine Interchangeable**
  - The safety and efficacy of a mixed-product is not confirmed
- **Duration of Protection**
  - Booster or not? The dosing interval?
- **More Information about Variants**



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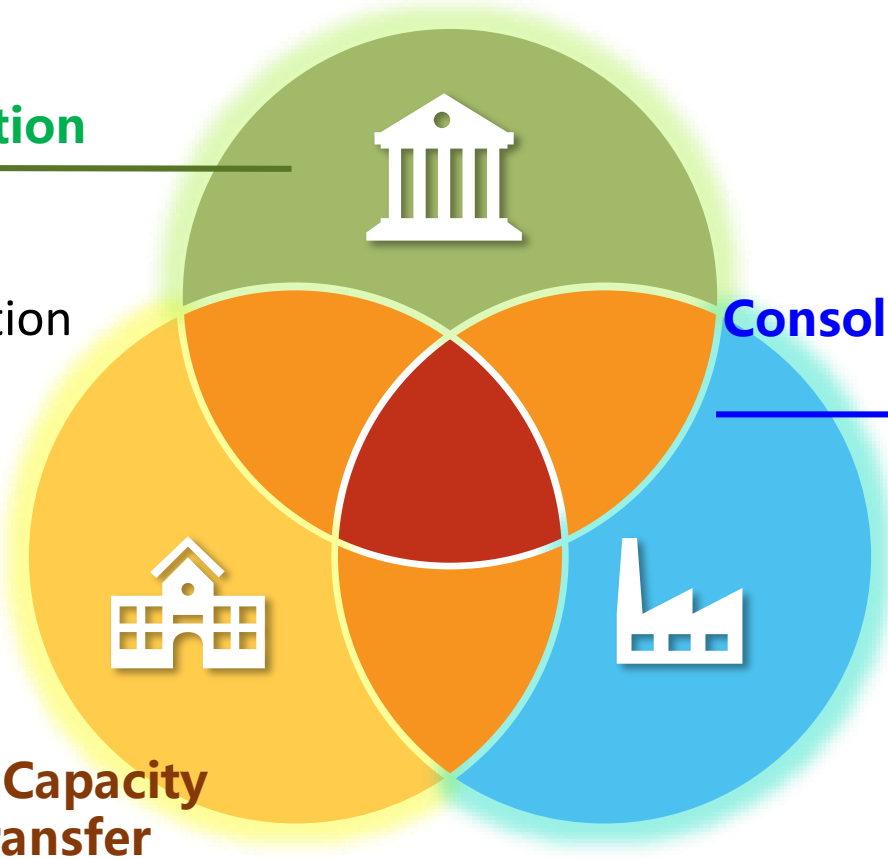
Public-Private Partnership

Government Resources Integration

- Inter-agencies collaborations
- Resources integration



Consolidate and Strengthen Industrial Chain

- Invest in therapeutics and vaccines development and manufacturing

Enhance Research Capacity and Technology Transfer

- Support development of research teams and facilitate technology transfer at early stage

Technical and Financial Supports

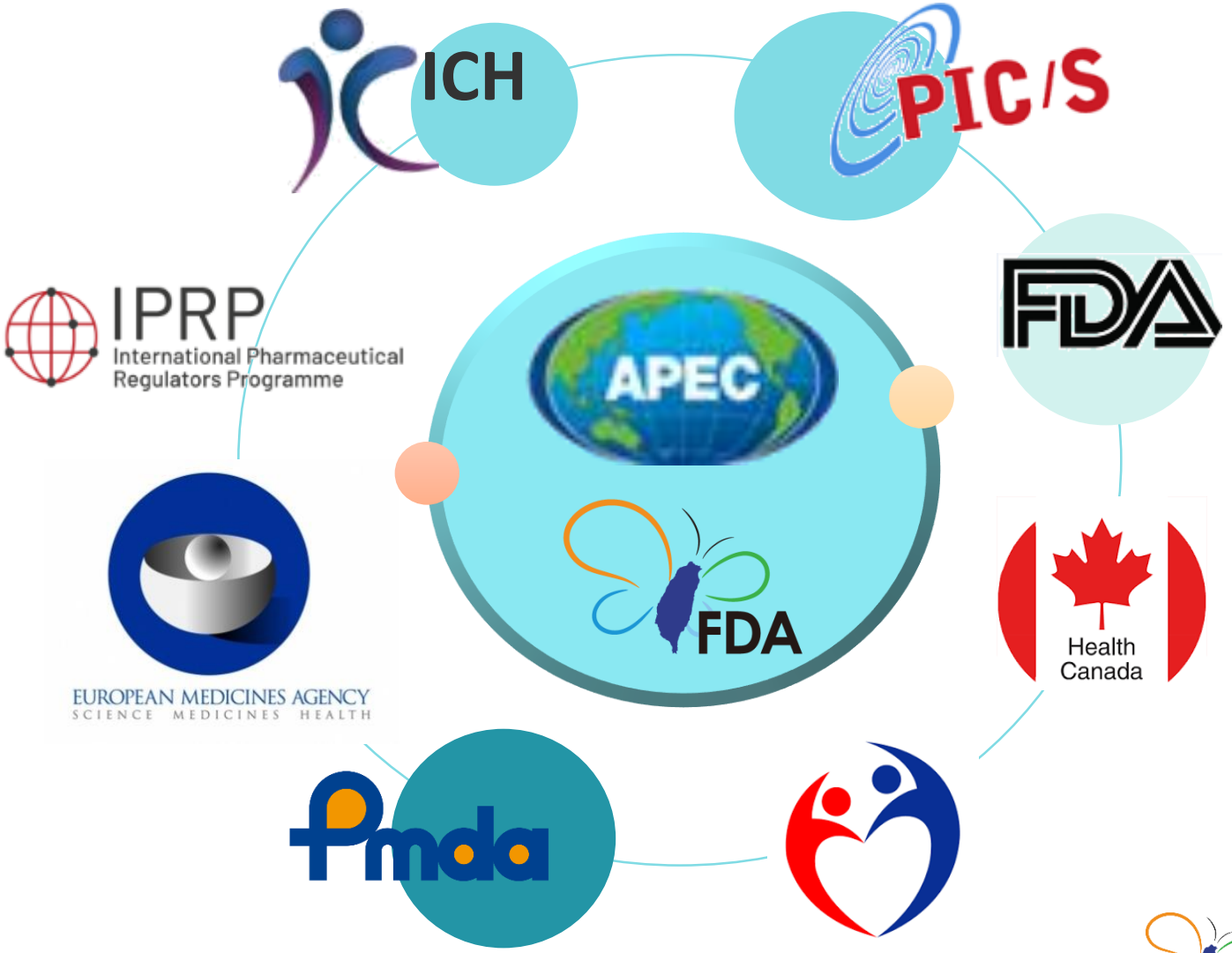
Technical Support Platform

- Support by **National Health Research Institute (NHRI)** and **Academia Sinica**
  - Provide animal study services, set up blood sample bank of COVID-19 confirmed cases
- **Department of Medical Affairs** and **Hospital and Social Welfare Organization Administration Commission**
  - Assist on accelerating the administrative process of clinical trials

Government Incentives / Subsidies

- **Subsidy program for domestic potential COVID-19 vaccines**
  - Supported by **Center for Disease Control (CDC)**, MOHW
  - Grants for the R&D and Clinical Trials of potential COVID-19 vaccines
- **A⁺ Industrial Innovation R&D Program**
  - Supported by **Department of Industrial Technology (DOIT)**, MOEA
  - Subsidies for industries to get involved in innovation, development and research programs

International Cooperation



Virtual Meeting on COVID-19

16th June, 2020

Actions taken by regulatory authorities on

(1) prevent **drug shortages**
(2) satisfy the increasing demands for **alcohol-based sanitizer products and personal protective equipment**
(3) fulfill the needs for **diagnostic test kits**

Future Prospects

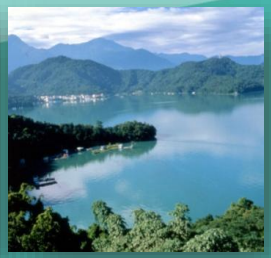
Timely access to the COVID-19 vaccines or drugs through risked-based regulatory decision making while not compromising products' quality, safety and efficacy

Enhance **post-vaccination surveillance** to monitor the safety and effectiveness

Promote **international regulatory cooperation**, information sharing and reliance







Thank You
For Your Attention

Dr. Yi-Chu (Judy), Lin
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John Lim
Executive Director, Centre of Regulatory Excellence
Duke-NUS Medical School

Regulatory Agility
During and After COVID-19

Professor John CW Lim
Executive Director, Duke-NUS Centre of Regulatory Excellence
Core Lead (Policy), SingHealth Duke-NUS Global Health Institute
Senior Advisor, Ministry of Health Singapore
Chairman, Consortium for Clinical Research & Innovation Singapore

CoRE
Centre of Regulatory Excellence
@ Duke-NUS Medical School

Scope

- Enabling Good Regulation in the Asia-Pacific
- Pre-COVID-19 Regulatory Trends
- Regulatory Agility during COVID-19
- Regulatory Trends to 2030
- Advancing Regulatory Agility & Innovation

Good Regulation is an Enabler

Regulation impacts global & national socio-economic-political environment

Regulation as an enabler

- Health Products
- Health Services
- Industries that impact health

Promotes access to:

- Essential medicines, medical devices and vaccines
- High quality health services
- Health-promoting environment

Health Systems Benefits & Outcomes → **Economic Benefits & Outcomes**

Ensuring sustainable development

Asia-Pacific Regulatory Enablers

1. Adopt **risk-based approaches** to help overcome resource limitations

2. Promote **regulatory cooperation**, recognition and reliance to facilitate convergence and harmonisation

3. Develop **regional platforms** for engagement, collaboration and capacity building

Lim JCW, Chan CL, Green A. *Global Challenges in Regulatory Capacity and Capability Building: Extrapolating Lessons Learned From the HSA.* Clinical Pharmacology & Therapeutics, Advance on line publication, November 20, 2018. DOI: 10.1002/cpt.1253

Global Trends impacting Regulatory Science since 2010

1. Expanding digital health opportunities due to rapidly advancing Infocomm Technology (ICT), e.g. AI, block-chain

2. New and enhanced treatment modalities and platform technologies, e.g. innovative & advanced therapies, vaccines

3. Precision medicine and personalised healthcare

4. Demand for responsive, on-demand healthcare

5. Accelerating health products access through multilateral cooperation

6. **Increasing importance of adopting agile approaches**

Pre-COVID-19 Regulatory Trends

1. Steady development of **regulatory convergence initiatives** supporting regulatory agility and regulatory science & policy development

2. Strengthening of **WHO initiatives** in cooperation, convergence & Good Reliance Practice

3. **Pan-global organisations**, e.g. ICMRA

4. **Regional initiatives**, e.g. APEC LSIF RHSC* with KPI identification to track convergence progress, ASEAN harmonisation efforts

   * Life Sciences Innovation Forum Regional Harmonisation Steering Committee

5. **Cross-regional initiatives**, e.g. ACCESS Consortium (Australia, Canada, Switzerland, Singapore, UK)

6. **Academic capacity building and think tank centres**, e.g. APEC RHSC COEs*, PMDA Asia Training Center, Duke-NUS CoRE

   * Centers of Excellence

Regulatory Agility during COVID-19

- National Regulatory Authorities (NRAs) facilitated access to essential COVID-19 health products through **effective, agile regulation**

  Mak TK, Lim JCW, Thanaphollert P, Mahlangu GN, Cooke E, Lumpkin MM. ***Global regulatory agility during covid-19 and other health emergencies.*** *BMJ. 2020*

- **Regulatory Agility** refers to adoption of *risk-based, context-driven approaches* and *regulatory cooperation* predicated on *sound scientific evidence and information*

- Involves non-traditional approaches to robust regulatory decision-making while not compromising safety, quality and efficacy

- "Agility" is preferable to "flexibility" which may connote unsafe cutting of corners

Regulatory Agility during COVID-19

- The pandemic has advanced
  (a) ***regulatory coordination and information exchange***
  (b) use of ***reliance, referencing*** **and** ***convergence***

- Speedy vaccine approval facilitated by
  (a) ***parallel development*** processes
  (b) ***rolling data reviews***
  (c) ***emergency use authorisations*** and ***conditional approvals***
  (d) on-going adverse event and ***real world monitoring***

- Use of *regular virtual & online meetings* by WHO, ICMRA, regional regulatory groupings and NRAs

The COVID-19 Crisis as an Opportunity to Strengthen Global Regulatory Coordination for Sustained Enhanced Access to Diagnostics and Therapeutics. Clinical and Translational Science. 13 Dec 2020. DOI: 10.1111/cts.12954

Regulatory Agility during COVID-19

- *Emergency use authorisation and conditional approval approaches* for new diagnostics, therapeutics and vaccines while awaiting more data for full approval

  https://www.duke-nus.edu.sg/core/think-tank/core-regulatory-perspective/making-sense-of-emergency-use-authorisations-(euas)-for-covid-19-vaccines-and-considerations-for-the-road-ahead

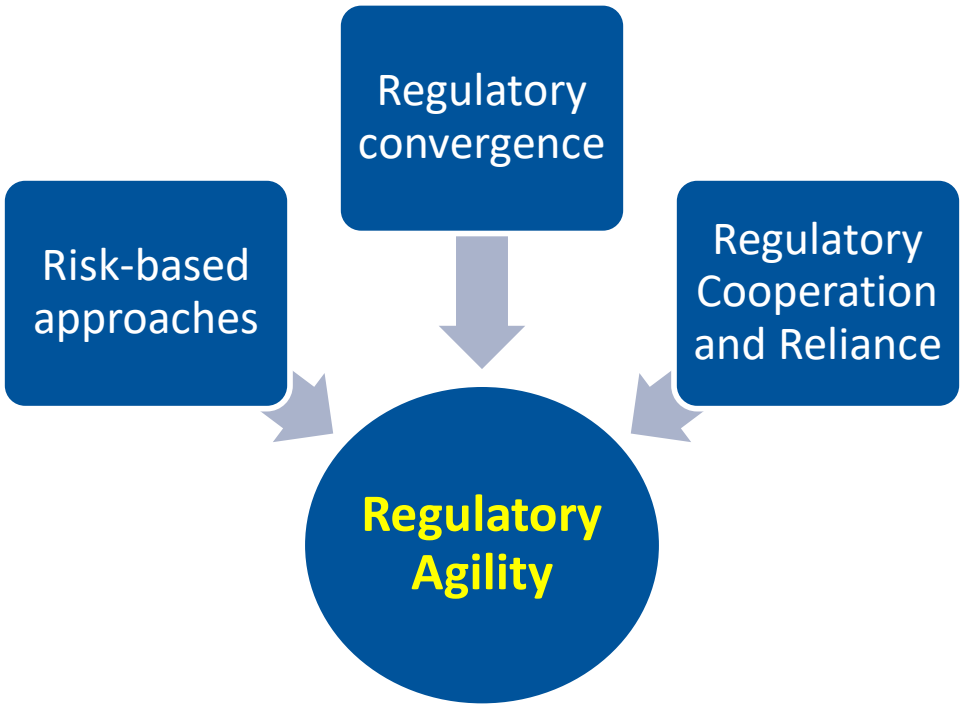
- Preliminary guidelines on *updating currently available vaccines* for *new SARS-CoV-2 variants* by NRAs (e.g. US FDA, EMA) and regulatory consortia (e.g. ACCESS)

  https://www.duke-nus.edu.sg/core/think-tank/core-regulatory-perspective/regulatory-agility-and-global-coordination-to-meet-the-challenge-of-covid-19-variants-preparing-for-the-next-generation-vaccines

Regulatory agility should become part of **regulatory "new normal"** to support innovation and future public health challenges

The COVID-19 Crisis as an Opportunity to Strengthen Global Regulatory Coordination for Sustained Enhanced Access to Diagnostics and Therapeutics. Clinical and Translational Science. 13 Dec 2020. DOI: 10.1111/cts.12954

Building Regulatory Agility

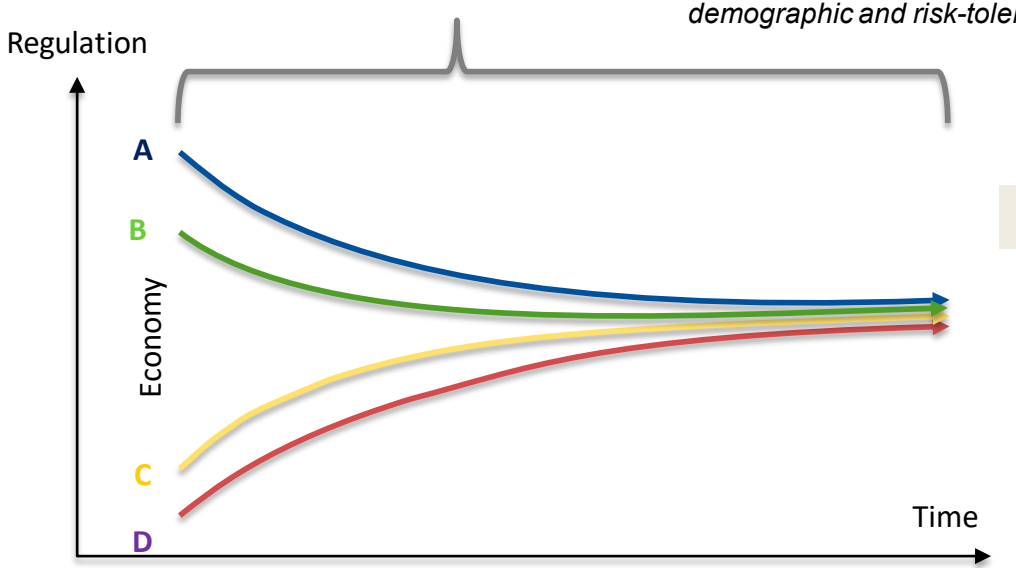


Timely Patient Access to Health Products

Convergence supports Regulatory Agility

Convergence =

*Regulatory requirements become **more aligned over time** with adoption of internationally recognised technical guidance documents, standards and scientific principles, while taking into account distinctive national legislative, demographic and risk-tolerance factors*



World Health Organization

APEC Asia-Pacific Economic Cooperation

Regulatory Harmonization Steering Committee
APEC Life Sciences Innovation Forum

Duke-NUS Centre of Regulatory Excellence

Enhance regional health systems & policy

Strengthen regulatory systems for health-related products in Asia-Pacific

Networking & Collaboration

Provide a neutral academic platform for engaging and connecting a diverse range of stakeholders

CoRE's Strategic Focus Areas Based on Regulatory Trends to 2030

1. **Patient Engagement** – promote patient involvement in Asia-Pacific health systems, e.g. Coalition to Advance Patient Engagement (CAPE)
2. **Digital Health** – define scope, domains and relevant regulatory frameworks
3. **Innovative Therapies** – enhance coordinated regulatory frameworks and capacity
4. **MedTech** – enhance regulatory frameworks and capacity
5. **Innovative Clinical Trials** – clarify regulatory positions, e.g. RWE, digital endpoints, interoperability, security
6. **Outbreak Vaccines, Therapeutics & Diagnostics** – promote regulatory agility & robust decision frameworks

Digital Health

(as an Example)

- Digital technologies are essential component and enabler of sustainable health systems and universal health coverage
- WHO promotes Infocomm Technology in health development through research, guidelines, capacity, policy and advocacy support
- Wide scope and issues, e.g. AI, Mobile Health, Big Data Analytics, RWE, Blockchain, Cybersecurity, Interoperability, Software as Medical Device, Electronic Health Records…….
- All have regulatory implications and challenges

Due to multi-stakeholder interest and lack of legacy regulatory frameworks, opportunity exists for coordinated solutions

7 Pre-requisites for Regulatory Agility

1. **Trust -** fundamental for adoption of *innovative therapies (e.g. vaccines)*, assuring *patient data confidentiality*, and advancing *personalised digital health & telemonitoring solutions*

2. **Transparency** – data capture and use

3. **Training** – level up regulatory capabilities for therapeutic and policy innovations

4. **Testing** – regulatory sandboxes, e.g. telemedicine

5. **Trans-national bodies** – for coordination, convergence and information exchange, e.g. WHO, ICMRA, APEC

6. **Transfer** - cross-jurisdictional frameworks to promote interoperability and data exchange

7. **Timeliness**

Advancing Regulatory Agility & Innovation

To advance regulatory agility and innovation over the next decade:

- **Institute Regulatory Enablers** – risk-based regulation, regulatory cooperation, regulatory stakeholder platforms, capacity building
- **Benchmark** other economies' regulatory frameworks but understand context, e.g. *APAC Personalised Health Index*
  https://futureproofinghealthcare.com/asia-pacific-personalised-health-index
- **Apply COVID-19 Lessons for Agile Regulation** - risk-based, cooperation, sound scientific evidence
- **Commit to Collaborate**

Thank You

Webinar Series: The Role of Vaccination in Maintaining Health and the Economy During Pandemics

Building the Right Regulatory Environment for COVID-19 Response & Long-Term Health Resilience

8 July 2021 21:00 (Washington, DC)

9 July 2021 9:00 (Singapore)

13:00 (Auckland)

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Health Canada

Health Canada Santé Canada

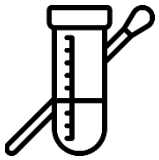
Canada

Health Canada's Regulatory Response to COVID-19: Expediting Access to Critical Health Products

YOUR HEALTH AND SAFETY... OUR PRIORITY.

Health Canada mobilized quickly to help limit the spread of COVID-19 in communities and support the healthcare system

Central to the public health response was an **urgent need for medical supplies and health products** to test for, treat and prevent COVID-19, such as:



Testing Devices And Supplies

Personal Protective Equipment for Medical Purposes

Hand Sanitizers and Disinfectants

Investigational Drugs and Vaccines

Our agile regulatory response is facilitating expedited access to needed products without compromising safety

Our approach:

Regulatory and administrative agilities
to expedite access to safe and effective COVID-19 health products

Outreach and engagement
to provide guidance, advice, and priority information to businesses eager to mobilize products

International collaboration
to advance global solutions and ensure alignment with key regulatory partners

International Collaboration

Working with our international partners on a coordinated and well-aligned approach to respond to the COVID-19 pandemic:

- This involves discussing, collaborating and leveraging resources on issues related to:
  - clinical trials and investigational testing
  - drug and medical device market authorizations
  - health product risk assessments
  - potential drug and medical device shortages

ICMRA: Health Canada is playing a leadership role in helping align policy approaches and regulatory agility

- Health Canada co-chairs, with the UK Medicines and Healthcare products Regulatory Agency (MHRA), the ICMRA COVID-19 working group. This group actions and provides recommendations on priority topics and issues raised during the ICMRA COVID-19 policy discussions by heads of agencies.
- Health Canada also co-chairs the ICMRA COVID-19 committee for global regulatory cooperation on real-world evidence and observational research with the European Medicines Agency (EMA).
- We also actively engage in the proceedings of the ICMRA international regulatory workshops on the development of COVID-19 vaccines and treatments as well as vaccine vigilance.

International Regulatory Initiatives

Health Canada leveraged existing partnerships during COVID-19, including:

- International Coalition for Medicines Regulatory Authorities (ICMRA) as an executive committee member and plays a leadership role in aligning policy approaches and regulatory agility
- World Health Organization's research and development (R&D) blueprint vaccines plan to develop a COVID-19 vaccine
- Pan American Health Organization as a member of its COVID-19 task group
- ACCESS Consortium: Points to consider for strain changes in authorised COVID-19 vaccines in an ongoing SARS-CoV2 pandemic

Important temporary measures are providing agility in a time of crisis

Health Canada's COVID-19 Interim Orders help to ensure:

such as testing kits and medical supplies stay in supply.

for needed drugs, medical devices, and foods for a special dietary purpose.

for promising therapies are conducted in Canada.

are quickly and safely made available.

caused directly or indirectly by COVID-19 are prevented.

We are responding to industry needs during the pandemic

Examples of additional administrative agilities and guidance provided to support industry in meeting the urgent need for health products:

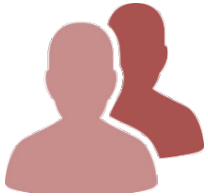
Interim policy measures to…

- Prioritize the review of all COVID-19 related health product applications
- Support the sale and distribution of sanitizers and disinfectants
- Promote electronic and virtual processes where possible, such as conducting remote inspections

Guidance on…

- Acceptable process adaptations for clinical trial sponsors
- Developing serological antibody tests
- Importing or selling COVID-19 supplies, such as medical gowns, gloves, ventilators, and respirators
- Manufacturing hand sanitizers

Anticipated benefits



Patients

Would see timely access to promising new innovative products that can positively impact their health.

Health Care System (including PTs)

Would see efficient access to promising advanced therapeutics while remaining confident that the health and safety of Canadians are being protected.

International harmonization

Would be facilitated, making Canada a market that is aligned with other major jurisdictions such as like the US and EU.

Health Product Innovators

Would see an opportunity to bring innovative products to market which current regulations cannot accommodate, and Canada as a more competitive space to do business.

Our swift regulatory actions have enabled access to thousands of products for communities and healthcare professionals

Since March 2020, Health Canada approved:

4,875	**702**	**72**
Hand sanitizers	Medical devices	Testing devices
103	**2**	**5**
Clinical trials	Drug treatments	Vaccines

COVID-19 Food and Drug Regulation objectives

Allow continued and timely access to safe and effective COVID-19 drugs for Canadians by normalizing the review, authorization and oversight of COVID-19 drugs under the *Food and Drug Regulations*

1) Enable the sale and advertising of COVID-19 drugs after the Interim Order ceases to have effect, and once authorized under the Regulations

2) Enable both COVID-19 drugs that were authorized under the ISAD Interim Order and new COVID-19 drugs to seek authorization under the Regulations with similar flexibilities as had been provided under the Interim Order

3) Permit continuity of the post-market regulatory obligations after expiration of the ISAD Interim Order

4) Continue to allow the early importation (pre-positioning) of a promising COVID-19 drug, for which a Government of Canada contract for its procurement is in place, prior to that drug receiving market authorization in Canada

5) Continue a flexible framework for Drug Establishment Licences (DELs) that authorizes regulated activities in respect of COVID-19 drugs

Canada Gazette Publication

On March 31, 2021, transitional provisions to the Food and Drug Regulations were published in the Canada Gazette, Part II and the accompanying Guidance on amendments to the Food and Drug Regulations for drugs for use in relation to COVID-19.

Certain provisions of the amendments came into force on March 18, 2021, while others will come into force on the date that the IO expires on September 16th.

The Regulatory Impact Analysis Statement and published guidance document that contains additional information for drug sponsors.

Authorization of COVID-19 drugs under the Regulations with similar flexibilities as under the Interim Order

Notice of Compliance (NOC) and Terms and Conditions

- Continue to accept **rolling submissions** by accepting new evidence as it becomes available during the review period, supported by a **plan for information** that is filed by the sponsor at time of initial submission
  - Vaccines and novel treatments will likely gain market access through a rolling submission, potentially with international collaboration

- Maintain regulatory **flexibilities on data requirements** and the ability to impose or amend terms and conditions on the DIN (drug identification number)
  - Examples of terms and conditions can include a risk management plan and/or pharmacovigilance and risk minimization measures and/or Phase IV trials

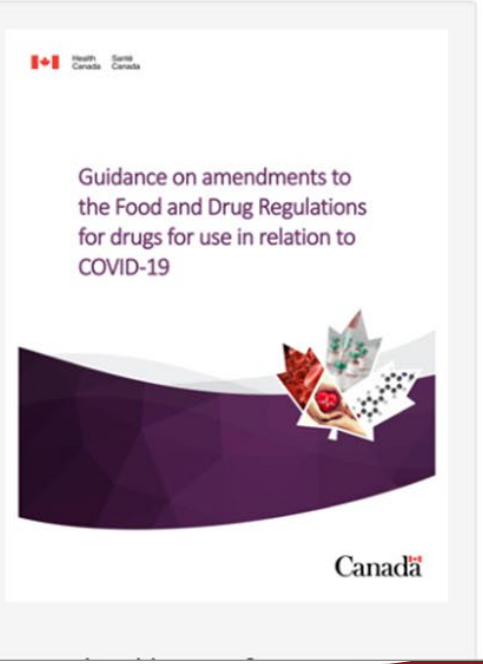
- Maintain the flexibility related to no requirement for brand name assessment and label mock-ups

Guidance on amendments to the Food and Drug Regulations for drugs for use in relation to COVID-19: Overview

Overview	Preparing a submission	Drug establishment licences and good manufacturing practices
Intellectual property	Post-market requirements	Pre-positioning of COVID-19 drugs
Submission scenarios, reference documents and key contacts		

This guidance applies to sponsors of new COVID-19 drug submissions as well as sponsors seeking a Notice of Compliance (NOC) for COVID-19 drugs that received temporary authorization under the Interim order respecting the importation, sale and advertising of drugs for use in relation to COVID-19 (ISADIO). It also applies to new COVID-19 drug establishment licences under the *Food and Drug Regulations*.

This document will help manufacturers prepare a submission for a Notice of Compliance for a COVID-19 drug under the *Regulations.* It also outlines the process for meeting the post-market regulatory requirements.



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Guidance for market authorization requirements for COVID-19 vaccines: Overview

Overview	Rolling submissions, non-clinical and clinical requirements	Quality, manufacturing and lot release requirements
Labelling and post-market requirements	Requirements for vaccines to address SARS-CoV-2 variants	Review process, communications and transparency

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Background

COVID-19 is the infectious disease caused by the most recently discovered coronavirus, SARS-CoV-2. This new virus and disease were unknown before the outbreak began in December 2019 and have since spread around the world.

Requirements for vaccines to address SARS-CoV-2 variants

- Variant strains of SARS-CoV-2 are emerging that may affect the level of protection provided by currently authorized COVID-19 vaccines. As a result, manufacturers are adapting authorized COVID-19 vaccines to provide protection against infection and disease caused by virus variants.

The submission type for a variant COVID-19 vaccine will depend on the specific vaccine, taking into account:

  - the platform used
  - whether the proposed variant vaccine is a version of an already authorized COVID-19 vaccine
  - the extent of change from the previously authorized version

- Vaccine manufacturers seeking to obtain market authorization for a variant COVID-19 vaccine should consult with us to discuss their regulatory filing plans.

Quality, non-clinical, clinical and post-market requirements

- Health Canada have collaborated with the Access Consortium to develop a guidance document to support regulatory alignment on the minimal requirements for variant COVID-19 vaccine authorization.

- Sponsors should refer to the Access Consortium points to consider for strain changes in authorized COVID-19 vaccines in an ongoing SARS-CoV-2 pandemic for specific guidance on the quality, non-clinical, clinical and post-market information required to support authorization of a variant COVID-19 vaccine.

- The Access Consortium guidance is closely aligned with international regulators, including guidance released by the European Medicines Agency (EMA) and US FDA.

- An updated Risk Management Plan (RMP), including a Canadian-specific addendum, should be submitted to ensure that adverse events can be appropriately captured for both the variant and prototype vaccine versions. The safety specification, pharmacovigilance plan and risk minimization plan should be updated for both variant and prototype vaccine versions. Traceability of the brand and batch, and distinguishing suspected AEFIs with new and old formulations should be a key focus of the updated RMP.

COVID-19 required an unprecedented regulatory response to make sure Canadians had access to needed health products

Our approach:

Proactive engagement and collaboration

with stakeholders and health system partners to provide timely advice and guidance, as well as heightened collaboration with international regulators to ensure alignment.

Emergency regulatory pathways and measures

to prioritize and expedite the review and licensing processes, including use of agile regulatory tools and approaches (e.g., T&Cs, rolling reviews).

Enhanced post-market surveillance

of safety and effectiveness, including life-cycle oversight of approved products, adjusting T&Cs based on emerging information, real-time response to and information sharing of safety signals.

Increased communications and transparency

including release of clinical data, to support high demand for information and data from broad range of stakeholders on regulatory requirements and decisions.

5 vaccines

2 treatments

600+ medical devices

4500+ sanitizers & disinfectants

Questions and comments