ThermoFisher SCIENTIFIC

Association of Medical Diagnostic Manufacturers

Global COVID-19 Submission Pathways

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Sr. Director, Global Regulatory Affairs, Clinical & Compliance
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Introducing

Kelli L. Tanzella, Ph.D.

Sr. Director Global Regulatory Affairs Clinical & Compliance

Thermo Fisher Scientific

- 25+ years in regulatory and quality in pharmaceutical and medical device industry
- 19 years at Thermo Fisher Scientific
- Areas of expertise include
  - Pre-market clearance and approvals relevant to both the pharmaceutical and medical device (IVD) industries.
  - Extensive experience in the development and implementation of regulatory strategies to enable business opportunities in NGS, CDx and Cell Therapy solutions.

Agenda

1. Global Regulatory Landscape
2. COVID-19 Regulatory Pathways around the globe
3. Lessons Learned
4. Q&A

Global Regulatory Landscape

Global Regulatory Landscape

- COVID 19 has brought many disruptions including delays in R&D, manufacturing, supply chain, and almost all the components essential to development that led to regulatory decisions and patient access to innovative devices and drugs.

- Interactions with regulatory agencies have become unpredictable with longer wait times to hear back from agencies or review teams that are critical to move along the development process.

- The regulatory landscape has also shifted with acceleration in many areas.
  - Regulatory bodies have released guidance in an effort to allow clinical trials to continue and to get COVID studies up and running in record. This has enabled the fast pace development of vaccines.
  - Additionally, close collaboration has become the norm among academia, industry and government agencies with commitment from all stake holders to move past the pandemic.

Changing Regulatory Landscape

Regulatory Agencies adapting quickly to the evolving COVID-19 environment by enacting temporary Policies and Guidelines to increase flexibility and proactively engage diagnostic and therapeutic manufacturers.

- Many Guidance and Policies are being enacted without a public comment period.
- Regulatory flexibility for the approval for of PPEs and stockpiling of drugs from domestic and foreign sources is underway.
- Regulatory oversight flexibility to safeguard product and personnel is in place, while continuing to provide submission assessments and remote auditing capability

What's the impact?

- Validated COVID-19 diagnostic tests are being made available for commercial distribution prior to formal regulatory reviews.
- Health authorities have taken measures to increase the availability of personal protective equipment (PPEs) and critical care equipment.
- Specific requirements for updates to approved products are being temporarily waived and permissions have been provided to simplify regulatory processes to promote market access.

COVID-19 Tests Test Types

Types of diagnostic tests

Antigen diagnostic tests

- Designed for the rapid detection of proteins from the virus that causes COVID-19.
- Antigen tests quickly detect fragments of proteins found on or within the virus by testing samples collected from the nasal cavity using swabs. One of the main advantages of an antigen test is the speed of the test, which can provide results in minutes. However, antigen tests may not detect all active infections, as they do not work the same way as a PCR test.

Molecular diagnostic (PCR) testing

- Detects genetic material from the virus and can help diagnose an active COVID-19 infection.
- Generally, authorized for qualitative detection of nucleic acid from SARS-CoV-2 in specific upper and lower respiratory specimens from individuals suspected of COVID-19 by their healthcare provider.

Serological tests

- Identify individuals who have developed an adaptive immune response to the virus, indicating recent or prior infection, by detecting antibodies to SARS-CoV-2 in human blood specimens.
- Serological (antibody) tests are generally authorized for the qualitative detection of antibodies to SARS-CoV-2 in blood, serum, and/or plasma, and are intended for use as an aid in identifying individuals with an adaptive immune response to SARS-CoV-2, indicating recent or prior infection.

Definitions

- **Point of care test (also known as near patient test):** an in vitro diagnostic medical device that is not intended for self-testing but is intended to perform testing outside a laboratory environment, generally near to, or at the side of, the patient by a health professional
- **Self-test:** an in vitro diagnostic medical device intended to be used by a layperson
- **Analytical sensitivity:** sensitivity of a measurement procedure quotient of the change in a measurement indication and the corresponding change in a value of a quantity being measured
- **Analytical specificity:** selectivity of a measurement procedure capability of a measuring system, using a specified measurement procedure, to provide measurement results for one or more measurands which do not depend on each other nor on any other quantity in the system undergoing measurement
- **Clinical (Diagnostic) Sensitivity:** ability of an IVD examination procedure to identify the presence of a target marker associated with a particular disease or condition
- **Clinical (Diagnostic) Specificity:** ability of an IVD examination procedure to recognize the absence of a target marker associated with a particular disease or condition (the above definitions of performance characteristics taken from BS EN ISO 18113- 1:2011, In vitro diagnostic medical devices — Information supplied by the manufacturer (labelling): Terms, definitions and general requirements)
- **Positive Percent Agreement:** calculated in the same way as Clinical (Diagnostic) Sensitivity, but indicate that a non-reference standard was used
- **Negative Percent Agreement:** calculated in the same way as Clinical (Diagnostic) Specificity, but indicate that a non-reference standard was used

COVID-19 Pathways around the globe

Global commercialization planning

In planning for global launch of COVID-19 diagnostics its important to develop a detailed commercial strategy and understand each country's regulatory pathway.

- Does the country have an emergency use pathway? If not, what is the pathway, i.e., traditional IVD pathway, CE IVD (self-declared)?
- Will the regulatory agency accept another countries emergency use submission, i.e., U.S. EUA or do they accept CE IVD (self-declared)?
- Are import permits required?
- Are local clinical studies required?
- Can authorization or approval be obtained prior to completing all testing requirements?
- What's the duration for the authorization?
- Reimbursement implications?

United States

Emergency Use Authorization Pathway

- Under the EUA process FDA can authorize the emergency use of unapproved medical products within weeks rather than months to years.
- FDA evaluates requests for authorization using available evidence and criteria, while balancing the risks and benefits of the product.

- Products that meet the EUA process require significantly less data than otherwise would be required for approval, clearance, or licensing by the FDA.

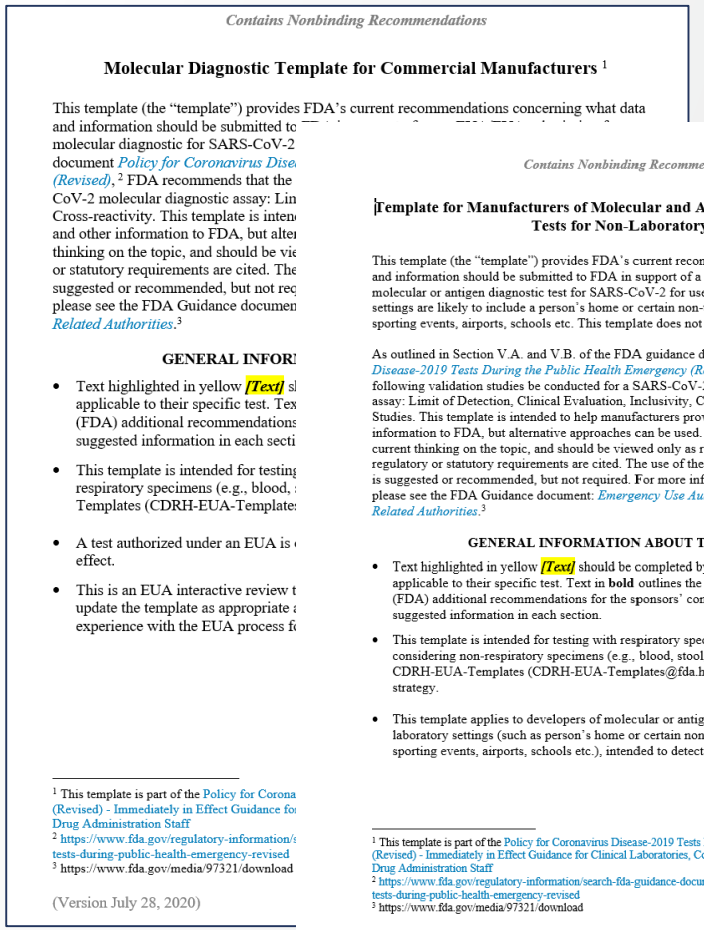
- EUAs are in effect until the emergency declaration ends but can be revised or revoked as the agency re-evaluates the needs during the emergency, or as products meet the criteria to become approved, cleared, or licensed by the FDA.

United States

Emergency Use Authorization Pathway

EUA Submission – templates are available on the FDA website

- The EUA request should include a well-organized summary of available scientific evidence related to the product's safety and effectiveness, risks (including the adverse event profile) and benefits, and any available, approved alternatives to the product.
- The type and amount of data needed to support the EUA may vary depending on the nature of the declared emergency or threat of emergency and the nature of the candidate product.
- FDA may request additional data and information. This will be on a case-by-case basis to ensure statutory criteria for issuance of an EUA are met.



Contains Nonbinding Recommendations

Molecular Diagnostic Template for Commercial Manufacturers [1]

This template (the "template") provides FDA's current recommendations concerning what data and information should be submitted to
molecular diagnostic for SARS-CoV-2
document *Policy for Coronavirus Dise*
(Revised), [2] FDA recommends that the
CoV-2 molecular diagnostic assay: Lin
Cross-reactivity. This template is inten
and other information to FDA, but alte
thinking on the topic, and should be vie
or statutory requirements are cited. The
suggested or recommended, but not rec
please see the FDA Guidance documen
Related Authorities.[3]

GENERAL INFOR

- Text highlighted in yellow ***[Text]*** s
applicable to their specific test. Tex
(FDA) additional recommendations
suggested information in each secti
- This template is intended for testing
respiratory specimens (e.g., blood,
Templates (CDRH-EUA-Templates
- A test authorized under an EUA is
effect.
- This is an EUA interactive review t
update the template as appropriate
experience with the EUA process f

[1] This template is part of the Policy for Corona
(Revised) - Immediately in Effect Guidance fo
Drug Administration Staff
[2] https://www.fda.gov/regulatory-information/
tests-during-public-health-emergency-revised
[3] https://www.fda.gov/media/97321/download

(Version July 28, 2020)

Contains Nonbinding Recommendations

Template for Manufacturers of Molecular and Antigen Diagnostic COVID-19 Tests for Non-Laboratory Use [1]

This template (the "template") provides FDA's current recommendations concerning what data and information should be submitted to FDA in support of a pre-EUA/EUA submission for a molecular or antigen diagnostic test for SARS-CoV-2 for use in a non-laboratory setting. Such settings are likely to include a person's home or certain non-traditional sites such as offices, sporting events, airports, schools etc. This template does not apply to home collection kits.

As outlined in Section V.A. and V.B. of the FDA guidance document *Policy for Coronavirus Disease-2019 Tests During the Public Health Emergency (Revised)*, [2] FDA recommends that the following validation studies be conducted for a SARS-CoV-2 molecular or antigen diagnostic assay: Limit of Detection, Clinical Evaluation, Inclusivity, Cross-reactivity, Usability and Flex Studies. This template is intended to help manufacturers provide these validation data and other information to FDA, but alternative approaches can be used. This template reflects FDA's current thinking on the topic, and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* means that something is suggested or recommended, but not required. For more information about EUAs in general, please see the FDA Guidance document: *Emergency Use Authorization of Medical Products and Related Authorities*.[3]

GENERAL INFORMATION ABOUT THIS TEMPLATE

- Text highlighted in yellow ***[Text]*** should be completed by the test manufacturer (sponsor) as applicable to their specific test. Text in **bold** outlines the Food and Drug Administration's (FDA) additional recommendations for the sponsors' consideration when completing the suggested information in each section.
- This template is intended for testing with respiratory specimens or saliva; if you are considering non-respiratory specimens (e.g., blood, stool, etc.), please contact FDA at CDRH-EUA-Templates (CDRH-EUA-Templates@fda.hhs.gov) to discuss your validation strategy.
- This template applies to developers of molecular or antigen diagnostic tests, for use in non-laboratory settings (such as person's home or certain non-traditional sites such as offices, sporting events, airports, schools etc.), intended to detect SARS-CoV-2 from individuals.

[1] This template is part of the Policy for Coronavirus Disease-2019 Tests During the Public Health Emergency (Revised) - Immediately in Effect Guidance for Clinical Laboratories, Commercial Manufacturers, and Food and Drug Administration Staff
[2] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/policy-coronavirus-disease-2019-tests-during-public-health-emergency-revised
[3] https://www.fda.gov/media/97321/download

(Version July 29, 2020) 1

Emergency Use Authorization of Medical Products and Related Authorities: Guidance for Industry and Other Stakeholder (Office of Counterterrorism and Emerging Threats) https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization
https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations

United States

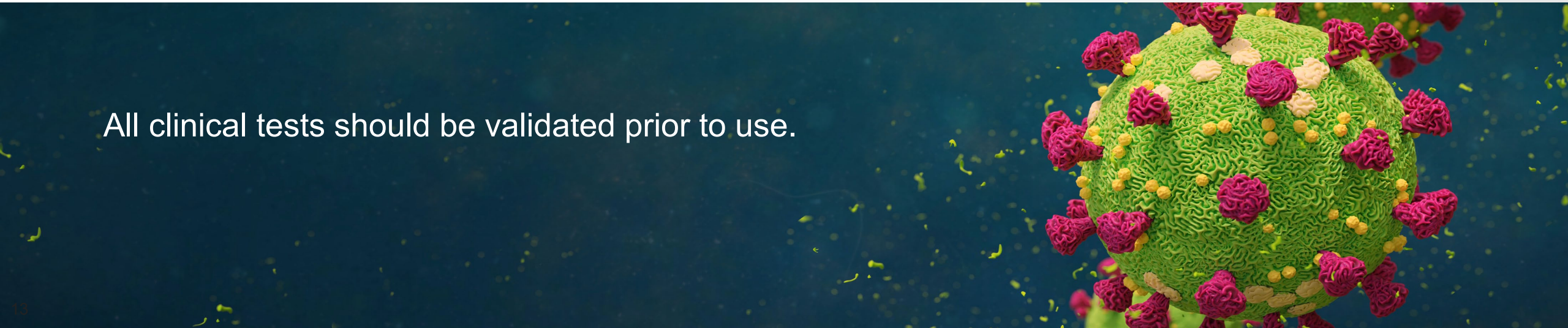
EUA contents

- Description of the product
- Intended use
- Where, when, and how the product is anticipated to be used; and/or the population(s) for which the product may be used
- Product FDA approval status

- Identification of any approved alternative products
- Adequacy for the proposed use
- Unmet needs the EUA would address
- Efficacy and safety information
- Data from clinical and nonclinical studies(*in vivo/in vitro)*
- Adverse event monitoring requirements

- Analysis of the risks/benefits
- Information on the chemistry, manufacturing, and controls of your product
- Fact sheet providing information on dosing, contraindications, warnings, and adverse events. For distribution to healthcare workers, clinicians and patients

All clinical tests should be validated prior to use.



Canada Emergency Use

Medical Devices that are Class II, III or IV

- HC outlined an Interim Order (IO) for the importation and sale of medical devices for use in relation to COVID-19.
- The IO was established in an effort to get unlicensed products into Canada that are approved in other jurisdictions. The IO allows HC to issue expanded indications for use to a device that either has been approved through this IO or granted a medical device license (MDL).
- The authorization is only valid as long as the IO is in effect. The IO is set to expire Fall 2021; but may be renewed based on the ongoing public health need. HC has proposed transition provisions for devices approved under IO for long-term regulatory approval in Canada.
- Further information will be provided by HC later in 2021.

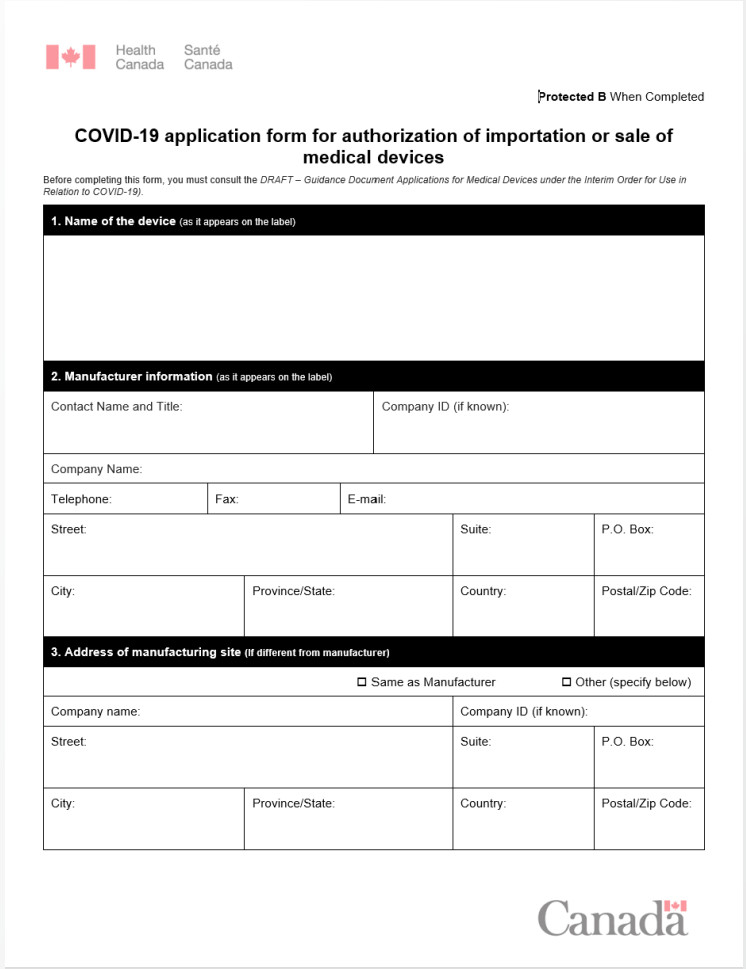
Interim Order No. 1 expired in March 2021 and has been superseded by Interim Order No. 2.

Canada – Interim Order Pathway

Interim Order

- A MDSAP certificate is not required; manufacturers are required to share information to demonstrate their products are of the appropriate quality.
- Submit an IO application electronically to hc.devicelicensing-homologationinstruments.sc@canada.ca; include: (“COVID-19 Device Application” in the subject line).
- Include device details of safety and effectiveness information.
- Include an Attestation to the availability of documented procedures for certain activities: Distribution Records, Complaint Handling, Incident Reporting and Recalls.
- HC is waiving application fees for COVID-19 medical devices subject to the IO.

Note: If a foreign jurisdiction waives all pre-market submission and evaluation requirements, this would not be considered a foreign regulatory approval for the purposes of the IO and therefore not eligible for IO.



Health Canada Santé Canada

Protected B When Completed

COVID-19 application form for authorization of importation or sale of medical devices

Before completing this form, you must consult the *DRAFT – Guidance Document Applications for Medical Devices under the Interim Order for Use in Relation to COVID-19).*

1. Name of the device (as it appears on the label)

2. Manufacturer information (as it appears on the label)

Contact Name and Title:		Company ID (if known):	
Company Name:			
Telephone:	Fax:	E-mail:	
Street:		Suite:	P.O. Box:
City:	Province/State:	Country:	Postal/Zip Code:

3. Address of manufacturing site (If different from manufacturer)

☐ Same as Manufacturer ☐ Other (specify below)

Company name:		Company ID (if known):	
Street:		Suite:	P.O. Box:
City:	Province/State:	Country:	Postal/Zip Code:

Canada

- Classification Guidance for COVID-19 Medical Devices
- COVID-19 Medical Devices - Information for manufacturers, distributors and health professionals
- New Transition Regulations for the IO Respecting the Importation and Sale of Medical Devices (COVID-19): Notice to Stakeholders
- https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/announcements/interim-order-importation-sale-medical-devices-covid-19/guidance-medical-device-applications.html

United Kingdom

MHRA focus

- CE marking under IVDD for COVID-19 assays as self declared under Article 9, Annex III, conformity assessment procedure, are recognized by MHRA.
  - Changes post-Brexit to comply with UKAC are required for implementation by 01Jan2022 for manufactures outside of the UK.
- Additionally, Target Product Profiles (TPPs), which are similar to product standards, have been developed by the MHRA and Department of Health and Social Care (DHSC). The aim is to help manufactures design and deliver COVID-19 tests that might be useful in contributing to the UK testing strategy.
- Manufacturers who think they meet the requirements of a specific TPP, may submit a proposal to DHSC.
- DHSC has a set process for the evaluation of diagnostic tests for COVID-19. If the test fulfils the DHSC evaluation process but does not yet have a CE mark, manufacturers can apply for a derogation from such requirement, which is considered by the MHRA.

https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/895745/TPP_Point_of_Care_SARS-CoV-2_Detection_Tests.pdf
https://www.gov.uk/government/collections/new-guidance-and-information-for-industry-from-the-mhra
https://www.gov.uk/government/publications/how-tests-and-testing-kits-for-coronavirus-covid-19-work/for-industry-and-manufactures-covid-19-tests-and-testing-kits
https://www.gov.uk/government/publications/how-tests-and-testing-kits-for-coronavirus-covid-19-work/for-industry-and-manufactures-covid-19-tests-and-testing-kits

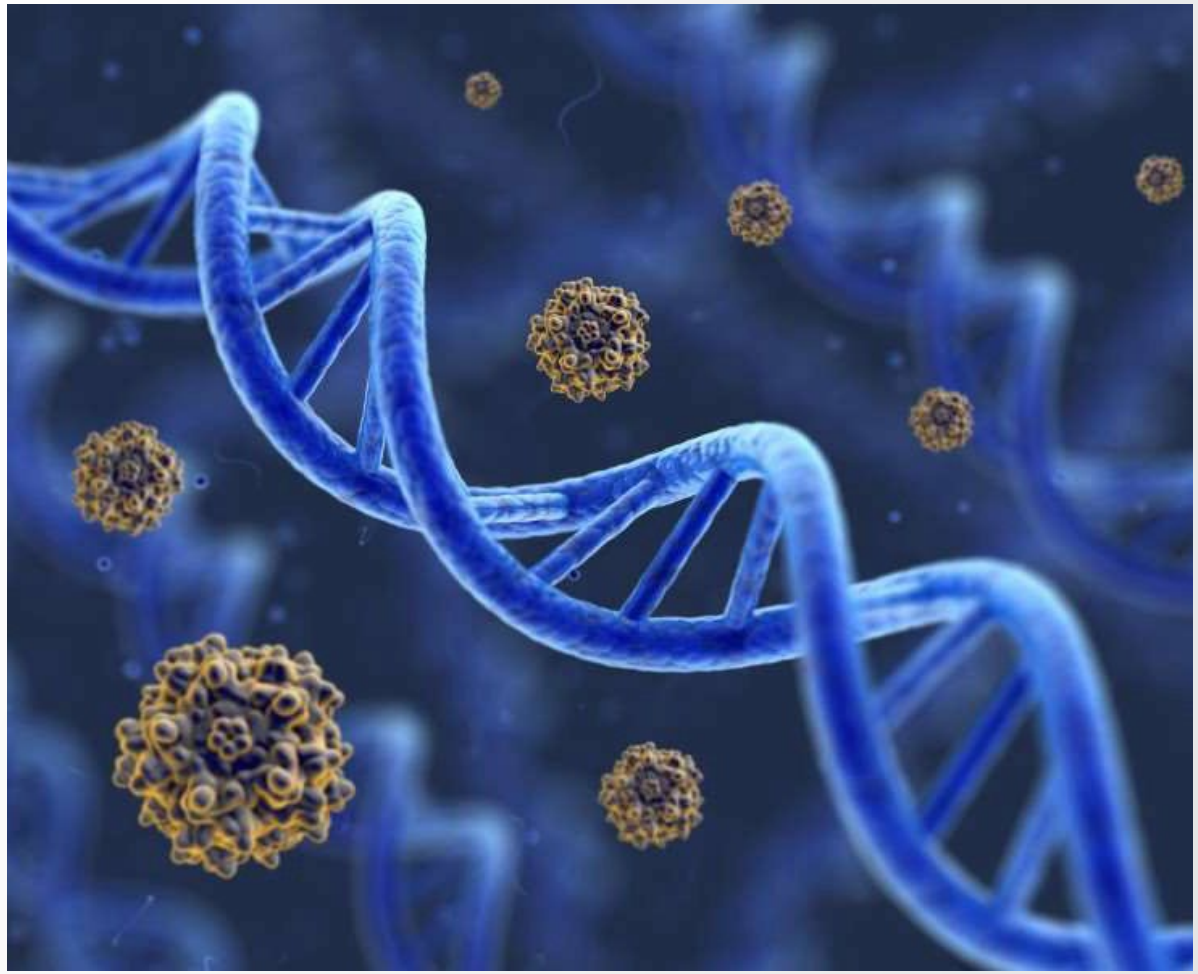
MHRA

Derogation Process

Derogation process includes sending an application to the MHRA with specific information including

- Instructions for use
- Clinical evidence base
- Details of other regulatory approvals
- Confirmation of completion of DHSC evaluation process
- Details of the product
- Expected time to gain CE certification
- And more…

Evidence that the device performs as intended is paramount for the derogation process



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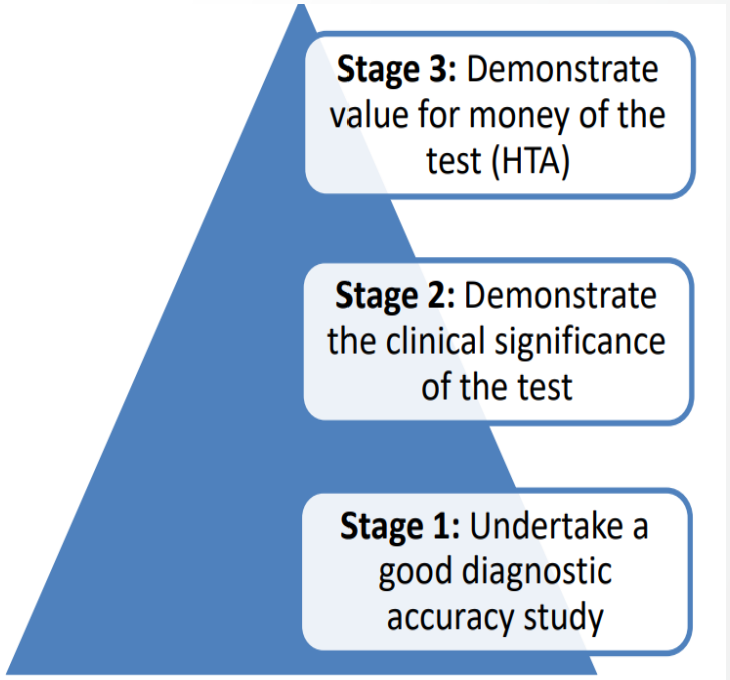
UK – NICE and MHRA

National Institute for Health Care and Excellence (NICE) and MHRA

- NICE developed an evidence-based standards framework for SARS-CoV-2 and anti-SARS-CoV-2 antibody diagnostic tests.
- It's a three-stage approach to collecting data and evidence in the short and long term, while tests are being quickly developed and validated.
- The framework aligns with the UK government's 5-pillar testing strategy
  - Pillar 1 & 2 including viral detection tests for current infection
  - Pillar 3 & 4 antibody tests for previous infection
- The framework assumes tests' analytical performance is already established, and developers are complying with ISO 13485 (manufacturers) and ISO 15198 or 17025 (laboratories)



- Framework applies to:
  - Diagnostic test manufacturers
  - Laboratories developing tests
  - Clinicians assessing tests
  - Clinical researchers collecting data on tests
  - Research funders and people who advise researchers on study design
  - Purchasers and other decision makers.

This process must be followed if a laboratory plans to be part of the UK governments testing strategy

European Union

- In April 2020, the European Commission published guidance indicating manufacturers must comply with the relevant provisions of the IVD Directive 98/79.
  - Technical files must be prepared that explicitly show the test is safe and performs as intended, by demonstrating compliance with the requirements in Annex I of the Directive.
  - Tests can be intended by the manufacturer for use by health professionals or by lay users (self-tests). For COVID-19 tests intended for use by health professionals, the CE-mark may be affixed following a declaration by the manufacturer that the requirements of the Directive are satisfied (declaration of conformity). Devices intended for self-testing require the involvement of a notified body which must carry out additional verification of the technical documentation.
  - CE marking under the IVD Directive 98/79 continues to be acceptable within the European Economic Area. Transition to the IVD Regulation 2017/745 is still slated for May 2022.

Under IVDR, COVID-19 test kits will be classified under Class D and require lot release testing.

Communication from the Commission Guidelines on COVID-19 in vitro diagnostics test and their performance (2020/C 122 I/01

European Union

IVD-Directive vs. IVD-Regulation Product classification

IVDD Classifications	
Annex II List A	Highest risk, blood group typing and HIV/Hepatitis testing.
Annex II List B	Medium risk: minor blood groups (Kidd,Duffy), HLA typing, sexual diseases, trisomy 21, PSA, blood sugar analysis.
Self certified	All other devices
No notified body review for self-certified devices needed (greater than 85% of IVDs on the market prior to IVDR).	

IVDR classification (based on 7 rules)	
Class A	low patient risk/ no public health risk (instruments, culture media, etc.)
Class B	medium patient risk / no public health risk
Class C	high patient risk / no or moderate public health risk (genetic tests or CDx)
Class D	high patient risk / high public health risk
All except Class A will require notified body involvement (~85%)	

COVID-19 devices are considered **Class D** under IVDR due to high public health risk

IVDD and IVDR Requirements Comparison

Item		Required for IVDD	Required for IVDR
Analytical studies			
	LoD	Yes	Yes
	Accuracy/method comparison	Yes	Yes
	Precision (Reproducibility/repeatability)	Yes	Yes
	LoD	Yes	Yes
	Analytical Reactivity (Inclusivity)	Yes	Yes
	Analytical Specificity (Exclusivity, cross reactivity, interference)	Yes	Yes
	Carry-Over/X-Contamination	Yes	Yes
	Specimen Storage/Shipping	Yes	Yes
	Clinical Evaluation	Yes	Yes
	Clinical Validation	Yes	Yes
	Stability (Shelf-Life, in use, shipping)	Yes	Yes
Other requirements			
	Clinical validation	Yes	Yes
	Manufacturing process overview	Yes	Yes
	Software validations	Yes	Yes
	EMC and safety testing	Yes	Yes
	Labeling (user guides, product labels)	Yes	Yes
	Translated user guides	Yes	Yes
	Performance evaluation plan and report	No	Yes
	Scientific validity report	No	Yes
	Analytical performance evaluation plan and report	No	Yes
	Clinical performance evaluation plan and report	No	Yes
	Post market performance follow up plan	No	Yes
	Post market surveillance plan	Yes	Yes

CE IVD recognition within EEA and Reimbursement

Countries that recognize the IVD Directive

- European Economic Area includes:
  - Austria, Belgium, Bulgaria, Croatia, Republic of Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, and Sweden.
- Part of EEA but not EU
  - Iceland, Liechtenstein, and Norway

- Following Competent Authority notification, additional documents are required to be submitted for reimbursement in the following countries:
  - Germany
  - Italy
  - Switzerland
  - Belgium
  - France
  - Netherlands
  - England
  - Denmark
  - Norway
  - Sweden
  - Austria
  - Spain
  - Portugal
  - Ireland
  - Poland

Countries that recognize CE IVD under IVD Directive

Asia Pacific	Latin America	Middle East
• Malaysia • Thailand • India • Vietnam • Indonesia	• Brazil • Mexico • Ecuador • Argentina • Colombia • Costa Rica • Ecuador • Bolivia • Panama • Guatemala • Chile • Guiana	• Dubai • Israel • Morocco • Saudi Arabia • Turkey • Bahrain • Kuwait • Jordan • Lebanon • Oman • Pakistan • Qatar • UAE

CE Marked product is accepted with additional documentation. If using local distributors or local company offices Power of Attorney is required plus Free Sale Certificates issued by the Competent Authority,

Brazil

Emergency Use Pathway

- Emergency Use has been re-opened.
- ANVISA has made special allowances for products used to combat the pandemic, included under the additional regulations for devices related to COVID-19 or SARS-CoV-2.
- Registration via the special route must follow RDC 03/2010.

Due to the international COVID-19 crisis, products on the WHO for COVID-19 testing are exempt from registration requirements, and importation is allowed for health services and health public or private entities. The importer must:

- Meet the regulatory rules to market the devices,
- Maintain traceability records,
- Have in place post-market procedures,
- Provide labels and IFU in Portuguese, and
- Comply with RDC 483/2021 and other regulations.

RDC 03/2010: describes the rules for registration evaluation of medical devices in emergency routes.

Brazil

Emergency Pathway

- IVDs that detect COVID-19 need to follow RDC 36/2015. If performance studies are not available, justification must be provided that allows the evaluation of the reliability of results and effectiveness of the product.
- If stability data is available for similar products, and all other criteria are met according to RDC 36/2015, the shelf-life of the product will be 6 months (except in situations where comparative studies indicate a shorter period). A shelf-life longer than 6 months will be allowed when supported by real-time data.
- The registrations (Class III and IV) approved by RDC 348/2020 are valid for 1 year. During this period, an application must be submitted through the normal route to maintain the products on the market.
- Labels must include “Aprovado para uso Emergencial” (Approved for emergency use).
- ANVISA RDC 377/2020 allows COVID-19 rapid tests (immunochromatographic assays) to be sold to drugstores. The tests included in scope are to evaluate the presence of coronavirus antibodies or antigens, without the purpose of confirmatory diagnosis, and must be registered with ANVISA. The test must be performed by a pharmacist. All product complaints must be notified to ANVISA within 5 days.
- The importer must send at least 100 units of diagnostic kits of each batch, within a maximum period of 5 days starting from the date of customs clearance, for analysis by the Institute National Quality Control – INCQS.
- For all IVDs that detect COVID-19 that are not registered with ANVISA, the importer (healthcare institution for an example) must prove and ensure the sensitivity and specificity of the IVD.

Mexico

Emergency Pathway

- Following recommendations of the WHO, the Ministry of Health established the Institute of Diagnostic and Epidemiological Reference (InDRE) to evaluate IVD tests for detection of COVID-19.
- InDRE can grant a technical approval letter, which importers can deliver to COFEPRIS to obtain an immediate marketing authorization.
- Dossier will then be evaluated and, if considered compliant, the Ministry of Health will release a valid 5-year health registration.
- PCR tests:
  - InDRE developed a special testing protocol for each device, for sensitivity, specificity, and repeatability testing.
- Serological tests:
  - Expedited review of IgG and IgM serological tests for COVID-19 was passed in June 2020. COFEPRIS developed an evaluation protocol along with the National Institute of Nutrition and Medical Science. All serological tests submitted for approval are evaluated according to the protocol (performed by TecSalud).

Japan

PMDA and MHLW oversight

- Requirements
  - Manufacturing sites must have received Foreign Manufacturer Accreditation (FMA) for Japanese Medical Devices by the Ministry.
  - Additionally, your Japan local site or distributor must be registered for compliance with labeling, packaging and under the Japanese Pharmaceutical Law by the Ministry of Health.
  - Valid ISO 13486:2016 or MDSAP certificate
  - Local Study concordance data with the method provided by the National Institute of Infections Disease Clinical samples:
    - Positive sample: more than 10 samples
    - Negative sample: more than 15 samples

Japan Requirements

	#	Items
For the Product Notification dossier	1	Intended Use
	2	Device Description - Test Principle - Measurable Parameters - Sample types - Reagents and Consumables and required, etc.
	3	Appearance, Dimensions, Weight - Overview drawings and photos - Dimensions of the instrument and PC etc. - Weight of the instrument and PC etc.
	4	Electrical Rating
	5	Block Diagram
	6	Materials for Components - Main materials name
	7	Product Performance Specification - Through put - Assay principle - testing procedures and the specs for the performance check, etc.
	8	Standards for designating the quality, safety and effectiveness
	9	Operation Procedures
	10	Manufacturing Method - Mfg. flow chart - Design controller's name and address - Manufacturer's name and address
	11	Japanese Package Insert
	12	Design Life of Instrument
For the launch	13	Japanese Label on Instrument
	14	Function Test / Final Inspection at Marsiling site - Testing Procedure and the specs. - Report template
	15	Original labels of the consumables and reagents required for Dx run

Australia

TGA Emergency Pathway

- TGA implemented emergency exemptions that allow for the importation and sale of COVID-19 IVD test kits and gives expedited registration for applicable products.
- All COVID-19 test kits must be approved for inclusion in the Australian Register of Therapeutic Goods (ARTG), in order to be legally supplied in Australia.

Note: *The emergency exemption that previously allowed supply of COVID-19 tests directly to accredited pathology laboratories* ***ended on 31 July 2020****. All COVID 19 tests must be included in the ARTG prior to supply, with the exception of Class 4 in-house IVDs being used to perform donor screening under the new emergency exemption which is in effect until 30 June 2021*

GA's information webpage: Coronavirus (COVID-19): Information on medicines and medical devices
Australian Government Department of Health information webpage: Coronavirus (COVID-19) health alert
Expedited COVID-19 medical device application process
Applying for TGA assessment of a COVID-19 test for inclusion in the ARTG

Australia

Expedited Assessment for COVID-19 test

- All COVID-19 tests included in the ARTG are based on an expedited assessment process are subject to additional non-standard conditions, that inform post-market validations as experience and knowledge around COVID-19 diagnostic testing grows.
- The conditions require that additional evidence to support the ongoing safety and performance of the devices be provided to the TGA within 12 months of inclusion on the ARTG.
- Additional conditions are being imposed on the supply of COVID-19 serology-based tests (i.e., serological rapid screening tests) and rapid antigen tests for use at the point-of-care as it is considered that the correct interpretation of results obtained from these tests requires the involvement of a suitably qualified healthcare professional.

Australia

Emergency Pathway requirements

- Sponsors must submit manufacturer's evidence (conformity assessment certification) to the TGA prior to submitting the IVD application.
- Once an IVD application is submitted and the application fee paid, the TGA will contact you and advise what information is required.
- The TGA website provides guidance on the information required in the technical files of an application and a step-by-step guide to the ARTG inclusion process.

Declaration of Conformity which declares that the device complies with:

- The applicable provisions of the essential principles
- The classification rules
- An appropriate conformity assessment procedure
- The declaration requires the manufacturer to provide details that are relevant to the conformity assessment procedure and the manufacture of the IVD medical device covered by the declaration.
- Templates are published to assist in the preparation of declarations of conformity.
- It is the responsibility of the manufacturer signing a declaration to ensure that it is drawn up correctly and meets all the legal requirements.

Medical device inclusion process

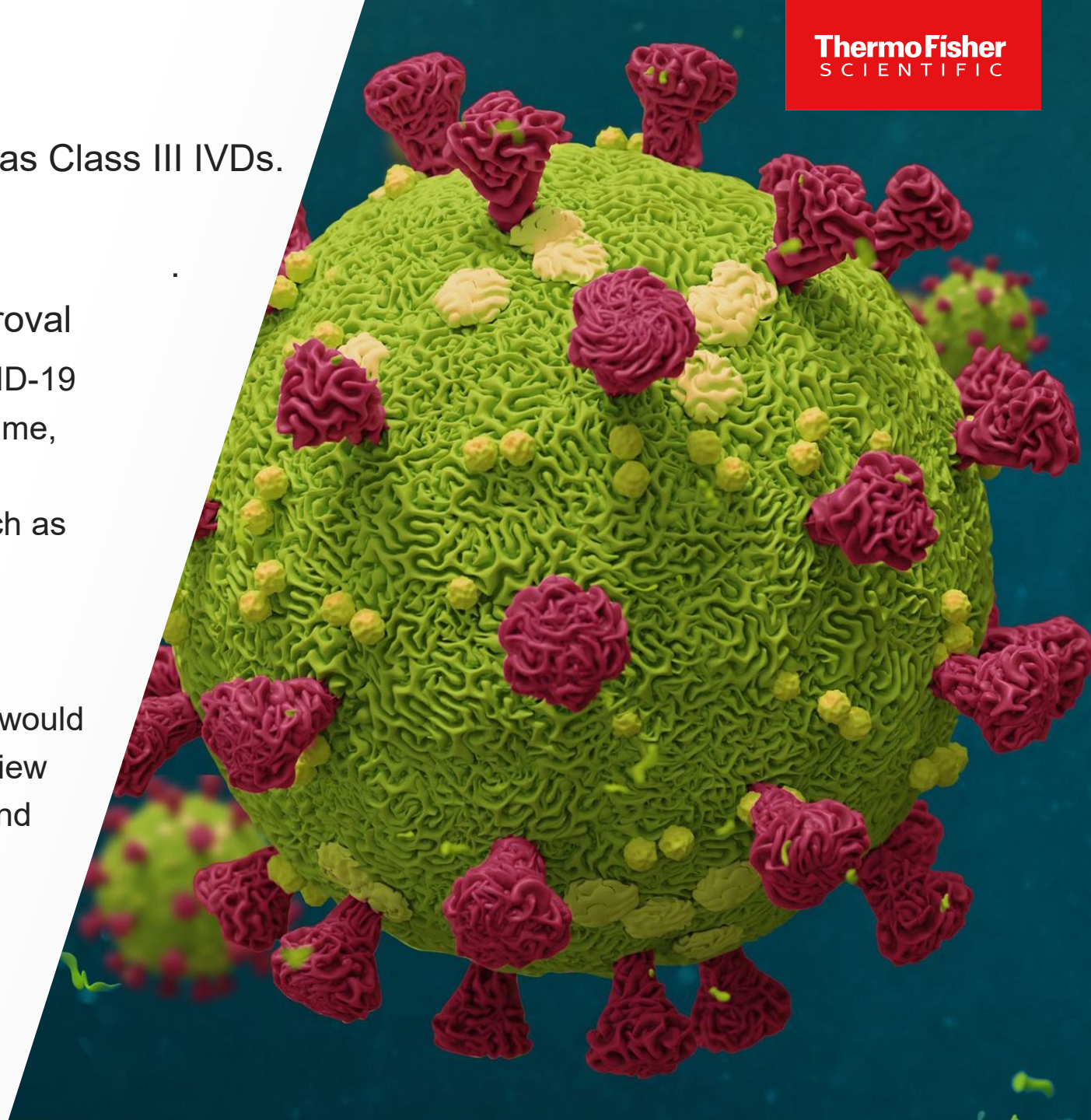
Overview of medical devices and IVD regulation

China

The NMPA classifies COVID-19 detection reagents as Class III IVDs.

Many devices no longer eligible for emergency approval

- It appears that the NMPA is only approving some COVID-19 IVDs through the emergency registration route at this time, and other Class III devices may not be accepted for emergency approval. Additionally, some provinces (such as Henan, Zhejiang, and Hunan) have closed emergency approval for all Class II devices.
- As a possible alternative for a faster review, interested manufacturers could try to confirm whether a province would accept their device for the “Green Channel” priority review route. Different provinces have varying requirements and criteria



http://www.nmpa.gov.cn/WS04/CL2582/

World Health Organization

WHO

Emergency Use License (EUL)

- The WHO Emergency Use Listing Procedure (EUL) is a 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 process aids 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 for EUL

IVDs eligible for EUL submission

Manufacturers interested in an EUL submission are invited to contact diagnostics@who.int to arrange a pre-submission meeting/call.

NOTE: Applications will not be accepted without prior consultation with WHO.

Currently, the following IVDs are eligible for EUL submission:

- Assays for the detection of SARS-cov-2 nucleic acid
- Immunoassays for the detection of SARS-cov-2 specific antibodies
- Rapid diagnostic tests for the detection of SARS-cov-2 antigens.

WHO recognizes CE marked product

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

WHO EUL Process

Application Requirements

- Product name and product code
- Name and address of the legal manufacturer
- Title and name of the authorized contact for the EUL assessment
- Sites of manufacture
- Information on whether or not the product is a rebrand of an existing issued an authorization product for emergency use or equivalent.

EUL Process Requirements includes review of the following

- Quality Management Systems Review and Plan for Post-Market Surveillance
  - Includes a paper audit of the quality management system of the manufacturing site
- Product Dossier Review
- Reportable incidents and change notification are requirements of post-market surveillance per WHO.

WHO publishes on their website and makes publicly available the following information in connection with the assessment process:

- The names of products and manufacturers that have applied for EUL, the product code(s) submitted for EUL and the EUL status of each application;
- WHO EUL public report summarizes the findings of the EUL assessment; and any negative outcomes of the EUL assessment.

http://www.who.int/diagnostics_laboratory/EUL/en/index.html

Lessons Learned

Lessons Learned

- Develop a detailed commercialization plan and have a Plan B; No matter how carefully a project is planned, something may still go wrong with it.
- Prioritize countries by Tier 1, 2, 3 based on the market for your product; All countries is not a priority list and EU is not a country…
- Resource the teams appropriately
- Set expectations internally and then over communicate
- Understand limitations of your product and that it may not meet the sensitivity and specificity requirements in all countries
- Timelines for authorizations or approvals by regulatory agencies are subject to change during the pandemic – communicate this internally
- Don’t forget about Post-Market Surveillance; resource appropriately

Thank you