Ministry of Health & Family Welfare
Government of India

厚生労働省
Ministry of Health, Labour and Welfare
Japan Ministry of Health, Labour and Welfare (JMHLW)

5th India-Japan Medical Products Regulatory Symposium

(Through WEBEX, 21st & 22nd Dec. 2021)

IVD

(CLINICAL INVESTIGATION REQUIREMENTS) (INDIA)

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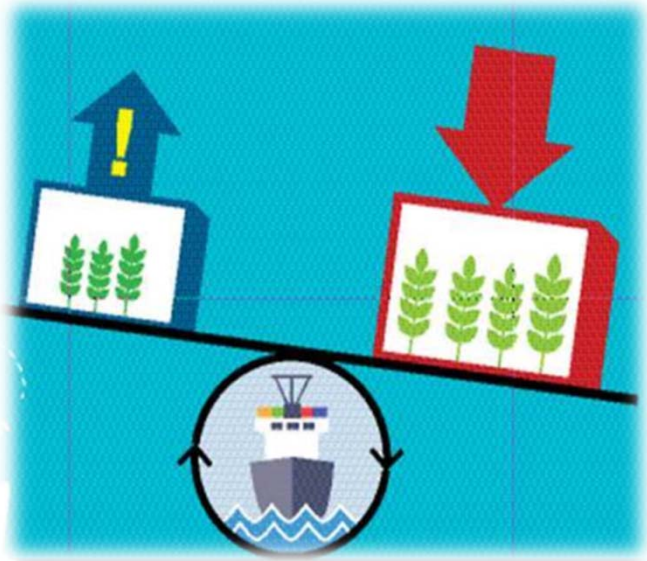
CENTRAL DRUGS STANDARD CONTROL ORGANIZATION
CDSCO CDSCO
सत्यमेव जयते
MINISTRY OF HEALTH, GOVERNMENT OF INDIA

Pmda
独立行政法人 医薬品医療機器総合機構
Pharmaceuticals and Medical Devices Agency

Content

- Introduction
- Regulation of In-vitro Diagnostic Medical Devices in India
- Laboratories identified for validation of IVD kits in India
- Regulatory pathway for approval of New In-vitro Diagnostic Medical Device
- Clinical Performance Evaluation requirements for In- vitro Diagnostic Medical Device

Introduction



- Current market size of the In-vitro Diagnostic Medical Device industry in India ~ $ 2 bn .
  Import: ~ US $ 1.5 bn ;
  Export: ~ US $ 0.5 bn
- ~ 80 % of the IVD Reagents/Kits, Analyzers, Instruments including software are imported.
- Approx. 175 of IVD kit manufacturers in India.
- All IVD Reagents/ kits are regulated under Medical Devices Rules, 2017.

Scope of Medical Devices Rules, 2017

Medical Device Rules, 2017 is applicable to:

i. substances used for in vitro diagnosis and surgical dressings, surgical bandages, surgical staples, surgical sutures, ligatures, blood and blood component collection bag with or without anticoagulant covered under sub-clause (i) of section 3 of the Drugs and Cosmetics Act, 1940 (23 of 1940);

ii. substances including mechanical contraceptives (condoms, intrauterine devices, tubal rings), disinfectants are notified under sub-clause (ii) of section 3 of the Drugs and Cosmetics Act, 1940 (23 of 1940); and

iii. devices notified from time to time under sub-clause (iv), of clause (b) of section 3 of the Drugs and Cosmetics Act, 1940 (23 of 1940);

Regulatory Authorities

IVD MD Risk based Classification ; Activity	Class A	Class B	Class C	Class D
Import	CLA	CLA	CLA	CLA
Manufacture	SLA	SLA	CLA	CLA
Permission to conduct CI /CPE	Permission from CLA			
Sale	SLA			
QMS Verification	Notified Body**	Notified Body**	CLA	CLA
FSC	SLA	SLA	CLA	CLA
MSC / NCC	SLA	SLA	CLA	CLA
Neutral/Special code	CLA	CLA	CLA	CLA

* CLA: Central Licensing Authority, SLA: State Licensing Authority, CPE: Clinical Performance Evaluation, NCC: Non Conviction Certificate, MSC: Market Standing Certificate, FSC: Free Sale Certificate

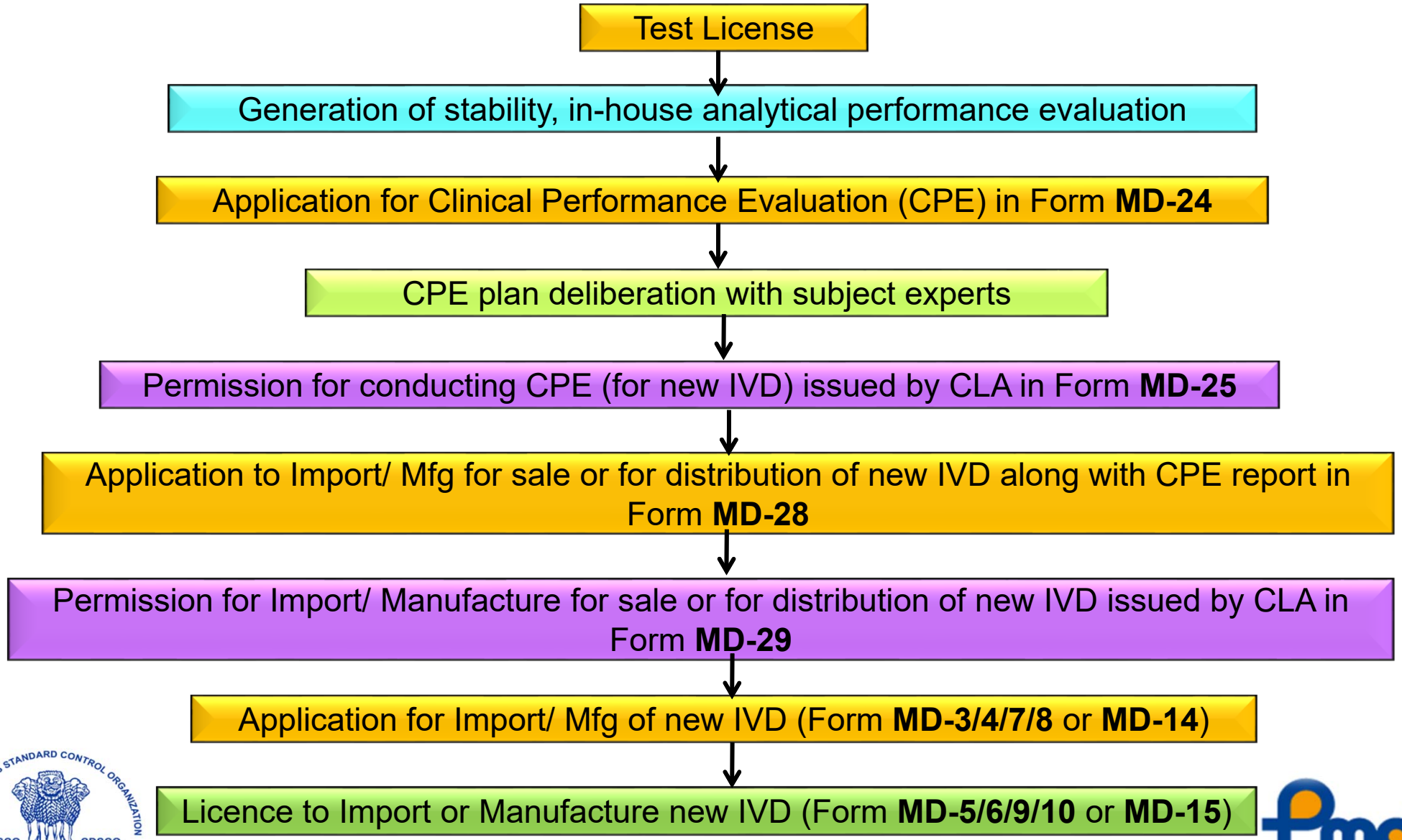
** Note: Notified Bodies shall be registered with Central Licencing Authority. Prior inspection shall not be required before the grant of manufacturing of Class A devices.

Performance Evaluation / Validation

- List of Laboratories identified for validation of IVD kits available in CDSCO website.
- Prior to issue of Import/ manufacturing permission, PE/ Validation require for In-vitro Diagnostics Reagents/ Kits used for the detection of :

1. HIV
2. HBV
3. HCV
4. Blood Grouping reagent
5. Cancer
6. Tuberculosis
7. Malaria
8. Dengue
9. Chikungunya
10. Syphilis
11. Typhoid
12. Influenza
13. Toxoplasma Gondii
14. Cytomegalovirus
15. Pneumonia
16. Methicilline-Resistant Staphylococcus Aureus
17. Entero Virus (A/B)
18. Markers for Congenital disorders
19. Neisseria Gonorrhoeae
20. Human Papilloma Virus infection
21. Autoimmune Disorders
22. Human Genetic testing
23. Other life threatening infections/agents (eg. COVID-19, Nipah Virus, Zika Virus etc.)

Regulatory Pathway for Approval of New In-vitro Diagnostic Medical Device



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Clinical Performance Evaluation requirements for IVDs

Permission to conduct CPE for New IVD

Form MD-24

+

Documents

+

Treasury Challan of Rs. 25000

- Ethics Committee approval
- Regulatory status in other countries
- Undertaking by investigators
- Undertaking by the sponsor

CPE Plan/ Study Protocol :

- Rationale for the study
- Objective of the study
- IVD description, labeling
- Description of test methods and interpretation of results
- In-house performance evaluation data
- Study Population, Study sites
- Study site training and monitoring
- Specimen type, Sample Size
- Specimen collection, preparation, handling and storage
- The scheduled duration for evaluation
- Inclusion and exclusion criteria
- Limitations
- Warnings & Precautions
- Data collection and management
- Required materials
- Case Report Form

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Selecting a Reference Test

- ✓ Product should have a known and appropriate level of clinical performance with the same specimen types.
- ✓ Product should have well-characterized with known state-of-the art performance characteristics.
- ✓ Product should be Manufactured under a stringent quality management system.
- ✓ Product should have regulatory approval

Expert Committee panels for IVDs

- Blood grouping sera
- Human Leukocyte Antigen (HLA)
- COVID-19 Reagents/ Kits
- Blood Glucose Diagnostic Devices an
- Cancer diagnostic devices and reagents
- HIV, HBV, HCV, Influenza, Syphilis and STD diagnostic devices and reagents
- Malaria, Dengue, Chikungunya, Typhoid and Leishmaniasis diagnostic devices and reagents
- Tuberculosis diagnostic devices and reagents

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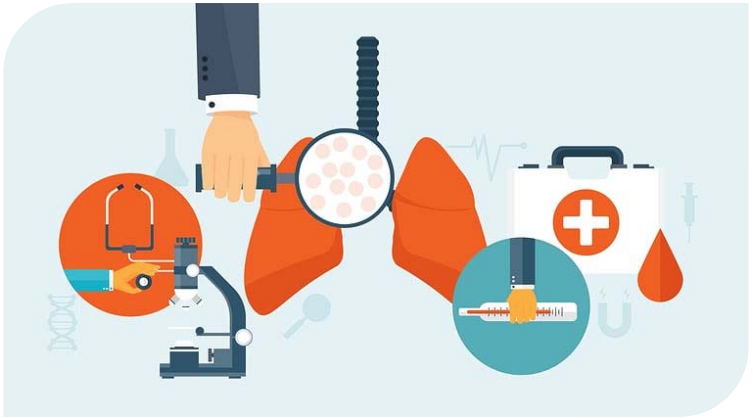
Source of Experts (Govt. Institutions)

- National Institute of Biologicals (NIB)
- Indian Council of Medical Research (ICMR)
- All India Institute of Medical Sciences (AIIMS)
- National Centre for Disease Control (NCDC)
- National AIDS Research Institute (NARI)
- National Institute of Virology (NIV)
- National Institute of Malaria Research (NIMR)
- National Institute for Research in Tuberculosis (NIRT)

Conditions for permission to conduct of Clinical Performance Evaluation

- No person or sponsor shall conduct any CPE in respect of a new IVD without the permission granted by the CLA.
- CPE shall be conducted in accordance with the approved CPE plan and GCP Guidelines.
- CPE shall be initiated after approval of CPE plan by the registered Ethics Committee



- CPE shall be registered with the Clinical Trial Registry of India before enrolling the first participant.

Cont..

- Annual status report of each CPE, shall be submitted to the CLA by the sponsor, and in case of termination of any CPE, the detailed reasons for the same shall be communicated to the CLA within thirty days of the date of termination.

- The laboratories or other institutions taking part in the evaluation study or the sponsor including their employees, subsidiaries and branches, their agents, contractors and sub-contractors, and clinical investigation sites shall be open for inspection by the regulators.

- CPE shall be initiated within a period of one year from the date of grant of permission, failing which prior permission from the CLA needs to be obtained.

Conditions for Permission to Import/ Manufacture IVDs

- IVDs shall conform to the specifications submitted along with the application
- The permission holder of Form MD-29 shall submit the PSUR to the CLA from the date of launch in the market (submit every six months for first two years followed by annually for two more successive years).
- The permission holder shall inform the date of launch of IVDs in the market to the CLA.
- The permission holder shall submit the suspected unexpected serious adverse event within fifteen days of the awareness of the event to the CLA.

Specification/ Criteria for IVDs

Product	Type	Specification/Criteria
HIV HBsAg	ELISA / RAPID	Sensitivity 100% Specificity ≥ 98%
HCV	ELISA	Sensitivity 100% Specificity ≥ 98%
HCV	RAPID	Sensitivity ≥99% Specificity ≥ 98%
Rapid Plasma Reagin (RPR) Test And TPHA (Hemagglutination) Test for Syphilis	ELISA / RAPID	Sensitivity ≥ 85% Specificity ≥ 93%
Malaria Antigen Detection of Pf / Pv (Plasmodium falciparum / Plasmodium vivax)	RAPID	1. For the detection of Pf / Pv in all transmission settings the panel detection score (PDS) should be at least 75% at 200 parasite/µL. 2. False positive rate should be less than 10% 3. The invalid rate should be less than 5%

Acceptance Criteria for SARS-CoV-2 IVD Kits

Type of Kit	Acceptance Criteria
RT-PCR Kit	Sensitivity: 95% and above Specificity: 99% and above
RNA Extraction Kit	At least 95% concordance among positive At least 90% concordance among negative samples > 95 % samples showing amplification in internal control
VTM	100% concordance among spiked samples 100% samples showing amplification in internal control
Antibody Rapid Kit	Sensitivity: 90% and above Specificity: 99% and above
ELISA / CLIA Kit	IgM: Sensitivity- 90% and above Specificity- 99% and above IgG: Sensitivity- 90% and above Specificity- 95% and above
Rapid Ag Test Kits	• Validated as a Point of Care Test (POCT) without transport to a laboratory setup: Sensitivity: 50% and above; Specificity: 95% and above • Validated in a laboratory setup with samples collected in Viral Transport Medium (VTM): Sensitivity: 70% and above; Specificity: 99% and above

Fast track Approval for COVID-19 IVD Kits/Reagents

- Fast track clearances of COVID-19 IVD kit applications from March 2020 to till date.
- Latest list of approved COVID-19 kits are being uploaded in CDSCO website. As on 13.12.2021, following kits for the detection of COVID-19 infection have been approved by this office.

Rapid / Elisa / CLIA (Serology based)	RT-PCR (Molecular based)	Antigen Test	Antigen Home Test / Self Test
152	235	81	06
Importer - 96	Importer - 154	Importer - 36	Importer–01
Indigenous - 56	Indigenous - 81	Indigenous – 45	Indigenous - 05

Awareness

- **List of banned IVDs**

  Central Govt. vide G.S.R 432(E) & 433(E) dated 07/06/2012 prohibit Import, manufacture, sale, distribution and use of "Serodiagnostic test kits for diagnosis of tuberculosis".

  Central Govt. vide S.O 1352(E)dated 23/03/2018 prohibit Antibody Detecting Rapid Diagnostic Tests for routine diagnosis of malaria.

- **Launch of Support Cells for WHO PQS for IVDs in India**

  for providing guidance to the Indian manufacturers for the WHO Prequalification of *In Vitro* Diagnostics Programme in India

  1) National Institute of Biologicals in North India
  2) Andhra Med-tech Zone in south India

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Thank You

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