ISSUE No. 58

SILVER JUBILEE YEAR 2016

TAMILNADU PHARMACEUTICALS SCIENCES WELFARE TRUST

25 Years

Pharma Web

Newsletter of Tamilnadu Pharmaceutical Sciences Welfare Trust

Apr. - May. - Jun. 2023

Delvin Formulations

Destiny for Innovation

MOVING GLOBALLY

R & D and Manufacturing of API

R & D and Manufacturing of Formulations

International Marketing

Domestic Marketing

Medical Devices

Surgical

Pharmaceuticals

NURAY CHEMICALS PVT. LTD.	HIBROW	Sai Mirra Innopharm	Numen Healthcare	Delvin Formulations	Inventz Lifesciences	Dr. KALAM COLLEGE OF PHARMACY
API (Bulk Drug)	Formulation R & D - Manufacturing	Formulation R & D - Manufacturing	International Marketing - Based at Singapore	Domestic Formulation Marketing	OTC with Spring Board Ventures	Educational Institution

Healthcare

i2H SOLUTIONS	LIFE SPAN DIABETES CLINICS	SCITUS
Diagnostic Care @ Home	Chain of Diabetic Clinics	Clinical Research Organisation

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Tamilnadu Pharmaceutical Sciences Welfare Trust

Pharma Web

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ISSUE : 58 Apr. - May. - Jun. 2023

CONTENTS **Page No.**

TAMILNADU PHARMACEUTICAL SCIENCES WELFARE TRUST
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e-mail : pictrust89@gmail.com Website : www.pictrust.com

EDITORIAL

Dear Readers,

We are happy to publish the 58th issue of Pharma Web Newsletter for **Apr – Jun 2023.**

This 58th issue contains the program highlights as well as the following articles published by eminent person in Pharma industry.

- **Diethylene Glycol Contamination in Cough Syrups -**
  Shri. Ganadhish Kamat, Quality Professional, Hyderabad

- **Indian IVD Regulatory Landscape – Dr. Sella Senthil,**
  Asst. Drugs Controller (India), IVD-Division, CDSCO, MoHFW, New Delhi

We have also published the various Gazette Notifications pertaining to the amendment of Drugs & Cosmetics Act & Rules, important circulars issued by DCGI pertaining to Drugs & Pharmaceuticals.

Important news items connected to our Pharmacy profession appeared in various national newspapers & Parliament Question & Answers relevant to our Pharmacy profession are published

We are very much thankful to M/s. Delvin Formulations, M/s. Medopharm, M/s. Tablets (India) Ltd., for the continuous support by giving advertisement, in order to sustain the cost of publishing of this newsletter.

Our special thanks to M/s. Fourrts (India) Laboratories Pvt. Ltd., for supporting Pharma Web advertisement and also awarding meritorious award for B. Pharm Students of The Tamilnadu Dr. MGR Medical University, Guindy, Chennai.

Hope this Newsletter will benefit our Pharma professionals. Any suggestions to improve our news letter are welcome.

With Best Regards,

R. NARAYANASWAMY

Chief Editor

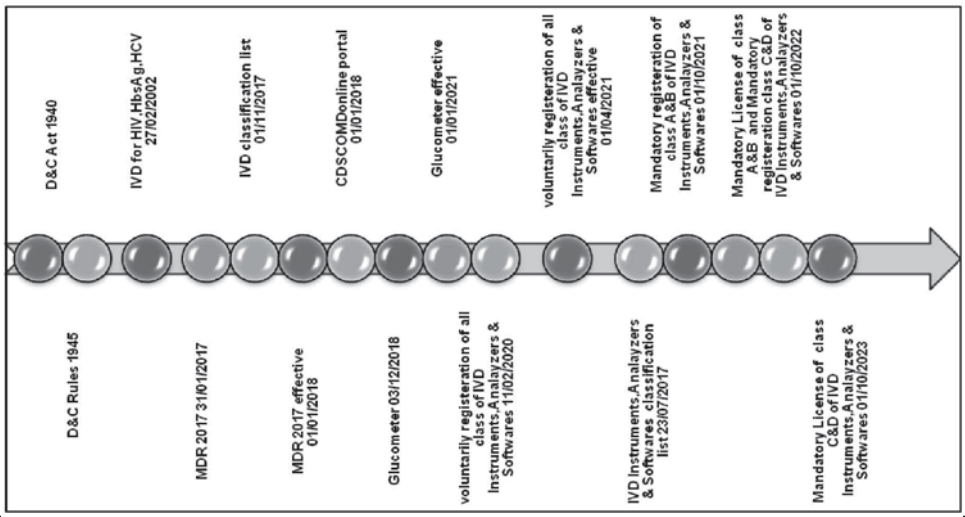
ARTICLES

Indian IVD Regulatory Landscape

Dr. Sella Senthil
Asst. Drugs Controller (India), IVD-Division, CDSCO, MoHHW, New Delhi

Lecture Delivered during Webinar organized by JSS College of Pharmacy, Mysuru, on 5th August 2023

Phased Regulatory Controls of IVDs



Introduction

In India, import, manufacturing, Clinical Performance, sale and distribution of In Vitro Diagnostic Medical Devices are regulated under Drugs and Cosmetic Act and MDR-2017 Rules.

(I) Low risk - Class A;
Eg. specimen receptacle. Etc.,

(ii) Low moderate risk- Class B;
Eg. Glucose test, clinical chemistry .Etc.,

(iii) Moderate high risk- Class C;
Eg. Cancer marker, Malaria, Dengue .Etc.,

(iv) High risk- Class D;
Eg. Blood Grouping, HIV, HBV, HCV, .Etc.,

Key Comparison of MD vs IVD vs Drugs

Medical Devices	In Vitro Diagnostic Medical Devices	Drug
In vivo and/or ex vivo use	In vitro use	In vivo use
Diagnostic or therapeutic intended uses	Diagnostic intended use	Therapeutic intended use
Active Components Generally based on mechanical, electrical, and materials engineering	Key components are. Antibodies / Antigen	API
Performance of Devices	Performance of Devices (e.g. sensitivity, specificity)	Drug content (eg.Assay, dissolution)
Clinical investigation New MD	Clinical performance Evaluation –New IVD	Clinical trails – New Drugs

Key Comparison of MD vs IVD vs Drugs

Medical Devices	In Vitro Diagnostic Medical Devices	Drug
Stability studies in real time & Accelerated condition	studies in real time Stability Accelerated In use stability Transportation stability	Stability studies in real time & Accelerated condition
Generally stored at room temperature	Generally stored at 4°-8°C	Generally stored at room temperature
Generally long shelf life	Generally short shelf life	Generally long shelf life

Medical Device Definition

All devices including an instrument, apparatus, appliance, implant, material or other article, whether used alone or in combination, including a software or an accessory, intended by its manufacturer to be used specially for human beings or animals which does not achieve the primary intended action in or on human body or animals by any pharmacological or immunological or metabolic means, but which may assist in its intended function by such means for one or more of the specific purposes of —

- diagnosis, prevention, monitoring, treatment or alleviation of any disease or disorder;
- diagnosis, monitoring, treatment, alleviation or assistance for, any injury or disability;
- investigation, replacement or modification or support of the anatomy or of a physiological process;
- supporting or sustaining life;
- disinfection of medical devices; and
- control of conception.

Important notifications

MINISTRY OF HEALTH AND FAMILY WELFARE

(Department of Health and Family Welfare)

NOTIFICATION

New Delhi, the 11th February, 2020

S.O. 648(E).— In pursuance of sub-clause (iv) of clause (b) of section 3 of the Drugs and Cosmetics Act, 1940 (23 of 1940), the Central Government, after consultation with the Drugs Technical Advisory Board, hereby specifies the following devices intended for use in human beings or animals as drugs with effect from the 1st day of April, 2020, namely:—

All devices including an instrument, apparatus, appliance, implant, material or other article, whether used alone or in combination, including a software or an accessory, intended by its manufacturer to be used specially for human beings or animals which does not achieve the primary intended action in or on human body or animals by any pharmacological or immunological or metabolic means, but which may assist in its intended function by such means for one or more of the specific purposes of—

(i) diagnosis, prevention, monitoring, treatment or alleviation of any disease or disorder;

(ii) diagnosis, monitoring, treatment, alleviation or assistance for, any injury or disability;

(iii) investigation, replacement or modification or support of the anatomy or of a physiological process;

(iv) supporting or sustaining life;

(v) disinfection of medical devices; and

(vi) control of conception.

[F.No. X.11035/281/2018-DRS]

Dr. MANDEEP K. BHANDARI, Jt. Secy.

MINISTRY OF HEALTH AND FAMILY WELFARE

(Department of Health and Family Welfare)

NOTIFICATION

New Delhi, the 11th February, 2020

G.S.R. 102 (E).— Whereas a draft of certain rules further to amend the Medical Devices Rules, 2017, was published as required by under subsection (1) of section 12 and sub-section (1) of section 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940), vide notification of the Government of India in the Ministry of Health and Family Welfare (Department of Health and Family Welfare) number G.S.R. 797 (E), dated the 18th October, 2019, in the Gazette of India, Extraordinary, Part II, Section 3, Sub-section (i), inviting objections and suggestions from persons likely to be affected thereby, before the expiry of a period of thirty days from the date on which the copies of the Official Gazette containing the said notification were made available to the public;

And whereas copies of the Official Gazette were made available to the public on 18th October, 2019;

And whereas objections and suggestions received from the public on the said rules have been considered by the Central Government;

Now, therefore, in exercise of the powers conferred by section 12 and section 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940), the Central Government, after consultation with the Drugs Technical Advisory Board, hereby makes the following rules further to amend the Medical Devices Rules, 2017, namely:—

1. (i) These rules may be called the Medical Devices (Amendment) Rules, 2020.

(ii) These rules shall come into force on the 1st day of April, 2020.

2. In the Medical Devices Rules, 2017 (hereinafter to be referred as said rules), after CHAPTER III, the following CHAPTER IIIA shall be inserted, namely:—

"CHAPTER IIIA

REGISTRATION OF CERTAIN MEDICAL DEVICES

19A. (1) This Chapter shall be applicable to all devices notified under clause (b) of section 3 of the Act except the medical devices and devices specified in the Annexure of Eighth Schedule of these rules.

(2) The Medical devices referred in sub-rule (1) shall be registered with the Central Licensing Authority through an identified online portal established by the Central Drugs Standard Control Organisation for this purpose:

Key Definitions

- **In vitro diagnostic medical device** - substances used for in vitro diagnosis shall be referred as in vitro diagnostic medical device.
- **Reagent** - a chemical, biological or immunological component, solution or preparation intended by the manufacturer to be used as in vitro diagnostic medical device
- **New in vitro diagnostic medical device**- any substances used for in vitro diagnosis that has not been approved for manufacture for sale or for import by the Central Licensing Authority and is being tested to establish its performance for relevant analyte or other parameter related thereto including details of technology and procedure required.
- **Performance evaluation**- systematic investigation by which data is assessed and analysed to establish or verify performance of the in vitro diagnostic medical device for its intended use.
- **Clinical performance evaluation-** systematic performance study of a new IVD on a specimen collected from human participants to assess its performance
- **Specimen receptacle-** means a device, whether vacuum type or not, specifically intended by its manufacturer for the primary containment of specimens derived from human or animal body.
- **Transmissible agent** - an agent capable of being transmitted to a person, which causes communicable, infectious or contagious disease.

Regulatory Authorities

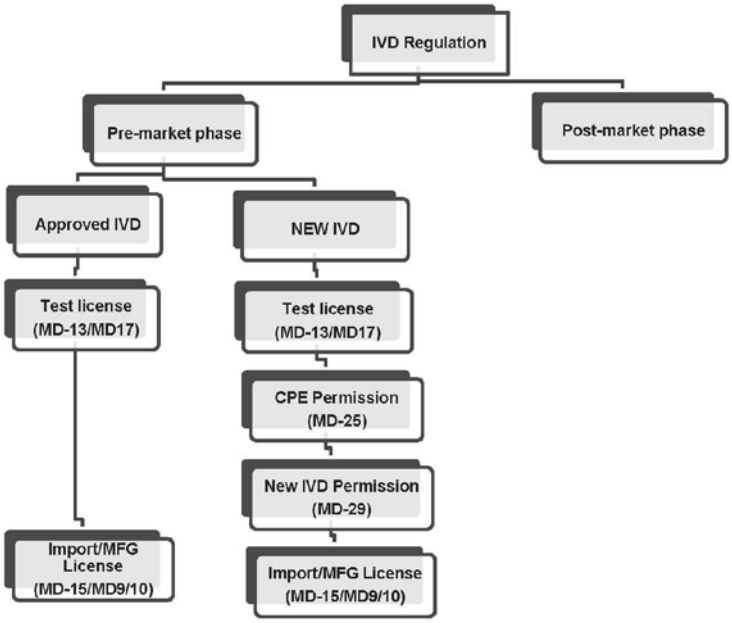
IVD Risk based Classification Activity	Class A Low Risk	Class B Low Moderate Risk	Class C Moderate High Risk	Class D High Risk
Import	CLA	CLA	CLA	CLA
Manufacture	SLA	SLA	CLA	CLA
Permission to conduct CPE	Permission from CLA			
Sale	SLA			
QMS Verification	Notified Body**	Notified Body**	CLA	CLA
FSC	SLA	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.

IVD Regulatory Pathway



What IVDs require PER/External evaluation

SLA/ CLA may require the Performance Evaluation Report for the following In-vitro Diagnostics

1.HIV	2. HBV	3. HCV	4. Blood Grouping reagent	5. Cancer
6. Tuberculosis	7. Malaria	8. Dengue	9.Chikungunia	10.Syphlis
11.Typhoid	12.Influenza	13.ToRCH (Toxoplasma gondii, Rubella virus, Cytomegalovirus, Herpes simplex virus)	14.Chlamydia	15.Pneumonia
16.Methicilline-Resistant Staphylococcus Aureus	17.Entero virus	18.Marker for congenital disorder e.g. Screen test for Down's Syndrome	19.Sexually transmitted agent i.e. Treponema pallidum, Neisseria gonorrhoeae, Human Papilloma Virus, Herpes Virus	20.Other life threatening Infections / agent.

Central medical devices testing laboratory (CMDTL)

Name of Laboratory	Category of medical device
The National Institute of Biologicals, Noida	In-Vitro Diagnostics for human Immunodeficiency virus, Hepatitis B Surface Antigen and Hepatitis C Virus, Blood Grouping sera, Glucose Test Strip, Fully Automated Analyser Based Glucose Reagent, RT-PCR Kits for Diagnosis of Covid-19, Ribonucleic acid (RNA) Extraction Kits for Diagnosis of Covid-19, Viral Transport Medium (VTM) for Diagnosis of Covid-19, RTLAMP Kit for diagnosis of Covid-19

Under Rule19 of MDR 2017. **Central medical device testing laboratory**.
(1) The Central Government may, by notification, establish Central medical devices testing laboratory for the purpose of,
(a) testing and evaluation of medical devices; or
(b) functioning as an appellate laboratory; or
(c) to carry out any other function as may be specifically assigned to it.
(2) Without prejudice to sub-rule (1), **the Central Government may also designate any laboratory having facility for carrying out test and evaluation of medical devices as central medical devices testing laboratory for the purposes specified in sub-rule (1):**
Provided that no medical devices testing laboratory, shall be so designated unless it has been duly accredited by the National Accreditation Body for Testing and Calibration Laboratories.

Medical devices testing laboratory (MDTL) registered for testing of IVDs on behalf of the manufacturer

Name of Laboratory	Category of medical device
M/s, Star Imaging & Path Lab Pvt. Ltd. situated at 4B/4, TILAK NAGAR, West Delhi, Delhi - 110018	Bilirubin (Total and Direct), Creatinine test reagent / kit, Aspartate Amino Transferase, Alanine Amino Transferase, Uric Acid Test reagents / kits, Total Protein test reagents /kits , Activated partial, PT (Prothrombin Time) Test

Medical devices testing laboratory" means any institute, organisation registered under sub-rule (3) of rule 83 for
carrying out testing or evaluation of any medical device on behalf of a licencee for manufacture for sale

CDSCO specified Labs for carryout PER of high risk IVDs

1 National Institute of Biologicals, Plot No. A-32, Sector-62, Institutional Area, Noida, Uttar Pradesh 201309
2. ICMR-National AIDS Research Institute. (ICMR). 73, 'G'-Block MIDC Bhosari, Pune - 411026, Maharashtra India
3 ICMR- National Institute of Virology, 20/ A, Dr.Ambedkar Road, Post Box No. 11 Pune 411001, India
4 ICMR- National Institute for Research in Reproductive Health, Jehangir Merwanji Street, Parel, Mumbai, Maharashtra 400012
5 ICMR-National Institute of Cholera and Enteric Diseases, P-33 C.I.T. Road, Scheme-XM, Beliaghata Kolkata-700010
6 Christian Medical College & Hospital, Ida Scudder Road, Vellore, Tamil Nadu 632004
7 Department of Clinical Virology, Institute of Liver & Biliary Sciences, D-1, Vasant Kunj New Delhi-70
8 All India Institute of Medical Sciences, Division of Clinical Microbiology & Molecular Medicine, New Delhi-110029
9 All India Institute of Medical Sciences, Dept. of microbiology, Sijua, Patrapada, Bhubaneswar, Odisha 751019
10 All India Institute of Medical Sciences, Division of Genetics, Dept. of Paediatrics', New Delhi
11 Dept. of Microbiology, The Postgraduate Institute of Medical Education and Research, Chandigarh, Sector 12, Chandigarh, 160012
12 Division of Genetics, Dept. of Paediatrics', Maulana Azad Medical College, New Delhi
13 ICMR- Institute of Cytology and Preventive Oncology (ICPO), I-7, Sector - 39, Noida 201301 Uttar Pradesh, INDIA/ National Institute of Cancer Prevention & Research

CDSCO specified Labs for carryout PER of high risk IVDs

14 ICMR- National Institute for Research in Trible Health, Nagpur Road, Near NSCB Medical College Jabalpur, Madhya Pradesh, 482003
15 ICMR- National Institute for Research in Tuberculosis, Mayor Sathiyamoorthy Road, Chetpet, Chennai – 600 031, India
16 ICMR- National Institute of Eipidemiology, R 127, 3rd Avenue, Second Main Road, Tamil Nadu Housing Board, Ayapakkam, Near Ambattur, Chennai, Tamil Nadu 600077
17 ICMR- National Institute of Immunohaematology, 13th floor, New Multistoreyed Building, KEM Hospital Campus, Parel, Mumbai, Maharashtra 400012
18 ICMR- National Institute of Malaria Research (NIMR), Sector 8, Dwarka, Delhi-110077 (India)
19 ICMR- National Institute of Pathology, Sadarjang Hospital Campus, Ansari Nagar West, New Delhi, Delhi 110029
20 ICMR- National Jalma Institute of Leprosy and other mycobacterial diseases P.O BOX 101, Dr. M. Miyazaki Marg, Tajganj, Agra – 282001
21 ICMR- Vector Control Research Centre, Medical Complex, VCRC Road, Indra Nagar, Priyadarshini Nagar, Puducherry, 605006
22 ICMR-Regional Medical Research Centre, N.E. Region, P.O.- Lahowal, Dibrugarh - 786 010 Assam, INDIA
23 ICMR-Regional Medical Research Centre, NALCO Nagar, Chandrasekharpur, Bhubaneswar, Odisha 751023
24 National Reference Laboratory for Tuberculosis,Department of Microbiology, Bhopal Memorial Hospital & Research Centre, under ICMR, DHR,Raisen Bypass Road, Near Karond Chouraha,Bhopal – 462038

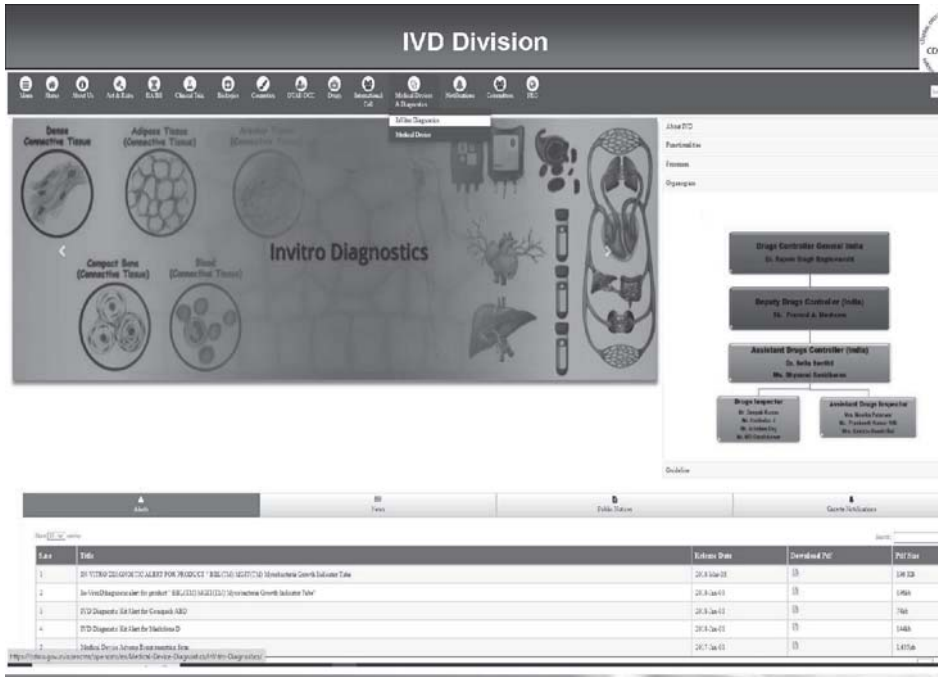
CDSCO specified Labs for carryout PER of high risk IVDs

24 National Reference Laboratory for Tuberculosis,Department of Microbiology, Bhopal Memorial Hospital & Research Centre, under ICMR, DHR,Raisen Bypass Road, Near Karond Chouraha,Bhopal – 462038
25 Indian Red Cross Society, 1, Red Cross Road, New Delhi
26 King Institute, Guindy Flyover, Guindy Institutional Area, SIDCO Industrial Estate, Guindy, Chennai, Tamil Nadu 600032
27 Medical College and Hospital (Department of Oncology/ Medical Oncology), 88, College St, Calcutta Medical College, College Square, Kolkata, West Bengal 700073
28 National Institute of Tuberculosis & Respiratory Diseases, Sri Aurobindo Marg, Near Qutub Minar New Delhi- 110030
29 National Tuberculosis Institute, 8, Bellary Road, Bangalore 560 003, India
30 Rajan Babu T.B. Hospital, Kingsway Camp, GTB Nagar, Delhi 110009
31 Sawai Man Singh Medical College, Jawahar Lal Nehru Marg, Gangawal Park, Adarsh Nagar, Jaipur, Rajasthan 302004
32 Shantabai Devarao Shivaram Tuberculosis Research Centre & Rajiv Gandhi Institute of Chest Diseases, Someshwara Nagar 1st Main Road, Dharmaram College Post, Bangalore - 560 029
33 Tata Medical Center, 14 MAR (E-W), New Town, Rajarhat, Kolkata 700156
34 Tata Memorial Hospital, Dr. E Borges Road, Parel, Mumbai - 400 012 India

Specification/Criteria for IVD

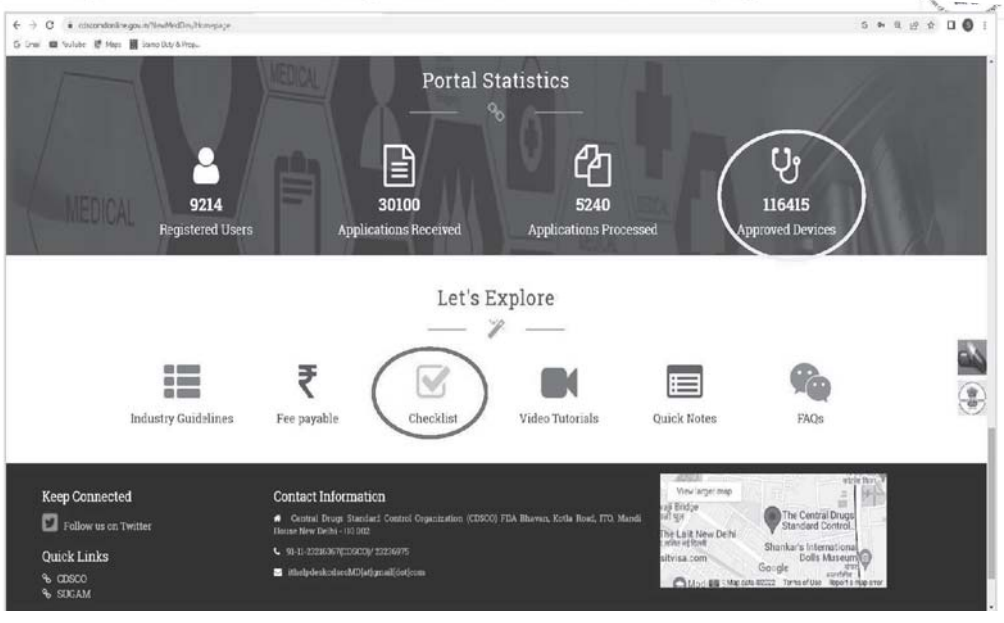
Product	Type	Specification/Criteria
HIV HBsAg	ELISA / RAPID	Sensitivity 100% Specificity ≥ 98%
HCV	ELISA	Sensitivity 100% Specificity ≥ 98%
HCV	RAPID	Sensitivity ≥99% Specificity ≥ 98%
Rapid Plasma Reagin (RPR) Test And TPHA (Hemagglutination) Test for Syphilis	ELISA / RAPID	Sensitivity ≥ 85% Specificity ≥ 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%


https://cdsco.gov.in/opencms/opencms/en/Home/
Central Drugs Standard Control Organization
Directorate General of Health Services
Ministry of Health & Family Welfare
Government of India
Drugs Controller General of India
Dr. Rajeev Singh Raghuvanshi


IVD Division
Invitro Diagnostics

https://cdscomdonline.gov.in/NewMedDev/Homepage

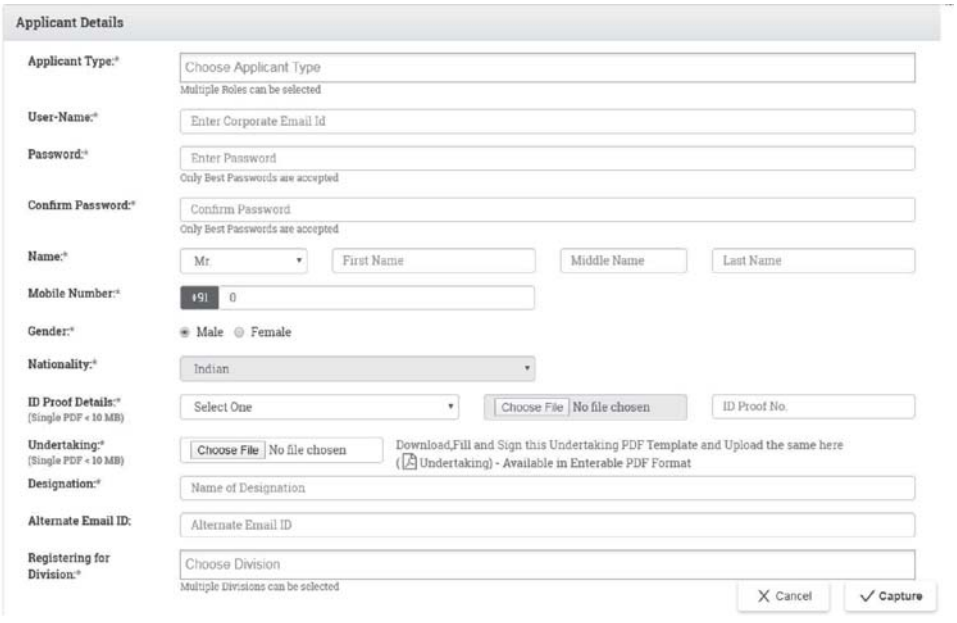
https://cdscomdonline.gov.in/NewMedDev/Homepage



Salient Features of Online Portal

- Establish single window platform for application for Import license/manufacturing license through online portal.
- Establish uniformity w.r.t. the requirement of documents for different type of applications throughout India.
- Greater outreach of citizen centric information
- Ease for stakeholders
- Accountability, transparency, reliability and timely process of the applications
- Real time trending of application.

Applicant Registration



Registered Indian Address *(This address will be referred in all the forms submitted to CDSCO office)*

Organization Name:* Name of Organization

Organization Type:* Select

CIN (Corporate Identification Number): CIN No

Address Line * Address Line 1

Country* India

State* Select

District* Select

City/Taluka/Mandal/Tehsil* City/Taluka/Mandal/Tehsil

Pin Code* 0

Contact No.* (Please include STD Code - Phone Number)
+91 STD Code - Contact Number
Multiple Contact Numbers can be added with comma separation

Fax No.* (Please include STD Code - Fax Number)
+91 STD Code - Fax Number
Multiple Fax Numbers can be added with comma separation

Upload Your Corporate Address Proof Details (Certificate of Incorporation):* (Single PDF < 10 MB) Choose File No file chosen

Copy of Manufacturing License or Wholesale Licenses (In case, you are first time applicant & not holding any licenses,please upload the justification for the same) :* (Single PDF < 10 MB) Choose File No file chosen

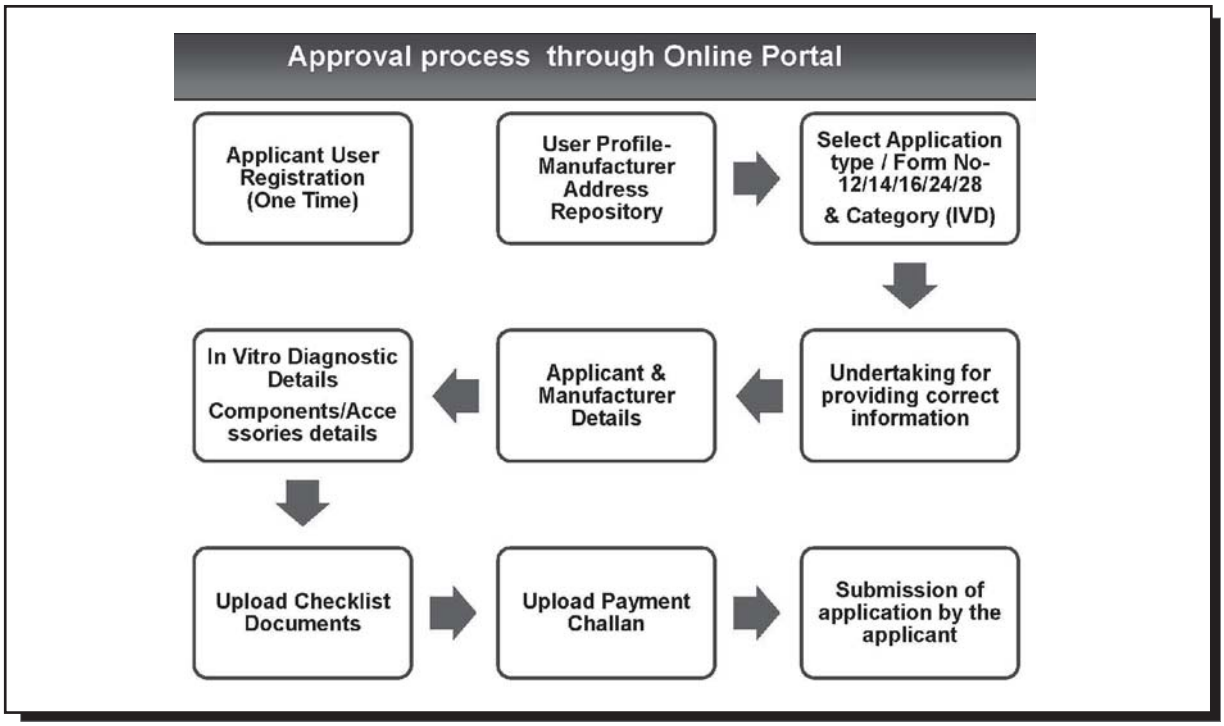
Please tick (✓) this option if you want to receive SMS alerts.

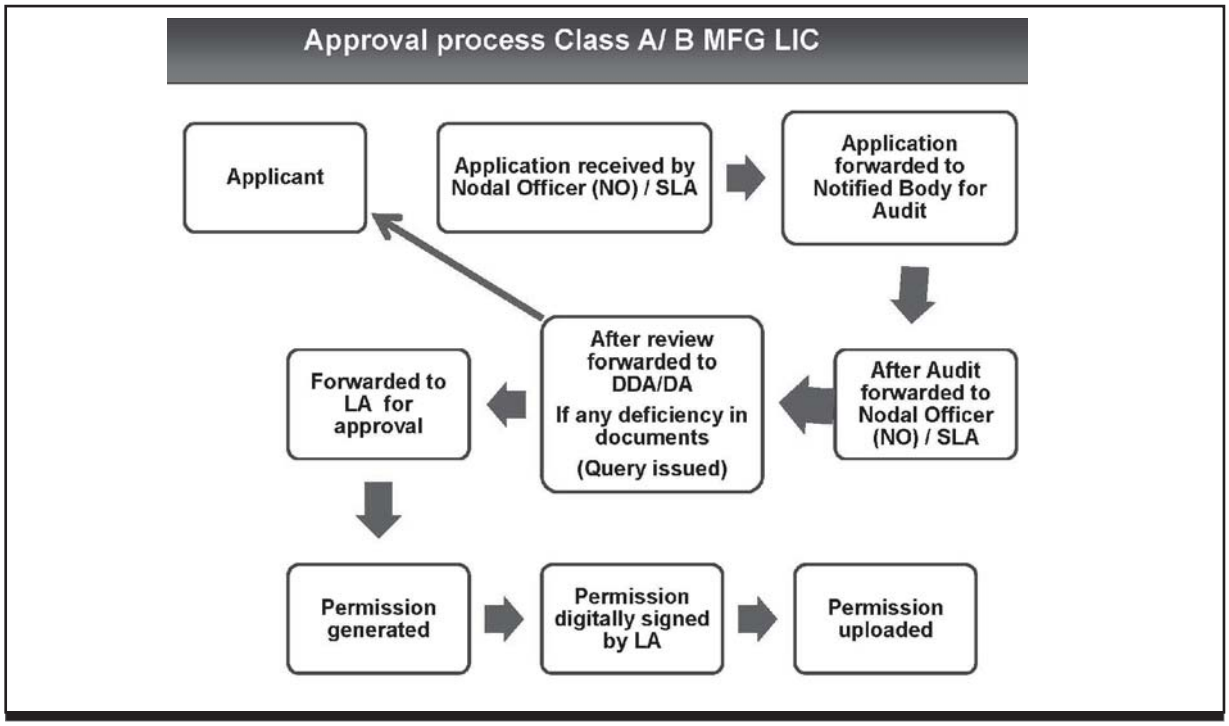
87454

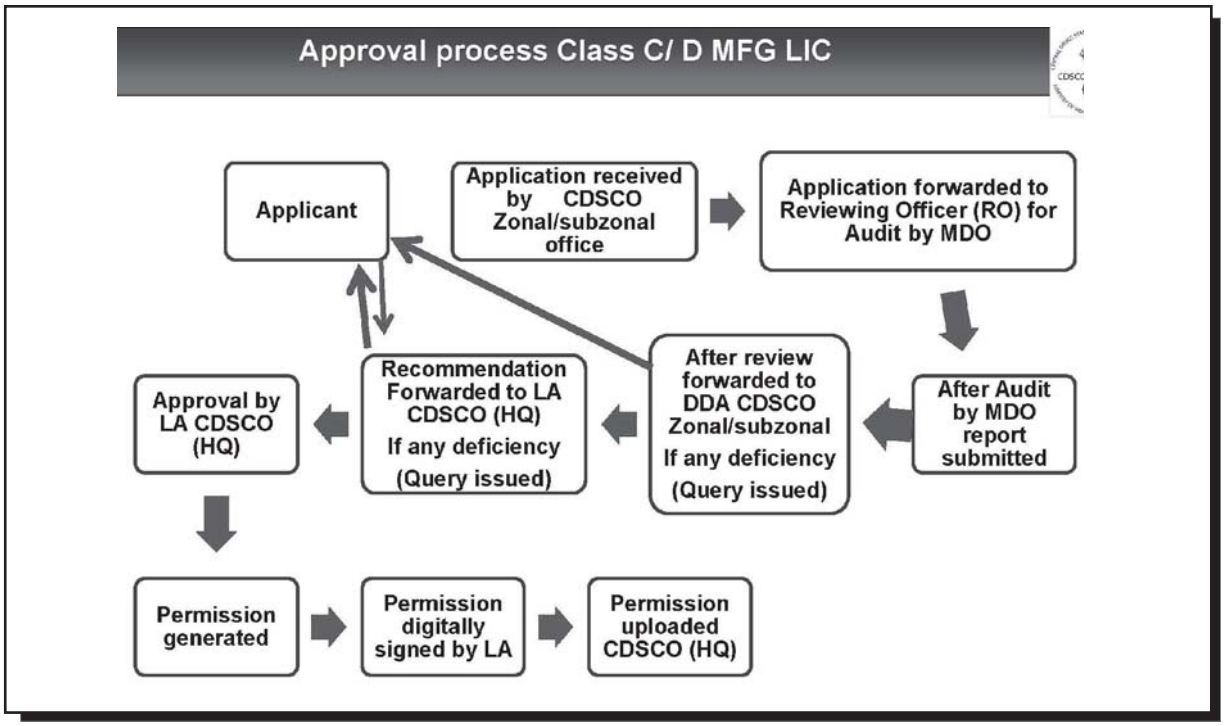
I agree to the terms, conditions and privacy policy laid down by Central Drugs Standard Control Organisation, DGHS, Ministry of Health & Family Welfare for availing the online services provided under this portal. *

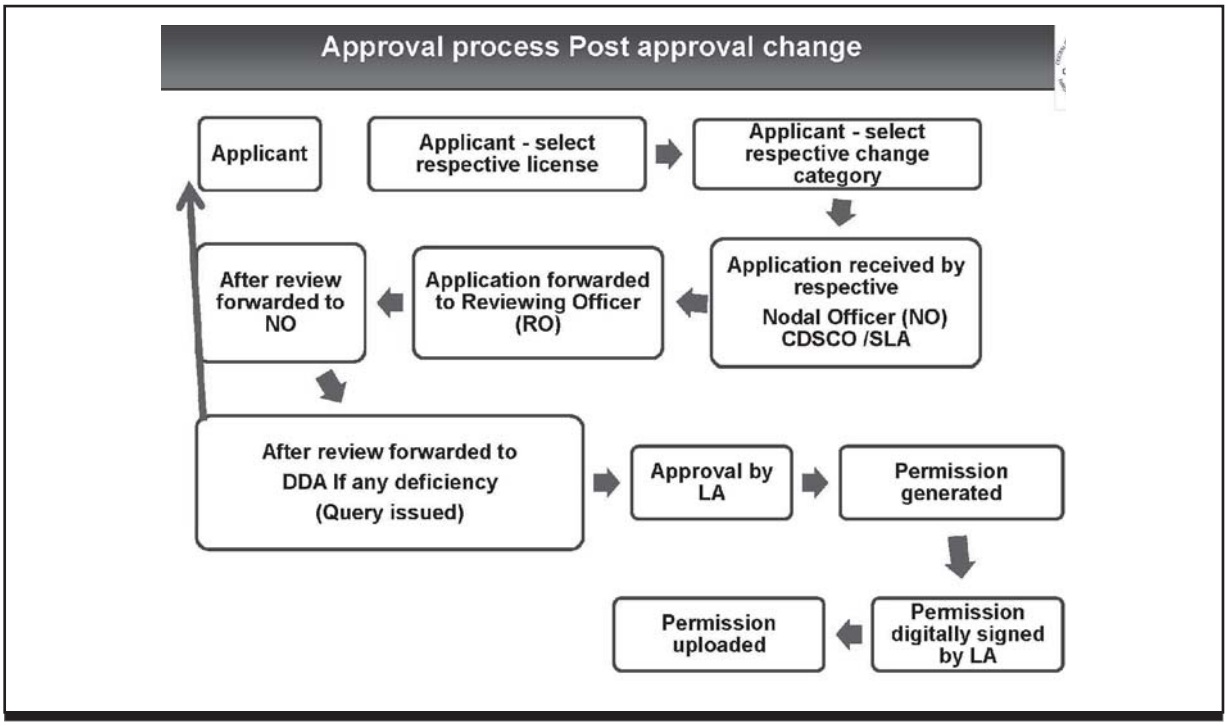
Previous | Submit | Cancel | Capture

Online Submission & Real-Time Tracking of Application

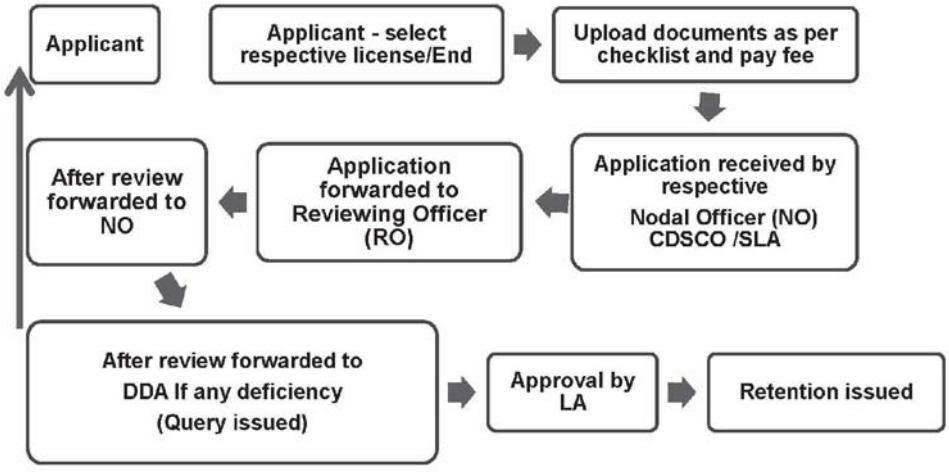

Approval process through Online Portal
Applicant User Registration (One Time)
User Profile- Manufacturer Address Repository
Select Application type / Form No- 12/14/16/24/28 & Category (IVD)
Undertaking for providing correct information
Applicant & Manufacturer Details
In Vitro Diagnostic Details Components/Acce ssories details
Upload Checklist Documents
Upload Payment Challan
Submission of application by the applicant


Approval process Class A/ B MFG LIC
Applicant
Application received by Nodal Officer (NO) / SLA
Application forwarded to Notified Body for Audit
After Audit forwarded to Nodal Officer (NO) / SLA
After review forwarded to DDA/DA If any deficiency in documents (Query issued)
Forwarded to LA for approval
Permission generated
Permission digitally signed by LA
Permission uploaded


Approval process Class C/ D MFG LIC
Applicant
Application received by CDSCO Zonal/subzonal office
Application forwarded to Reviewing Officer (RO) for Audit by MDO
After Audit by MDO report submitted
After review forwarded to DDA CDSCO Zonal/subzonal If any deficiency (Query issued)
Recommendation Forwarded to LA CDSCO (HQ) If any deficiency (Query issued)
Approval by LA CDSCO (HQ)
Permission generated
Permission digitally signed by LA
Permission uploaded CDSCO (HQ)


Approval process Post approval change
Applicant
Applicant - select respective license
Applicant - select respective change category
Application received by respective Nodal Officer (NO) CDSCO /SLA
Application forwarded to Reviewing Officer (RO)
After review forwarded to NO
After review forwarded to DDA If any deficiency (Query issued)
Approval by LA
Permission generated
Permission digitally signed by LA
Permission uploaded

Approval process Retention of license



Nodal Officer - Dashboard

Regulation of Covid-19 IVD Regents/Kits

IVD type	COVID-19 IVD RT-PCR	COVID-19 IVD RAPID/ ELISA/ CLIA	COVID-19 Home-based Antigen testing kit	Viral transport (VTM)	RNA/DNA Extraction	Molecular transport medium (MTM)
Device Class	Class C	Class C	Class C	Class A	Class C	Class C
Import	CLA	CLA	CLA	CLA	CLA	CLA
Manufacture	CLA	CLA	CLA	SLA	CLA	CLA
Requirements of `MD-25	Abbreviate, defer, or waive On national emergency	Abbreviate, defer, or waive On national emergency	Abbreviate, defer, or waive On national emergency	NIL	NIL	NIL
Requirements of MD-29	As post license condition On national emergency	As post license condition On national emergency	As post license condition On national emergency	NIL	NIL	NIL
PER Requirements	NIL for USFDA (EUA), PMDA (Japan), TGA (Australia), WHO (EUL) Approved	NIL for USFDA (EUA), PMDA (Japan), TGA (Australia), WHO (EUL) Approved	NIL for USFDA (EUA) Approved	NIL for USFDA (EUA) Approved	NIL for USFDA (EUA) Approved	NIL for USFDA (EUA) Approved
	1 lot Prior approval and 2 lot post marketing (within 04 months time) ; for Non-USFDA/PMDA/TGA/WHO or Indigenous	3 lot Prior approval for Non-USFDA/PMDA/TGA/WHO or Indigenous	3 lot Prior approval for Non-USFDA/PMDA/TGA/WHO or Indigenous	1 lot Prior approval	1 lot Prior approval	1 lot Prior approval

REGULATORY PATHWAY FOR DOMESTIC MANUFACTURING OF COVID-19 IVD REAGENTS/KITS

Obtain Test licence for small quantity of IVD kit for in-house testing & ICMR validation in **Form MD-13** by applying in Form MD-12 along with fee for each IVD INR 500 and documents as per the checklist available on the MD Online portal (Link https://cdscomdonline.gov.in/NewMedDev/viewChecklistReport) available on the MD online portal (Link https://cdscomdonline.gov.in/NewMedDev/Homepage).

Obtain manufacturing license in Form MD-9 or MD-10 (loan license) by applying in Form MD-7 or MD-8 (loan license) along with fee for one site INR 50000 (fresh application) and per product INR 1000 and documents (SMF, DMF, Product and Process Validation reports, Product Stability Study reports,etc.) as per checklist available on the MD Online portal.

Form MD-9 or MD-10 is issued based on Site Inspection carried out by MDO(s) of CDSCO, compliance to QMS as per Fifth Schedule of MDR-2017, scrutiny of technical documentation and Validation report of IVD kit issued by ICMR designated laboratory as per the acceptance criteria for the sensitivity and specificity of COVID-19 IVD kits published by ICMR (Link https://www.icmr.gov.in/ckitevaluation.html).

- Above mentioned Applications ie (MD-12, MD-7/8) may be submitted simultaneously and processed parallelly.
- Application received , reviewed, audited (where applicable) and recommended to LA by concerned CDSCO zonal/sub zonal office in coordination with CDSCO(HQ)

REGULATORY PATHWAY FOR IMPORT OF COVID-19 IVD REAGENTS/KITS

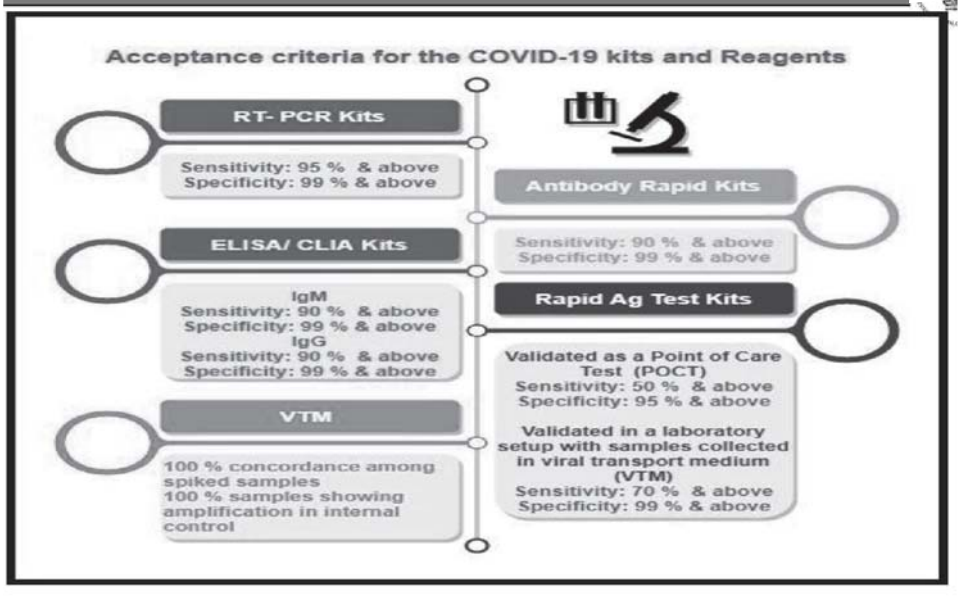
Obtain Import Test licence for small quantity of IVD kit for ICMR validation in **Form MD-17** by applying in Form MD-16 along with fee for each IVD $100 and documents as per the checklist available on the MD Online portal (Link https://cdscomdonline.gov.in/NewMedDev/viewChecklistReport) available on the MD online portal (Link https://cdscomdonline.gov.in/NewMedDev/Homepage).

Obtain Import license in Form MD-15 by applying in Form MD-14 along with fee for site $3000 (fresh application) and per product $ 500 and documents (SMF, DMF, Whole sale licence, POA, ISO 13485 certificate, FSC from the country of origin or issued by the competent authority of any of the countries namely, Australia, Canada, Japan, EU Countries or USA, etc.) as per checklist available on the MD Online portal.

Form MD-15 is issued based on scrutiny of submitted documents and Validation report of IVD kit (if applicable) issued by ICMR designated laboratory as per the acceptance criteria for the sensitivity and specificity of COVID-19 kits published by ICMR (Link https://www.icmr.gov.in/ckitevaluation.html).

- Above mentioned Applications ie (MD-16, MD-14) may be submitted simultaneously and processed parallelly.
- Application received, reviewed and recommended to LA by CDSCO(HQ).

Acceptance Criteria for SARS-CoV-2 Diagnostic Kits



Fast track Approval for COVID-19 IVD Kits/Reagents

Time line comparisons:

Application Type	Time line under MDR 2017	For COVID 19 IVDMD
Manufacturing Test license - MD12	30 days	Within 7 days (DCGI issued public notice dated 19-03-2020)
Import Test license – MD16	30 days	Within 7 days (DCGI issued public notice dated 19-03-2020)
Application for conduct clinical performance evaluation of new IVD MD – MD24	90 days	Abbreviate, defer, or waive Under MDR2017 (DCGI issued public notice dated 19-03-2020)
Application for permission to Import / manufacture New IVD MD – MD28	120 days	Abbreviate, defer, or waive Under MDR2017 (DCGI issued public notice dated 19-03-2020)
Application for manufacturing license for sale of IVD MD Form MD-7 or MD-8 (loan license) Class C/D	i. Scrutiny within 45 days ii. Site inspection within 60 days iii. License issued within 45 days of Inspection report	Expedited review and accelerated approval (DCGI issued public notice dated 19-03-2020)
Application for Import for sale of IVD MD Form MD-14	270 days	Expedited review and accelerated approval (DCGI issued public notice dated 19-03-2020)

Post market Surveillance

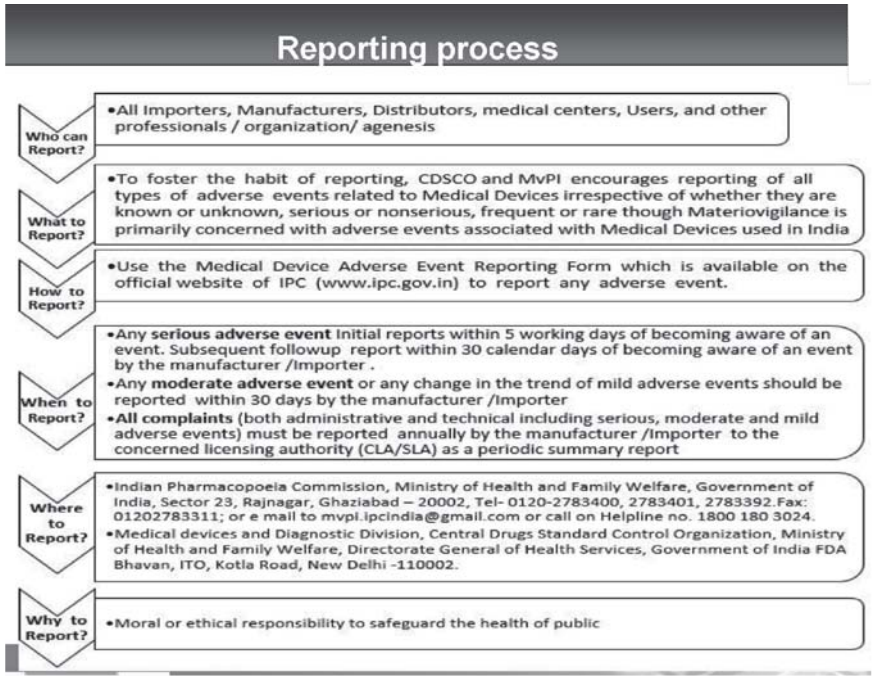
- "Post Marketing Surveillance" means systematic process to collect and analyse information gained from IVD that have been placed in the market.
- Manufacturer/Importer need to provide Device Master File/dossier (Medical device & IVD as per the Fourth schedule of MDR-2017, which should contain the Post Marketing Surveillance or Vigilance Reporting procedures and data collected by the manufacturer encompassing the details of the complaints received and corrective and Preventive actions taken for the same.
- In case of New IVD, PMS is critical, subsequent to approval of an, it shall be closely monitored for their clinical safety & performance once they are marketed.
- The PSURs shall be submitted every six months for the first two years after marketing approval of the IVD.

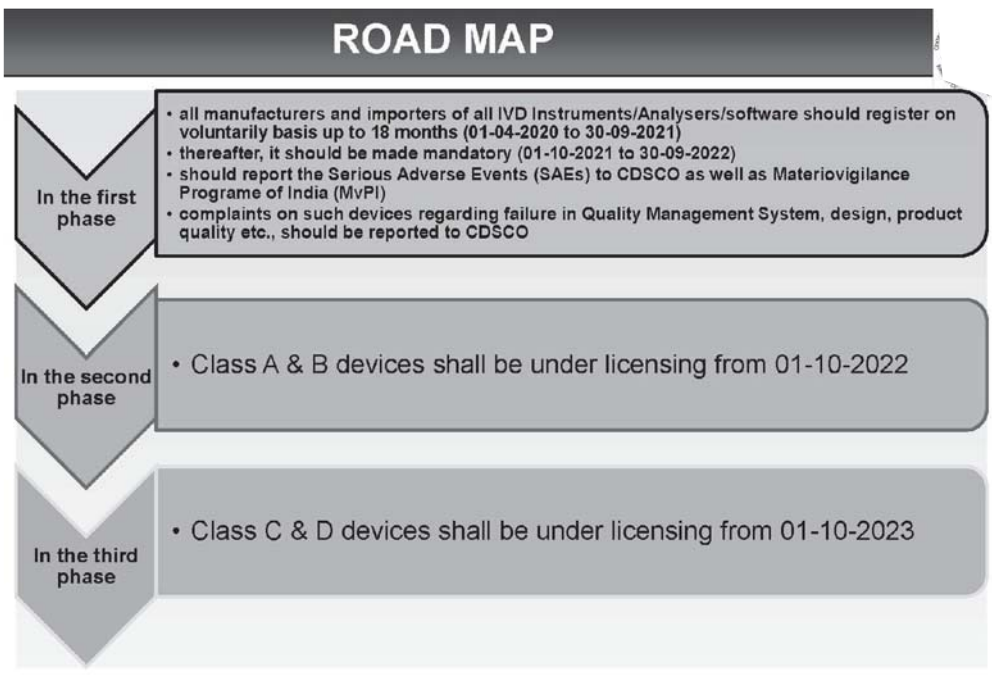
Responsibilities of the various parties in PMS

End users / procurers	Manufacturers or Importers	Licensing authorizes CDSCO /SLA	Testing Laboratories
•Use IVDs as per manufacturer's instructions •Maintain storage of IVDs •Identify problems •Document problems •Report complaints •Cooperate in sample verification testing	•Perform quality control lot release •Classify complaints •Report to concerned regulatory authority •Undertake root cause analysis •Take corrective action	•Conduct stringent pre-market assessment. •Designate testing lab for quality check of IVDs •Adopt Risk based approach •Collect reports of complaints •Oversee lot verification testing •Collect other post-market •Information. •Site inspecting / investigation (if required) •Take regulatory action	• Receive and store samples of test kits • Prepare and maintain lot verification testing panels • Conduct testing and record data • Analyze data and report a failures to Licensing authorizes (CLA/SLA).

Adverse event classifications and Examples

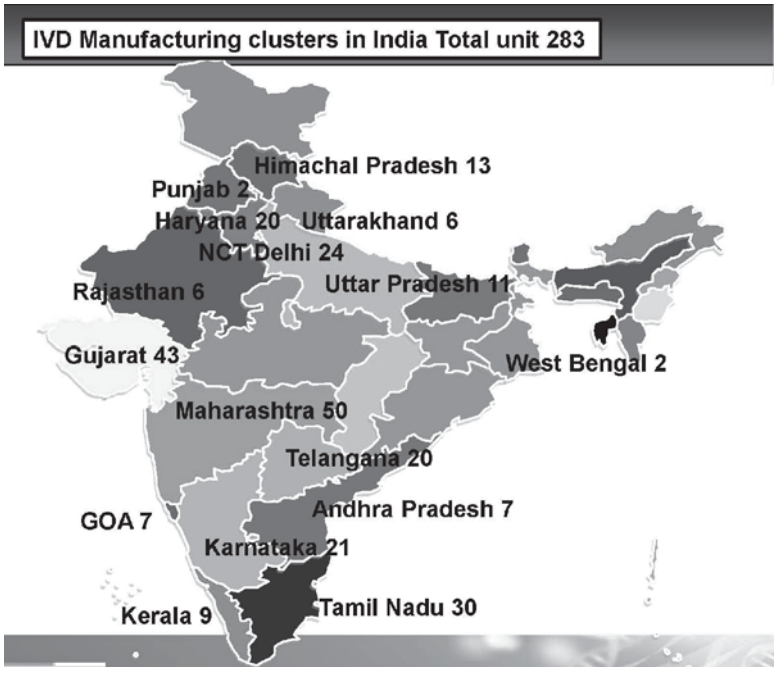
Classification	Description	Examples
Serious adverse event	. Death of patient, the user or other person . Any false negative result	. One or more individuals receive an COVID-19 contaminated blood product that was screened as COVID-19 negative by an COVID 19 RDT. An individual presenting for ART initiation has testing repeated to confirm their HIV diagnosis. The re-testing results are negative.
Moderate adverse event	Any false-positive result (that resulted in misdiagnosis)	. Invalid rate exceeds 5%. . High background for rapid diagnostic tests. . A component labeled lyophilized is found to be fluid, this is discovered by the user before use. . Greater than expected discrepant rate between assay 1 and assay 2 within a testing algorithm.
Mild adverse event	. Deficiency found by the user before use . The adverse event caused by a device exceeding its shelf life . Malfunction protection operated correctly	. The Control line does not appear . Desiccant has changed color.. . A component labeled lyophilized is found to be fluid, this is discovered by the user before use. . The packaging of a device is labeled with the caution 'do not use if the packaging is opened or damaged'. Before use


Reporting process
Who can Report?
•All Importers, Manufacturers, Distributors, medical centers, Users, and other professionals / organization/ agenesis
What to Report?
•To foster the habit of reporting, CDSCO and MvPI encourages reporting of all types of adverse events related to Medical Devices irrespective of whether they are known or unknown, serious or nonserious, frequent or rare though Materiovigilance is primarily concerned with adverse events associated with Medical Devices used in India
How to Report?
•Use the Medical Device Adverse Event Reporting Form which is available on the official website of IPC (www.ipc.gov.in) to report any adverse event.
When to Report?
•Any serious adverse event Initial reports within 5 working days of becoming aware of an event. Subsequent followup report within 30 calendar days of becoming aware of an event by the manufacturer /Importer .
•Any moderate adverse event or any change in the trend of mild adverse events should be reported within 30 days by the manufacturer /Importer
•All complaints (both administrative and technical including serious, moderate and mild adverse events) must be reported annually by the manufacturer /Importer to the concerned licensing authority (CLA/SLA) as a periodic summary report
Where to Report?
•Indian Pharmacopoeia Commission, Ministry of Health and Family Welfare, Government of India, Sector 23, Rajnagar, Ghaziabad – 20002, Tel- 0120-2783400, 2783401, 2783392.Fax: 01202783311; or e mail to mvpi.ipcindia@gmail.com or call on Helpline no. 1800 180 3024.
•Medical devices and Diagnostic Division, Central Drugs Standard Control Organization, Ministry of Health and Family Welfare, Directorate General of Health Services, Government of India FDA Bhavan, ITO, Kotla Road, New Delhi -110002.
Why to Report?
•Moral or ethical responsibility to safeguard the health of public


ROAD MAP
In the first phase
• all manufacturers and importers of all IVD Instruments/Analysers/software should register on voluntarily basis up to 18 months (01-04-2020 to 30-09-2021)
• thereafter, it should be made mandatory (01-10-2021 to 30-09-2022)
• should report the Serious Adverse Events (SAEs) to CDSCO as well as Materiovigilance Programe of India (MvPI)
• complaints on such devices regarding failure in Quality Management System, design, product quality etc., should be reported to CDSCO
In the second phase
• Class A & B devices shall be under licensing from 01-10-2022
In the third phase
• Class C & D devices shall be under licensing from 01-10-2023

Challenges

- Testing Labs and panel for PE & CPE
- Harmonisation of testing protocol and specification



Conclusion

- To ensure Safety, Quality, and Performance
- Harmonization with Global Regulations
- Promote the Growth of the industry
- Predictable, Transparent , simple regulatory process
- Support innovation

Achievements

- For addressing various questions on regulatory practices in IVD, Frequently Asked Questions (FAQ) on In vitro diagnostic medical devices is uploaded on CDSCO website. Also regular interactions are taking place with all the stakeholders to resolve their regulatory issues.
- CDSCO has also started Public relations office (PRO) to assist any start-up/ innovator/ industry person in facilitating regulatory clearances. Function from 10:00 am to 5.30 pm in all working days. Monday & Wednesday specific to IVD.
- Issued Draft guidance on Stability, PER & PMS for IVD.
- All licenses Import/ manufacturing, Permission of clinical performance evaluation, Permission for new IVD MD, Registrations of Private IVD MD testing Labs, Post approval changes ,FSC, MSC,NCC processed in online portal.
- Organized stakeholders training and awareness programs on NEW MDR 2017 and online portal.
- Fast track clearances of COVID-19 IVD MD applications from March 2020 to till date same appreciated by various stakeholders.
- Latest list of approved COVID-19 kits are being uploaded in CDSCO website. As on 19/03/2023, total 553 approved including 276 PCR kits, 100 Rapid Antigen Tests, 160 Rapid/ CLIA/ ELISA kits and 17 Antigen based Home test/self test kits for the detection of COVID-19 infection have been approved by this office.

Link for important IVD information

Copy of Gazette Notifications	https://cdsco.gov.in/opencms/opencms/en/Notifications/Gazette-Notifications/
List of IVDs (Kits & reagents) with Risk class	https://cdsco.gov.in/opencms/export/sites/CDSCO_WEB/Pdf-documents/medical-device/Classificationg1.pdf
Revised guidance list of Laboratories to be considered for conducting Performance Evaluation of In-Vitro Diagnostics	https://cdsco.gov.in/opencms/export/sites/CDSCO_WEB/Pdf-documents/GuidanceonPER-updated13-Feb2020-Final.pdf
FAQ in Vitro Diagnostic IVD Devices revised 2022	https://cdsco.gov.in/opencms/export/sites/CDSCO_WEB/Pdf-documents/IVD/FAQs/CDSCO-IVD-FAQ-03-2022-.pdf
List of IVDs (Analyzers ,Instruments &software) with Risk class	https://cdsco.gov.in/opencms/opencms/system/modules/CDSCO.WEB/elements/download_file_division.jsp?num_id=NzQ1Mg==
Draft Guidance document on Overview on Performance Evaluation / External Evaluation of In vitro Diagnostic Medical Device (IVDMD)	https://cdsco.gov.in/opencms/opencms/system/modules/CDSCO.WEB/elements/download_file_division.jsp?num_id=ODc2Ng==
Draft Guidance document on Guidance on Stability Studies of In-Vitro Diagnostic Medical Device (IVDMD)	https://cdsco.gov.in/opencms/opencms/system/modules/CDSCO.WEB/elements/download_file_division.jsp?num_id=ODc2OA==
Draft Guidance document on Guidance on Post-Market Surveillance of In-vitro Diagnostic Medical Device (IVDMD)	https://cdsco.gov.in/opencms/opencms/system/modules/CDSCO.WEB/elements/download_file_division.jsp?num_id=ODc2Nw==

Awareness

- 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'

"Without diagnostics, treatment is blind"

Diethylene Glycol Contamination in Cough Syrups

by

Shri. Ganadhish Kamat
Quality Professional, Hyderabad

Introduction:

Cough syrups have long been trusted as a remedy for relieving symptoms associated with respiratory illnesses, providing comfort during cold and flu seasons. However, the discovery of diethylene glycol (DEG) contamination in certain cough syrups has raised serious concerns about the safety and quality of these products. DEG, a toxic substance primarily used in industrial applications, poses significant health risks when ingested or absorbed by the human body. This article explores the issue of DEG contamination in cough syrups, its implications for public health, and the measures which should be taken to address this alarming problem.

Understanding Diethylene Glycol Contamination:

Diethylene glycol is an organic compound primarily used as an industrial solvent, particularly in the production of polymers, resins, and antifreeze. It is significantly cheaper than other common solvents and additives used in pharmaceutical dosage forms such as Propylene glycol and Glycerine. Unfortunately, its chemical properties and low manufacturing costs have led to instances of DEG being fraudulently or unintentionally used as a substitute or adulterant in the additives such as Propylene glycol and Glycerine used in pharmaceuticals including cough syrups.

Health Risks Associated with DEG:

The ingestion or absorption of diethylene glycol can have severe consequences for human health. It can cause kidney failure, damage the liver, affect the central nervous system, and even lead to death in extreme cases. Symptoms of DEG poisoning include nausea, vomiting, abdominal pain, dizziness, seizures, and respiratory issues. Children, due to their smaller body size, are particularly vulnerable to the toxic effects of DEG

Cases of DEG Contamination in Pharmaceuticals-

Over the years, several incidents of DEG contamination in cough syrups and other pharmaceuticals have come to light, causing significant harm and loss of life.

The first and one of the largest outbreaks, which resulted in 105 deaths, occurred in the United States of America (USA) in 1937. In this case DEG was used by development scientist as solvent for formulating sulphanilamide elixir due to lack of knowledge about it's toxicity. This incident led to the passing of the 1938 Federal Food, Drug and Cosmetic Act. The Act requires manufacturers to establish safety and efficacy of the drugs before they are introduced into the marketplace. Since that time, there have been no DEG mass poisonings in the USA, but many have occurred in the developing world.

Cough syrup contaminated with DEG led to the deaths of 33 of 36 children known to be affected in India in 1998 and 85 of 109 children known to be affected in Haiti in 1995–1996. In both outbreaks, patients had unexplained acute renal failure, a characteristic of moderate-to-severe DEG poisoning. In 1995, an American Physician volunteering in Bangladesh reported deaths in children due to Government issued cough syrup. Although the government denied that anything was wrong with the syrup, but the sample when tested in US was found to be contaminated with DEG. No specific actions to prevent recurrence were taken post these incidences.

A case of cough syrup containing DEG resulting in the deaths of 365 people, mostly children was reported in Panama in 2006-07. The diethylene glycol used in the contaminated syrup originated from a Chinese manufacturer, which exported it as industrial "TD glycerine" with a shelf life of one year. The letters "TD" were short for "substitute" in Chinese. When Panama-based company received the material from a Spanish trader, it changed the name to "glycerine" and the expiration date to four years before selling it to the government of Panama. Neither the trading companies involved nor the government lab in Panama that processed the ingredient tested the substance for verification. Responsible people were severely punished including death penalty to seniormost person involved.

In 2020-21, another 12 children died in India (J&K) after consuming cough syrups.

In death of more than 100 children were reported in Indonesia due to acute kidney injuries after consuming cough syrup contaminated with DEG and ethylene glycol.

Recently WHO reported deaths in more than 100 children in Marshall island, Gambia and Uzbekistan due to consumption of cough syrups made by three different drug manufacturers from India. After initial denial and attempts to prove that nothing was wrong in the cough syrups, CDSCO conducted audits at the manufacturing sites and eventually suspended their manufacturing licences due to lapses seen during the audits. Pharmexcil suspended the

membership of one of the company and Commerce ministry issued notice that all the cough syrups need to be tested at government laboratories before export.

Except for the first incident which occurred in US, no comprehensive measures have been taken to ensure that such incidences don't get repeated. For the incidences which occurred in India or related to products manufactured in India, I haven't seen any comprehensive investigation conducted by regulatory agency to understand the root cause/s and taking concrete actions to ensure that all medicines manufactured and distributed in India are safe.

Potential causes for DEG contamination

Based on limited information available in public domain related to these incidences and the knowledge of Pharmaceutical quality systems, following are likely causes for DEG contamination in cough syrups and other pharmaceutical preparations –

1. Intentional use of diethylene glycol by the manufacturer to save cost. This is highly unlikely because the toxic effects of DEG are now well known and no manufacturer with sane mind will intentionally add toxic chemical which can result in death, in their products, as it will damage their reputation and destroy their business.

2. Contamination of commonly used pharmaceutical ingredients such as Propylene glycol and Glycerine with DEG. Such contamination can occur due to intentional adulteration by manufacturer or the trader to reduce cost or accidental contamination due to mix-up or wrong labelling of containers if these chemicals are manufactured or handled in common facility.

3. Present in the ingredients, being by-product of manufacturing process.

Manufacturing processes of Glycerine & Propylene glycol

To understand what impurities can come from the manufacturing processes, we need to first understand various paths by which Glycerine and Propylene glycol are manufactured. Various commonly used manufacturing processes for the two ingredients and likely by-products by these routes are summarized below –

Ingredient	Method of production	Potential contaminants
Glycerine	Hydrolysis, saponification, alcoholysis of animal fats and vegetable oils	Tri methylene glycol, Formic acid, Various aldehydes, ketones, sulphur compounds, etc
	From petrochemicals (synthetic glycerine)	Acrolein, Methanol & Di chlorohydrin / Epichlorohydrin
	Microbial fermentation of sugars followed by purification using solvents	Residual solvents such as dioxane, ether, butanol By-products such as polyols and polyhydroxy alcohols.
Propylene glycol	Hydration of Propylene oxide	Di & Tri-propylene glycols along with other glycols, Chlorohydrin, Hypochlorous acid & Propylene oxide

Review of manufacturing processes and likely by-products did not indicate possibility of DEG contamination in these ingredients during manufacturing although there is possibility of formation of other toxic contaminants.

Based on above information the most likely cause for DEG contamination in Glycerine or Propylene glycol appears to be intentional adulteration for profiteering or un-intentional mix-up or wrong labelling.

While above are the technical causes for the contamination, the major underlying root cause for such repeated issues and poor quality of drugs in India is outdated drug laws and regulatory system. Some of the major flaws in our drug laws which have resulted in such incidences are –

1. The Central drug control organization does not have direct control over the state FDAs which work as parallel controlling agencies.

2. Lack of scientific evaluation of drug applications. After initial 4 years, state licensing authority can grant product permission. Each state follows different process for granting manufacturing licenses and many states grant such licences based on review of just limited administrative information without doing any technical evaluation to ensure safety and efficacy of the drugs.

3. There is no procedure for controlling changes to the process and product, So the manufacturers are at liberty to make any changes including changes in formulation, changes in vendors, changes in process etc without even informing to regulatory agency.

4. Recall process is extremely ineffective in India due to loose regulations.

5. There is no regulation for control of vendors and supply chain.

Corrective and Preventive actions required

Based on the potential causes identified earlier following controls need to be established to prevent recurrence of issues like DEG contamination and preventing occurrence of other serious contamination issues –

1. Vendor Qualification

The ingredients should be sourced only from approved vendor. Sourcing should be done directly from the manufacturer or their authorized distributor.

The vendor qualification should not be restricted to just review of self-assessment questionnaires and the data sheets provided by the vendor but should also include the audit of manufacturing site. The manufacturer as well as the distributor should be covered in vendor qualification process. Apart from reviewing the systems & processes and compliance to them, the audit should focus on understanding the manufacturing process to evaluate adequacy of process controls and specifications to effectively control the quality of the ingredients.

2. Quality agreement

Quality agreement should be signed with the vendor, clearly defining the terms and conditions, responsibilities and specifications. Responsibility of the vendor should include providing timely information about quality and process related changes to enable evaluation of the impact of those changes on the quality of the material and the drug product.

3. Incoming material inspection

Indian drug laws require all the raw materials to be used in Pharmaceuticals to be tested to ensure compliance to specifications. The law and rules thereunder however are silent about sampling process. Most companies collect sample from multiple containers selected from total containers, following inhouse developed sampling plans and make pool sample for performing the testing as per specifications which are largely derived based on the Pharmacopoeial monographs. IP and USP monographs for Glycerine and Propylene glycol have prescribed GC method for quantitative determination of Diethylene glycol and Ethylene glycol with limit of not more than 0.1%.

Just relying on testing of pool sample however provide very little assurance. For example, if out of total 10 containers received, company samples 4 containers following commonly used formula of $\sqrt{n+1}$, remaining 6 containers will not be sampled at all and if one or more of those contain DEG or EG fully or partially, it will go undetected. Similarly, if one of sampled container contain DEG or EG up to 0.3%, the pooled sample will show result below 0.1% and the material will get released. The syrup produced using one contaminated drum will however have higher level of DEG and may result in adverse event.

To address such issues following actions should be implemented in addition to vendor qualification described earlier.

1. At the time of receipt, it should be verified that the material is received in manufacturer's original container with manufacturers seal (preferably serialized).

2. Unless the ingredient is manufactured in a dedicated facility and the systems and processes including labelling process has been validated, each drum should be sampled and subjected to ID test. Since Identification tests for Glycerine and Propylene glycol in USP monograph includes test for DEG and EG, contamination in any drum will get detected. Unfortunately, the test for DEG and EG is not part of Identification test in IP monograph for Glycerine. So apart from ID check on all individual containers, DEG/EG check also needs to be conducted on individual samples.

3. Rest of the tests may be done on the pooled sample provided consistency in the supply has been assured based on audit of manufacturing facility and results of past shipments. Number of containers which can be pooled together should be based on the sensitivity of the method, limits and the criticality of the test.

4. Regulatory changes

Many Indian companies, especially those who are doing business in advanced countries have implemented all or some of above-mentioned controls. To ensure that all the Pharma companies operating in India adopt these controls, Indian regulatory agency need to overhaul the antiquated drug laws to incorporate them in the law. The process for review of drug applications needs to be strengthened to identify all possible contaminants and impurities and to ensure that adequate controls are in place to ensure safety of the product. Drug law should also include procedure for controlling changes to approved application to ensure that manufacturer's do appropriate risk assessment while doing changes to the product and process. It is also necessary to revamp Pharmacovigilance system in India. Most adverse events are not getting reported due to lack of awareness or simple laziness. This may result in failure to detect early warnings. Government should develop PV portal accessible to everyone where, patients and healthcare givers can report any adverse events noticed while using a drug. India currently has verry low causality determination rate in most states. Due to this many deaths occurring due to such issues may go unreported and may not get investigated resulting in delay in controlling further damage. Regulations need to make it mandatory to correctly determine the cause of death and recording in national data base. Any abnormal trends should be investigated. Government also need to develop effective recall system in India so that in the event of any serious defect detected in the distributed medicines, further distribution can be quickly stopped there by preventing further damage.

5. Consumer awareness

While regulatory measures are crucial, consumer awareness is equally important in mitigating the risk associated with DEG contamination and other serious quality defects. Consumers should be educated and encouraged to report any suspected side effects (adverse events) immediately to the healthcare professionals and also report to Pharmacovigilance cell of manufacturer or government portal. Any abnormal trends should be detected and investigated. AI could be good tool for such signal detection.

Conclusion:

The presence of diethylene glycol contamination in cough syrups and other medications poses a significant threat to public health. The ingestion or absorption of the toxic substance can lead to severe health complications, making it imperative to address this issue effectively. Governments, regulatory bodies, and pharmaceutical manufacturers must work collaboratively to implement stringent quality control measures and raise awareness among consumers. By ensuring the safety and integrity of medications, we can safeguard the well-being of individuals and restore public confidence in these essential medications.

INFORMATION

M.PHARM & PHARM D SCHOLARSHIPS 2022-23 AWARDED BY TNPSW TRUST

Profile of 2nd Rank

PHARMACEUTICS

Name: Ms. K. Priyadharshini

Project Title: Nanotechnology Driven Approach with Collagen and Silver Nanoparticles loaded Mupirocin in Chitosan Hydrogel for Burn Wound Infection

College: PSG College of Pharmacy, Coimbatore

Guide's Name: Mr. V. Shankar

PHARMACEUTICAL CHEMISTRY

Name: Ms. Ahamed Nisha. K

Project Title: Design, Synthesis and Characterisation of Some Novel Benzimidadazolyl Pyrimidine Derivatives as Potential Anticancer Agents Inhibiting MTHFD2 enzyme

College: College of Pharmacy, Madras Medical College, Chennai

Guide's Name: Ms. R. Priyadharshini

PHARMACEUTICAL ANALYSIS

Name: Ms. Suriyapriya. K

Project Title: RP-HPLC Method Development, Validation and Forced Degradation studies of an antiviral drug Molnupiravir.

College: KMCH College of Pharmacy, Coimbatore

Guide's Name: Dr. K. Suresh Kumar

PHARMACOLOGY

Name: Mr. Mohankumar. R

Project Title: Evaluation of Anti-Oxidant and Anti-Urolithiatic Activity of Nathai Choori Seeds by Ethylene Glycol and Ammonium Chloride Induced Urolithiasis In Male Albino Wistar Rats

College: College of Pharmacy, Madras Medical College, Chennai

Guide's Name: Dr. M. Sakthi Abirami

PHARMACOGNOSY

Name: Ms. S. Kirubavathi

Project Title: Formulation, Standardization and Evaluation of Herbal Gel of Tabernaemontana Coronaria for Anti-Rheumatic Activity

College: College of Pharmacy, Madras Medical College, Chennai

Guide's Name: Dr. R. Vijaya Bharathi

PHARMACY PRACTICE

Name: Mr. Manikandan. S

Project Title: Effectiveness of Iron Supplementation on Consecutive Versus Alternative Days In Women with Iron Deficiency Anemia- A Randomized Comparative Study.

College: SRM College of Pharmacy, Chennai

Guide's Name: Dr. S. Sarumathy. M

PHARM D

Name: Mr. S. Lokeshwaran, Ms. Saranya. S

Project Title: Study on Occurrence of Adverse Drug Reaction in Intensive Care Unit

College: Sri Ramakrishna Institute of Para Medical Sciences, Coimbatore

Guide's Name: Dr. G. Andhuvan

NOTIFICATION

File No.X-11026/35/2022-VD
Government of India
Directorate General of Health Services
Central Drugs Standard Control Organization
(Veterinary Division)

FDA Bhawan, Kotla Road,
New Delhi-110 002, India,
Dated: 19 JUL 2023

CIRCULAR

Subject: Online application for the issuance of Form 11 (Test Licence) for Veterinary Vaccines /Drugs – regarding.

In order to streamline the regulatory submission procedure, the submission of applications for issuance for Form 11 (Test Licence) for Veterinary Vaccines/Drugs is now functional on Online System of SUGAM portal (www.cdscoonline.gov.in) the applicants seeking for such certificate/license shall apply through online portal as per the checklist in the developed modules.

The facility of offline submission of applications in hard copy may not be available for processing.

(Dr. Rajeev Singh Raghuvanshi)
Drugs Controller General (India)

To,

1. All Stakeholders through CDSCO website.
2. State/UT Licensing Authorities (for information and necessary action)
3. CDAC team.

MINISTRY OF HEALTH AND FAMILY WELFARE

(Department of Health and Family Welfare)

NOTIFICATION

New Delhi, the 2nd June, 2023

G.S.R. 409(E).—Whereas a draft of certain rules further to amend the Medical Devices Rules, 2017 was published, as required under sections 12 and 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940) vide notification of the Government of India in the Ministry of Health and Family Welfare (Department of Health and Family Welfare) number G.S.R. 157 (E), dated the 1st March, 2023, in the Gazette of India, Extraordinary, Part II, section 3, sub-section (i), inviting objections and suggestions from persons likely to be affected thereby, before the expiry of a period of seven days from the date on which the copies of the Official Gazette containing the said notification were made available to the public;

And whereas, copies of the said Official Gazette were made available to the public on the 1st March, 2023;

And whereas, objections and suggestions received from the public on the said draft rules have been considered by the Central Government;

Now, therefore, in exercise of the powers conferred by sections 12 and 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940), the Central Government, after consultation with Drugs Technical Advisory Board, hereby makes the following rules further to amend the Medical Devices Rules, 2017, namely:—

1. (1) These rules may be called the Medical Devices (Amendment) Rules, 2023.

(2) They shall come into force on the date of their publication in the Official Gazette.

2. In the Medical Devices Rules, 2017 (hereinafter referred as the said rules), in rule 3, after sub-rule (zu), the following sub-rule shall be inserted namely:–

'(zua) "State Medical Devices Testing Laboratory" means a medical devices laboratory established or designated by the State Government under sub-rule (3) of rule 19'.

3. In the said rules, in rule 18, in sub-rule (1), after the words "Central Government", the words "or, as the case may be, the State Government" shall be inserted.

4. In the said rules, in rule 19,–

(a) for the marginal heading, the following marginal heading shall be substituted, namely:–

"Medical Device Testing Laboratories";

(b) after sub-rule (2), the following shall be inserted, namely: —

"(3) (1) The State Government may, by notification, establish State Medical Devices Testing Laboratory for the purpose of, –

(a) testing and evaluation of medical devices; or

(b) to carry out any other function as may be specifically assigned to it.

(4) Without prejudice to provisions of sub-rule (3), the State Government may also designate any laboratory having facility for carrying out test and evaluation of medical devices as State Medical Devices Testing Laboratory for the purposes specified in sub-rule (3):

Provided that no medical devices testing laboratory shall be so designated unless it has been duly accredited by the National Accreditation Body for Testing and Calibration Laboratories.".

[F. No. X.11014/7/2022-DR]
ARADHANA PATNAIK, Jt. Secy.

Note : The Medical Device Rules, 2017 were published in the Official Gazette vide notification number G.S.R. 78(E), dated the 31st January, 2017 and last amended vide notification number G.S.R. 777(E), dated the 14th October, 2022.

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Why are Indian Drugmakers Under the Lens?

What are the complaints? What are the regulatory processes for manufacturing, quality control and checks? What is the role of the Central Drugs Standard Control Organisation? What does India need to do to redeem its reputation in the global pharma industry?

The story so far: Since October last year, Indian Pharma companies have been under constant international scrutiny for exporting allegedly contaminated drugs, which have led to deaths of children. Recently, Nigeria raised the red flag on two oral drugs; Cameroon too sounded an alarm over another cough syrup reportedly made in India when several children died. Sri Lanka called out two drugs manufactured in India linking them to adverse reactions in several patients. In the latest move, Gambia has declared that from July 1, it is running strict quality control checks on all pharma products shipped into the country, before they leave Indian shores.

Has India launched a probe?

Soon after Gambia reported deaths of at least 70 children related to a contaminated cough syrup made in India, in December last year, reports from Uzbekistan of at least 18 children dying after consuming cough syrup contaminated with high amounts of diethylene glycol (DEG) or ethylene glycol poured in. The pharma company, Marion Biotech's licence was cancelled by the national watchdog — the Central Drugs Standard Control Organisation (CDSCO) — in March, but the Ministry of Health and Family Welfare has not answered any questions on the probe that was launched. A senior health official had earlier told The Hindu that the back-to-back allegations were a 'conspiracy' against the Indian pharma industry which is pegged at $42 billion.

The complaints from across the world on quality of Indian drugs does not seem to stop. The latest in line are alerts from Sri Lanka, where patients are reported to have died after being administered anaesthetic drugs made in India, and that an eye medication had caused visual impairment in 10 patients. Nigeria's National Agency for Food and Drugs Administration and Control found a batch of oral paracetamol and another cough medicine manufactured by companies based in Mumbai and Punjab to be sub-standard.

What has led to the loss of confidence?

While Gambia has appointed Mumbai-based Quntrol Labs to independently assess the manufacturing plants and drug samples of Indian exporters who ship drugs to Gambia from July onwards, The Hindu has learnt that it is not the first such African country to have a checking system in place. “Mozambique has been checking samples from all batches of medicines before they are exported from India to its shores,” Riddhi Jhaveri, founder of Quntrol Labs, told The Hindu. For instance, Ms. Jhaveri says, in the case of a sample of paracetamol drug — Azithromycin 500 mg — that was tested by Quntrol, it was found that there was only 20 mg of azithromycin instead of 500 mg. “We have a database of more than

500 exporters whose batch samples we analyse, and in the past several years we have picked up nearly 40 to 45 non-conformities in the samples," said Jhaveri.

In fact, Nigeria has been more careful. Not only does the Nigerian government get all pharmaceutical samples checked, it has also mandated that samples from all batches of chemicals, food, medical devices and cosmetics be checked by an independent assessor.

Why are regulators failing to take action against faulty manufacturing practices?

The issue of contaminated cough syrup batches seeping into the supply chain and finding their way to paediatric patients is not only limited to exports. India has recorded at least five major DEG poisoning events since 1972, killing at least 84 children. The incidents occurred in Chennai, Maharashtra, Bihar, Haryana, and the latest being the 2019 case in Jammu.

Take the Jammu case for instance, where the Himachal Pradesh Drug Control Administration (HPDCA) said in court that the errant manufacturer Digital Vision did not have the proper facility to test finished products for contamination. The pharma company, however, was not in the dock for the first time. It has a poor track record of at least 19 prior violations. State Food and Drug Administration bodies are not mandated to disclose the reports of inspections conducted by them on the pharma manufacturing facilities that fall under their jurisdiction.

Ideally, when a manufacturer is found to be violating laws especially in cases where there is a threat to life or alleged deaths, a criminal prosecution of the persons who are responsible for manufacturing and marketing the drug should be launched. Instead of doing that, the Ministry of Health, CDSCO and the state regulator HPCDA keep passing the buck. "Under India's convoluted drug regulatory law, the Centre is responsible for imports and approving new drugs based on safety and efficacy data but the licensing and prosecutions of pharma companies is the responsibility of State governments," write Dinesh Thakur and Prashant Reddy, co-authors of The Truth Pill, a book on how drug regulation works in India.

Why are pharma companies not punished?

Merely suspending or cancelling the manufacturing licence of a pharma company is not enough, says Ms. Jhaveri. "Suspension or cancellation of licence may lead the owners to start the same business but under a different name. This is not enough. But we rarely hear about criminal action being taken against the manufacturers under the law," she adds.

Under the Drugs and Cosmetics Act, 1940, manufacturers not adhering to good manufacturing practices can be subjected to a maximum punishment of imprisonment for life. Even when prosecutions are filed, the cases move at a snail's pace in courts. For instance, Thakur and Reddy note that in Andhra Pradesh, of the 54 judgments in cases filed against pharma companies between 1999 and 2017, the state was able to secure convictions

in only eight cases. Poor conviction rate was due to glaring errors committed by drug inspectors including shoddy paperwork, failure to seize, record its condition of storage and label the samples properly, as also the failure to complete the testing process of samples before its expiry date.

It does not help that the CDSCO is perennially reeling under a shortage of drug inspectors. A 2019 report titled 'Drug Regulation in India: The Working and Performance of CDSCO and SDRAs,' compiled by lawyers Shree Agnihotri and Sumathi Chandrashekaran, said that while there ought to be one drug inspector for every 50 manufacturing units and 200 pharmacists, there were vacancies in most States waiting to be filled. Karnataka was working at nearly half its sanctioned capacity for drug inspectors, while Himachal Pradesh had 27% vacant posts. In HP, nearly 15% posts were lying vacant.

Health experts say that if India wants to redeem its reputation, it will have to tighten the screws by ensuring robust pharma inspections and make sure that any slip-up by manufacturers is reported and prosecuted.

• Since October last year, Indian pharma companies have been under constant international scrutiny for exporting allegedly contaminated drugs, which have led to deaths of children. Recently, Nigeria raised the red flag on two oral drugs; Cameroon too sounded an alarm over another cough syrup reportedly made in India when several children died.

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Source: *The Hindu,* 2nd July 2023

Centre Mandates Drugs and Cosmetics Act's Schedule M for MSME Pharma Units

Small drugmakers in India will have to compulsorily follow good manufacturing practices detailed in the Schedule M of the Drugs and Cosmetics Act for better quality assurance, health minister Mansukh Mandaviya announced

The adherence by Pharma firms in the micro, small and medium enterprises sector to Schedule M, which details out practices related to shop floors, quality control system, quality check labs, production, cleaning of equipment and housekeeping, among others, will be implemented in a phased manner, the minister said after an interaction with industry representatives.

"This will help in quality assurance and also reduce compliance burden," Mandaviya said. "It is important for MSME pharma companies to be alert to quality of drugs and expeditiously move towards good manufacturing processes through self-regulation."

It is important for India to maintain its reputation as the pharmacy of the world, the minister stressed. The health ministry has been taking measures to ensure that the quality of medicines made in India is not compromised, especially after a few incidents of deaths globally, allegedly due to consumption of drugs made in the country.

In February, Tamil Nadu-based Global Pharma Healthcare recalled an entire lot of eye drops. Last year, cough syrups exported from India were linked to deaths of 66 and 18 children in Gambia and Uzbekistan, respectively.

"Our global position in the pharmaceutical sector is created through the quality of our products. We must undertake all possible steps to ensure that we strengthen this position in terms of value and quality. Hence, the role of self-regulation becomes critical," said Mandaviya.

The central government had in February conducted a workshop in Hyderabad with state drug regulators. As a part of the two-day camp, brainstorming sessions were conducted with a view to evolve a participative approach for time-bound implementation of policies and programmes.

The health minister has also directed the Drugs Controller General of India to take stringent action against those pharmaceutical manufacturing companies that are making spurious drugs.

He reiterated the government's zero tolerance towards manufacturers not adhering to quality compliance and making spurious medicines. "There shall be no compromise with the quality of drugs manufactured in India. Special squads have been formed to inspect drugs making companies across the country," he said.

In order to ensure the highest quality of pharma products, Mandaviya said regulatory authorities have started risk-based inspection and audit of manufacturing units. As many as 137 firms were inspected and action has been taken against 105 firms, the ministry said in a statement.

"Production has been stopped at 31 firms and 'Cancellation and Suspension of Product/Section Licenses' have been issued against 50 firms. In addition, a show cause notice has been issued to 73 firms, and warning letters to 21 firms," said the statement issued.

Source: *Hindustan Times,* 12th July 2023

More than 90 Million Indians Spend 'Catastrophic' 10-25% of Household Expenses on Healthcare

According to the Sustainable Development Goals (SDG) National Indicator Framework Progress Report 2023, a total of 31 million people living in families spend more that a quarter of their household expenditure on healthcare. The report indicated that the proportion of households spending between 10-25% of their expenditure on healthcare has shot up between 2017-18 and 2022-23.

Out of total 17 SDGs, the third goal aims at providing universal health coverage along with protection from catastrophic spending. This objective can be achieved by securing access to quality healthcare along with safe, affordable vaccines and medicines for everyone.

The report found that households with more than 10% spends on healthcare have raised from 4.5% to 6.7%. Similarly, families spending over 25% of their expenditures on healthcare have gone up from 1.6% to 2.3%.

Among several states, the maximum proportion of healthcare spending has been recorded in Kerala in 2022-23, with around 16% household spent over 10% of their expenditure and 6% of them spent over 25%. Other states that reported such significant increase in healthcare expenditure include Maharashtra, Karnataka, Uttar Pradesh, Odisha and Telangana.

According to NITI Aayog's June 2021 report, nearly 400 million Indians (30% of the population) lack any financial protection for health which leads to high out-of-pocket expenditure. The report also estimated that the actual number is likely to be higher due to uncovered population as a result of the existing coverage gaps in the PMJAY scheme.

Source: *Hindustan Times,* 1st July 2023

India's Pharma Exports Grew by 5% in April-May

Drug exports continue to be on the rise, despite instances of some desi pharmaceutical companies recalling their products from the US and reports of deaths in Gambia and Uzbekistan allegedly linked to cough syrups made in India last year. The pharmaceutical exports from the country recorded a 5% increase during April and May this year over the corresponding period in 2022.

S V Veeramani, chairman, Pharmaceuticals Export Promotion Council of India (Pharmexcil), set up by the Union ministry of commerce and industry said, India recorded pharmaceutical exports to the tune of $4.3 billion in April and May this year. “While there was a decline in exports of several commodities, the pharmaceutical exports have gone up 5% when compared with the corresponding period last year. While the US, which is the top market for India and accounts for more than 30% of our total pharmaceutical

exports, there is a 10% growth, Europe also witnessed a good growth. This is a testimony that the Indian pharmaceutical is not affected due to a couple of instances," he told TOI. He was speaking on the sidelines of 'Pharmac South 2023', a pharmaceutical expo inaugurated.

India's share in the global pharmaceutical exports market is 10% by volume. Known as the pharmacy of the world, India is home for 7,000 pharmaceutical units. Of this, 2,000 units have WHO's Good Manufacturing Practices certification, 700 are US Food and Drug Administration approved facilities and 600 approved by the European countries. The Indian pharmaceutical market was at $50 billion in FY23. While exports accounted for $25.4 billion, the rest is catered for the domestic market. "We are expecting around 10% growth this year," Veeramani added.

Daara B Patel, secretary general, Indian Drug Manufacturers' Association (IDMA) said, India caters to almost 200 countries in the world. "What has happened is unfortunate. But, I do not think that the industry will have a setback for the simple reason that the industry is very large in India," he said, responding to a query on the impact on the pharmaceutical sector due to the past instances.

Source: *The Times of India,* 15th July 2023

Drug Makers Convicted for 'Objectionable' Advertisement

A Chennai court convicted a drug manufacturer from Himachal Pradesh, distributors, and a retail pharmacy store for selling contraceptives with 'objectionable' advertisements on the wrappers.

The state drug control department received a complaint that a pharmacy in Kodambakkam had advertised that unplanned pregnancy could be avoided if women took one of their tablets' within three days after unprotected sex or failure of birth-control methods.

Based on this complaint, the Kodambakkam drug inspector inspected the pharmacy and found a carton containing tablet strips and leaflets on it.

The advertisement printed on them stated: "Postpone-72 needs to be taken as soon as possible but not later than 72 hours after unprotected sex. The earlier you take it the more effective it will be. Please refer to the enclosed leaflet for more information."

The inspector issued a show-cause memo to the pharmacy owner asking why action should not be taken against him and others involved in manufacturing and selling of the Levonorgestrel tablet.

Not satisfied with the replies, the inspector invoked the Drugs and Magic Remedies (Objectionable Advertisements) Act, 1954 a law which is rarely used by drug enforcement agencies in the country to book the Kodambakkam store, Acme Formulations in Himachal Pradesh, and Leeford Healthcare Limited in Punjab.

After obtaining the Tamil Nadu Drug Control Director's sanction order, the inspector filed a case with the Saidapet Metropolitan Magistrate Court in 2018. The counsel for the accused argued that the drug was licenced and even the advertisement was approved by the Union government.

The inspector in response stated that the government nod was to advertise only 0.15 mg tablets and not 1.5 mg tablets as printed on the seized cartons, leaflets, and strips. Overdose of oral contraceptives might lead to nausea, breast tenderness or vaginal bleeding, say doctors.

Therefore, the court found the accused guilty under section 7(a) of the said Act.

They were sentenced to pay a fine of 10,000 each and undergo one-month simple imprisonment.

Source: *The Times of India,* 25th July 2023

Tamil Nadu Intensifies Drive Against Substandard Drugs

The Tamil Nadu drug control department, which recently intensified its crackdown against substandard medicines, will soon start prosecution proceedings againts 17 drug manufacturers from Himachal Pradesh and Uttarakhand and four local drug makers.

Ever since reports emerged linking child deaths in the West Afrinacan nation of Gambia to drug makers in India, regulatory agencies across the country have stepped up vigil and officials in Tamil Nadu in the last four weeks have collected more than 7,000 samples from hospitals, retail pharmacies, drug manufacturing sites. Tests at government labs here showed 21 were Not Standard Quality (NSQ). Drug inspectors, who tracked the source to manufacturers in the northern states in 17 cases, observed lapses in medicine quality.

TN drug control authorities said that either the raw material or final product was stored in an improper manner making them prone to contamination and most were anti-diabetic, anti-hypertension, or cardiovascular drugs.

Doctors say consuming these substandard medicines will compromise the treatment of the disease. “For instance, we assume that a 10 mg tablet to a diabetic or cardiovascular patient will help bring down the blood sugar level or act as an effective blood thinning agent. But if the tablet is ineffective, then it will result in further complications in the long run,” said Dr AK Ravi Kumar.

Also, some of these substandard drugs might have preservatives to which some patients can develop allergies. To avoid further damage, the state drug control department has now obtained sanction orders to prosecute these manufacturers at the court of law.

This includes 16 stores which illegally sold habit-forming drugs (painkillers) which ideally should be sold only on doctors' prescriptions. Their licences have been temporarily suspended.

"There is no doubt erring retailers should be punished but of late we have reduced such cases to a large extent by conducting regular awareness sessions for our members.," said K K Selvan of Tamil Nadu Chemists and Druggists Association. At the same time, 80% of the anti-social elements arrested sourced the drug through online pharmacies. So, the government has to book them too, he said.

Source: *The Times of India,* 26th July 2023

Soon, You May Not be Forced to Buy Entire Strip of Tablets

You may not have to buy the entire strip of tablets or capsules when you need only a few of them in the near future.

The consumer affairs ministry is working on a plan with the industry to have perforated medicine strips, mentioning the manufacturing and expiry dates on each segment, so that even when you buy a few tablets, the torn strip will have all the necessary details. The other option being explored is to have either QR codes on medicine strips or on each table "depending on the viability".

Sources said the options were being explored in consultation with the industry after the National Consumer Helpline (NCH) run by the consumer affairs ministry saw an increase in complaints of chemists insisting customers on buying the entire strip.

The ministry recently held a round of consultations with senior representatives of the Pharma and medical devices industry which was attended by top officials of the Drug Controller General of India too. Officials said the issue was discussed and the ministry has suggested that new technologies should be explored for packaging medicines.

Officials said the forced buying of a full strip of medicine leads to wastage and puts unnecessary financial burden on customers. "We've suggestions to adopt perforation technology to cut the strip and also to print manufacturing and expiry date on each strip and even use QR code. The main focus is also to see that there is not much additional cost on consumers," said an official.

TOI has learnt that the industry representatives have pointed out that printing QR code on each tablet may cost less than 10 paise.

Source: *The Times of India,* 25th May 2023

Need to Amend Schedule P of D&C Act to Include Stringent Norms on Disposal of Unused & Expired Medicines

There is a growing concern about the lack of stringent norms on disposal of unused and expired medicines that pose a threat to health and the environment. The key issue is the lack of dedicated guidelines on the disposal under the Drugs & Cosmetics Act. Currently, only the Central Pollution Control Board mandates Biomedical Waste Management Rules.

Experts opine that one option could be to modify Schedule P of D&C Act that describes provisions for the shelf-life and storage conditions of various drugs, to incorporate 'Expired and unused medicines' from households. This could be through bins that can be kept with lock and key, at pharmacy outlets or any other designated place, until they are collected by the biomedical waste aggregators.

On the occasion of the World Environment Day observed annually on June 5, even if this year's theme is #BeatPlasticPollution, environmental experts call for a concerted effort in this direction on the disposal of unused and expiry dated medicines.

Scientifically it is proven that incineration of these medicines at prescribed specifications within the Bio-Medical Waste Guidelines, issued by the ministry of forest and environment is the only way to go. However, the weakest link in the entire process is collection/segregation of the unused and expired medicines from households. No guidelines are available for their storage at a location, permissible by law, prior to the final stage of disposal through incineration. The developed world has established take-back provisions from the community at designated time and place. Few countries that have a robust sewage system permit the use of toilet flushing, stated experts.

Data collected from surveys conducted by Delhi Pharmaceutical Trust reveals that almost 80% of such medicines collected from households are disposed either through the municipal waste dumps or by flushing through the toilet.

Quoting a 2020 study of a locality in Delhi, experts said for a population of 2.5 crore, comprising 50 lakh families average unused/expired in a household accounted for 15-30 units annually. The estimated expired medicines per family was 10 crore units. The trash was 6.3 crore units. The returns of expiry-unused drugs from pharmacies was 1.7 crore units. Those flushed down to the toilet was 1.3 crore units.

Such estimates, for the whole country, are not available, adding to lack of data hindering policy development. Studies conducted by other institutions reveal similar concerning results, they added.

In the absence of clear-cut guidelines, only some large and few MSME

pharmaceutical manufacturers dispose of them as per their standard operating procedures, incinerate and document disposal details. Pharmacy outlets too are seen to periodically put the stocks in boxes labelled as 'Expired medicines Not For Sale'. But experts noted that many a time disposal from pharmacy outlets are also not clearly known and uniformity may not exist.

Some experts feel that the nearest place that consumers can access is their pharmacy outlets, who can if permitted be a part of the chain to receive household unused and expired medicines.

Alternatively, municipal corporations may be asked to keep separate bins with lock and key at predefined locations for unused-expired medicines. “Since pharmacy outlets cannot account for these stocks, the provisions of the law need to be suitably amended. Involvement of the state drug regulators to provide guidelines or regulatory support is paramount. There is need for some pilot studies which are supported under Union government's Swachata Abhiyaan or other Sanitation programmes involving local authorities and drug controllers,” said a senior regulatory expert on condition of anonymity.

Source: *Pharmabiz,* 5th June 2023

379 of 89K Drug Samples Found Spurious, Rajya Sabha Told

Out of the 88,844 drug samples tested between April 2021 and March 2022, more than 2,500 were 'not of standard quality', while 379 have been found to be 'spurious', junior health minister Bharati Pravin Pawar told Rajya Sabha in response to a Parliament question.

In his written reply, Pawar said 592 prosecutions were launched for manufacturing, sale and distribution of spurious or adulterated drugs between April 2021 and March 2022, as per information received from drug controllers of various states and Union territories.

Health ministry sources said the government has stopped the production of drugs at 31 firms and cancelled or suspended the product licenses of 50 firms on finding non-adherence to quality control norms over the last few months. In addition, the sources said, show cause notice has been issued to 73 firms, and warning letters have been issued against 21 firms.

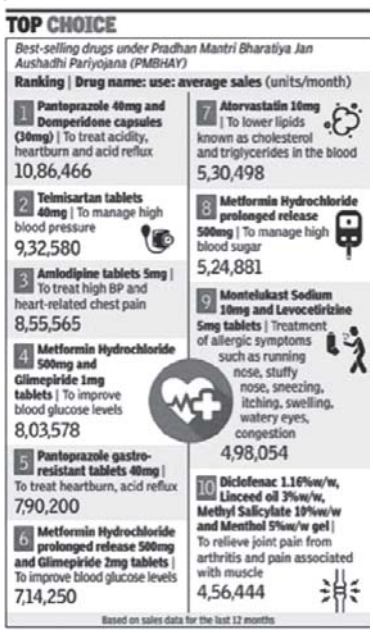
The action is result of a nationwide inspection of drug manufacturing units identified to be at the risk of manufacturing 'not of standard quality' being carried out by drug regulatory bodies in the backdrop of recent controversies over alleged adulteration in certain products, the sources said.

Source: *The Times of India,* 26th July 2023

Fixed-Dose Antacid Combo Top Drug at Jan Aushadhi Kendras

Pantoprazole (40 mg) and Domperidone (30 mg) capsules — a fixed-dose combination drug used for treating acidity-related problems — has emerged as the top selling product at Jan Aushadhi Kendras across the country. India has 9,484 Jan Aushadhi Kendras which sell generic drugs at affordable prices to the public under the Pradhan Mantri Jan Aushadhi Pariyojana (PMBJP).

According to sales data of these stores for the last 12 months, an average of 10.8 lakh units (each unit contains 10 capsules) of Pantoprazole (40 mg) and Domperidone (30 mg) capsules were sold at these stores on a monthly basis, the highest of all products sold by them. This was followed by Telmisartan (9.3 lakh units monthly sales) and Amlodipine (8.5 lakh units monthly sales), which are used to treat high blood pressure.



Ravi Dadhich, CEO, Pharmaceuticals and Medical Devices Bureau of India (PMBI), told TOI that the generic drugs sold at the Jan Aushadhi Kendras are 50%-90% cheaper than the branded alternatives, which is why more and more people are opting to buy them.

"Of the top 10 best-selling products at the Jan Aushadhi Kendras, 30% are products that are used to treat high blood pressure and diabetes. These are chronic conditions and treatment involves long-term medication. By opting for generic drugs, people can save a lot of money spent on drug purchase," he said.

The product basket of PMBJP comprises over 1800 drugs and 285 surgical equipment. Dadhich said that to ensure quality of products sold at the stores, all drugs are procured from World Health Organisation – Good Manufacturing Practices (WHO-GMP) certified suppliers. "Each batch of drug after its receipt at the warehouses is tested at laboratories accredited by 'National Accreditation Board for Testing and Calibration Laboratories' (NABL) for ensuring best quality," the PMBI CEO said.

The major therapeutic group of medicines available at the stores are: antibiotics and anti-infectives; cancer drugs; cardiovascular drugs; and vitamins and minerals among others. In 2019, the government also started selling sanitary napkins at Rs 1 per pad.

In 2014-15, there were only 80 Jan Aushadhi Kendras and their sales value stood at around Rs 7.29 crore.

Source: *The Times of India,* 17th June 2023

Medicines Patent Pool Deal to Make Cancer Drug Cheaper

In a move that would make certain cancer drugs more accessible and cheaper for patients, the Medicines Patent Pool (MPP) signed sub-licence agreements with three India-based companies, Eugia, Hetero and Dr. Reddy's Laboratories, along with Indonesian firm BrightGene to manufacture generic versions of Novartis' cancer treatment drug Nilotinib. The drug is used for the treatment of chronic myeloid leukaemia (CML), a type of blood-cell cancer.

These are the first sub-licence agreements that MPP has signed for a cancer treatment drug and are the result of a licence agreement signed between MPP and Novartis Pharma AG in October 2022 for their patented cancer medicine. Nilotinib is sold under the brand name Tasigna and marketed worldwide by Novartis.

According to information released by MPP, a United Nations-backed group working to increase access to, and facilitate the development of, life-saving medicines for low- and middle-income countries (LMICs), the selected manufacturers can manufacture generic versions of Nilotinib in India and seven middle-income countries and supply it in 44 territories included in the licence through a non-exclusive licence agreement, subject to local regulatory authorisation.

The licence includes the opportunity to develop and supply generic versions of Nilotinib in seven middle-income countries, namely Egypt, Guatemala, Indonesia, Morocco, Pakistan, the Philippines, and Tunisia, where patents on the product are pending or in force.

In 2020, the World Health Organization reported that more than 3.5 million new cancer cases were diagnosed in LMICs and premature deaths from cancer in these countries will rise from 2.3 million to 4 million in the next 20 years.

Charles Gore, executive director, MPP, said that they have worked with the four generic manufacturers to develop generic Nilotinib and bring an affordable treatment option to people diagnosed with CML in the selected countries. “Voluntary licensing is a truly impactful way of delivering affordable treatments to tackle the ever-rising burden of cancer in LMICs,” he said.

Lutz Hegemann, president of Global Health and Sustainability, Novartis, added that great gains have been seen in cancer survival in the richest countries over the last decade. “However, the benefit of our innovation is not reaching everyone, leaving a risk of cancer becoming a disease that disproportionately kills the poor. Through 'public-private partnerships', we aim to address barriers to healthcare and expand access to innovative treatment solutions for the long-term for as many people as possible — regardless of location or socio-economic situation. Today's announcement marks the next important step we are taking with our partner MPP as part of our commitment to the Access to Oncology Medicines (ATOM) Coalition,” he said.

Source: *The Hindu,* 22nd June 2023

India, US Will Work on Key Pharma Inputs to Cut China Reliance

India and the US have decided to collaborate on the development of active pharmaceutical ingredients and key vaccine input materials in what is being seen as an attempt to overcome the acute global dependence on China for the supply and production of crucial healthcare requirements.

The agreement to "seure, de-risk and strengthen" has been propelled by the experience of the two countries and the larger international community during the pandemic when China unsentimentally used its dominance of pharmaceutical ingredients, key starting materials and key vaccine input materials to the detriment of others. The crisis saw Chinese allegedly extorting huge profits for supplies that in many cases turned out to be sub-standard.

Currently, India is dependent on China and others for many pharmaceutical raw materials that are crucial for manufacturing drugs and vaccines. A collaboration with the US, site of cutting-edge research and India, with a well-developed pharmaceutical industry, will potentially ensure reliability and continuance of the supply chain in case there is any disruption in supply from the existing channels, experts said.

PM Modi and President Biden, in their joint statement, also underscored the need for strengthening the global collaboration network on research and development in medical countermeasures, vaccines, therapeutics and diagnostics to promote access to safe, effective, and innovative medical products in an affordable manner.

The leaders committed to holding a US-India Cancer Dialogue, hosted by President Biden's Cancer Moonshot, to bring experts together from both countries to identify concrete areas of collaboration to accelerate the rate of progress against cancer.

In their joint statement, PM Modi and President Biden applauded collaborations between research institutes of both countries on affordable cancer technology programs, including for the development of AI enabled diagnostic and prognosis prediction tools, and on diabetes research. They also called for expanded collaboration on digital health platforms including responsible use of cutting-edge technologies like AI, and to explore cooperation in research and the use of traditional medicine. President Biden lauded PM Modi's plan to eliminate tuberculosis in India by 2025, the statement said.

Source: *The Times of India,* 24th June 2023

Relaxing Norms for Biosimilars Risks Safety

A section of scientists and doctors has urged the Union Health Ministry and the Department of Biotechnology not to dilute norms for biosimilars (a biological medicine that is similar to an already approved biological medicine) as any such loosening of norms, in a bid to make such treatments affordable, risks compromising patient safety.

"Even when regulations are in place, about 3% of drugs are found to be of non-standard quality and the figure is higher (10%) for drugs supplied to the public sector," said Amitav Banerjee, Professor, Community Medicine and a Clinical Epidemiologist, referring to demands from some NGOs to ease guidelines for biosimilars with a view to both quickening their time to market availability and helping lower the cost of such medicines.

"Throwing the market open without proper quality checks for biosimilars, particularly in a country with a poorly functioning pharmacovigilance system to closely monitor long-term adverse events, will be hazardous," Dr. Banerjee cautioned.

He said for biosimilars that were copies of original innovator products, more studies were needed for regulatory approval to ensure that differences, if any, did not affect patient safety or drug efficacy, particularly since they were not generics.

Anurag S. Rathore, Professor Biopharmaceutical Technology, IIT-Delhi said: "Indeed, clinical trials continue to be the single largest contributor to the development and commercialisation of a biotherapeutic product. This is even true for a biosimilar, class of compounds for which the quantum of required clinical trials is already substantially reduced".

"It is also true that biosimilars cost significantly more than their pharmaceutical generic counterparts, thereby impacting their affordability and accessibility," Mr. Rathore observed. "These facts have been fuelling calls for the reduction or even elimination of clinical trials , as this would substantially lower the cost of manufacturing and make them more affordable. The regulators need to keep a delicate balance between affordability and patient safety," he added.

"If clinical trials are significantly curtailed or worse, totally eliminated, the probability of getting a therapeutic product with inadequate safety and/or efficacy increases," he warned.

Prof. Bejon Kumar Misra, founder director, Patient Safety and Access Initiative of India Foundation, an organisation that works in the area of patient safety, said: "Clinical trials and safety efficacy studies are vital requisites to ensure products launched in the market are safe and efficacious. The safety of patients cannot be negotiated for the sake of affordability".

"There is no denying that biosimilars can significantly bring down the price of essential biologics that are used for critical

diseases including cancer, but that does not mean biosimilars are allowed in the market without adequate safety studies," Mr. Misra added.

"In fact, because biologics are complex and difficult to develop, it is important that biosimilars undergo rigorous testing and clinical scrutiny to ensure they are safe and efficacious," he stressed. "Any slips, in the name of cost-cutting, could prove to be fatal for patients and for the industry," he added.

Source: *The Hindu,* 27th July 2023

HC Paves Way for Affordable Anaemia Drug

Decks have been cleared for the entry of affordable versions of intravenous anaemia therapy, ferric carboxymaltose. The Delhi high court has rejected the application by MNC drug firm Vifor, seeking an injunction against Dr Reddy's, MSN Labs and Corona Remedies, for manufacturing and marketing its generic versions. The development potentially paves the way for more companies including Cipla, to enter the market, bringing down prices further, industry and legal experts told TOI.

Ferric Carboxymaltose is an intravenous treatment of iron deficiency when oral iron preparations are ineffective. The drug is available in hospitals for around Rs 3,500. With generic versions and more launches now, the price could go down to under Rs 1,000, an over 50% reduction from the existing MRP. It loses patent protection on October 20, 2023. Over the last few years, and more recently in April, the Swiss company sued over a dozen players including La Renon, Suven, Alembic, Cipla and JB Chem to block the drug's entry. Interestingly, certain firms were successful in entering the market over a period of time. Some had launched the product which was being manufactured by Mumbai-based BDR Pharma, experts say.

In January 2012, Vifor licensed Pune-based Emcure Pharmaceuticals to commercialise the drug, which is marketed as Encicarb (now also sold under the brand names Ferium and Orofer FCM). It also has a marketing tie-up with Mumbai-based Lupin. Vifir claimed that the patent was for the product per se, and anyone making it would infringe it.

The judgment, a copy of which was accessed by TOI, said, "Since claim 1 is a 'product-by-process' claim, use of different process by the defendants to produce FCM cannot amount to infringement, as alleged. Defendants have arrived at a process, which is different from the process of Vifor and therefore cannot be accused of infringing."

However, a market player said the case has dragged on for several years, hence there isn't much commercial or patient benefit now.

Source: *The Times of India,* 27th July 2023

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