ISSUE No. 62

SILVER JUBILEE YEAR 2016

TAMILNADU PHARMACEUTICALS SCIENCES WELFARE TRUST

25 Years

Pharma Web

Newsletter of Tamilnadu Pharmaceutical Sciences Welfare Trust

Apr. - May. - Jun. 2024

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TAMILNADU PHARMACEUTICAL SCIENCES WELFARE TRUST
No. 608A, 6th Floor, Phase I, Spencer Plaza, 768 / 769, Anna Salai, Chennai – 600002
Ph: 044 - 28491232
e-mail : pictrust89@gmail.com Website : www.pictrust.com

EDITORIAL

Dear Readers,

We are delighted to present to you the 61st edition of the Pharma Web Newsletter covering **Apr – Jun 2024.**

This issue contains the program highlights as well as the following presentations given by eminent person in Pharma industry.

- **HVAC Qualification and Clean Room Validation -**
  Mr. V. Raja, Head – Engineering, M/s. Fourrts (India) Laboratories Pvt Ltd., Chennai

- **Computer System Validation in Pharmaceutical Industries -**
  Mr. T. K. Raghuraman, DGM, QA & QC M/s. Apex Laboratories Pvt Ltd., Chennai

Additionally, we've included various Gazette Notifications concerning the amendment of the Drugs & Cosmetics Act & Rules, as well as important circulars issued by the DCGI pertaining to Drugs & Pharmaceuticals. We've also curated significant news items from national newspapers that are relevant to our profession, providing you with a comprehensive overview of recent developments in the pharmacy sector.

We extend our heartfelt gratitude to M/s. Delvin Formulations, M/s. Medopharm, and M/s. Tablets (India) Ltd., for their steadfast support through advertisements, which helps us sustain the costs associated with publishing this newsletter.

A special mention goes to M/s. Fourrts (India) Laboratories Pvt. Ltd., for their support in Pharma Web advertisement and for their recognition through the meritorious award granted to B. Pharm Students of The Tamilnadu Dr. MGR Medical University, Guindy, Chennai. Their contribution to fostering talent in our field is commendable.

We hope that this Newsletter proves valuable to our Pharma professionals. Your feedback and suggestions for improvement are always welcomed and appreciated..

With Best Regards,

R. NARAYANASWAMY

Chief Editor

ARTICLES

HVAC Qualification and Clean Room Validation

by
Mr. V. Raja,
Head – Engineering, M/s. Fourrts (India) Laboratories Pvt Ltd., Chennai

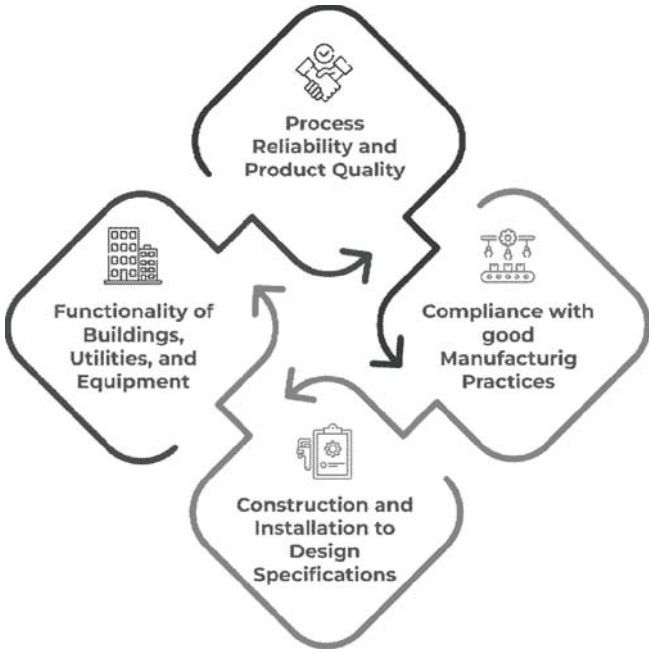
Lecture Delivered during webinar series conducted by IDMA, TNPKSB

Revised Schedule M in Qualification and Validation

- The purpose of qualification and validation is to prove, through documentation, that:
- **I Compliance with Good Manufacturing Practices** – The buildings, processes, equipment, and supporting utilities have been designed in compliance with good manufacturing practices requirements.
- **I Construction and Installation to Design Specifications** – The buildings, processes, and equipment have been constructed and installed in accordance with their design specifications.

Revised Schedule M in Qualification and Validation

- **Functionality of Buildings, Utilities, and Equipment** – The buildings, supporting utilities, and equipment function as intended.
- **Process Reliability and Product Quality** – A particular process will reliably yield a product that satisfies its predetermined specifications and quality attributes.



HVAC

1. Basics of HVAC

2. Qualification and validation of HVAC system in Pharmaceutical industry.

HVAC STANDS FOR

- H – HEATING
- V – VENTILATION
- AC- AIR CONDITIONING

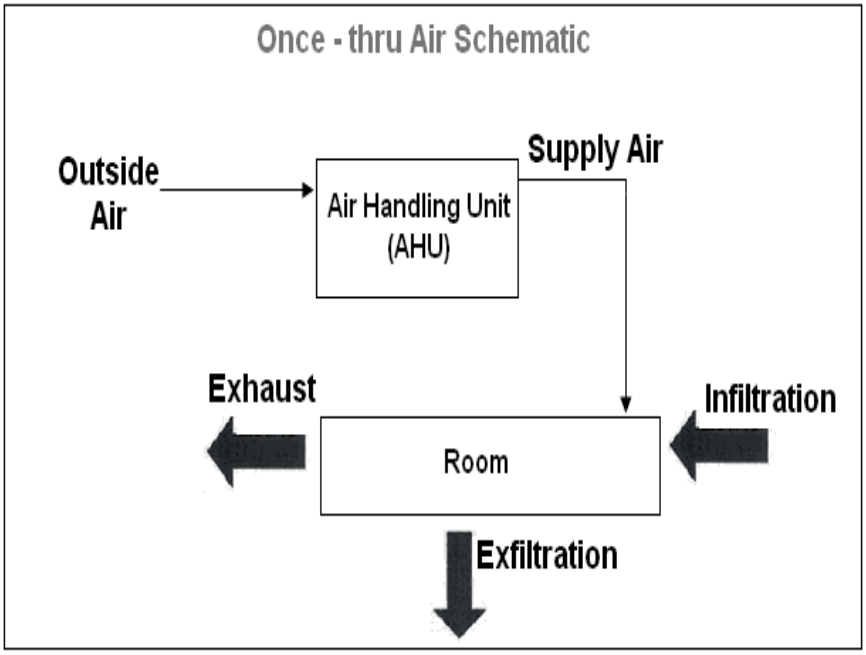
What is the use of HVAC system ?

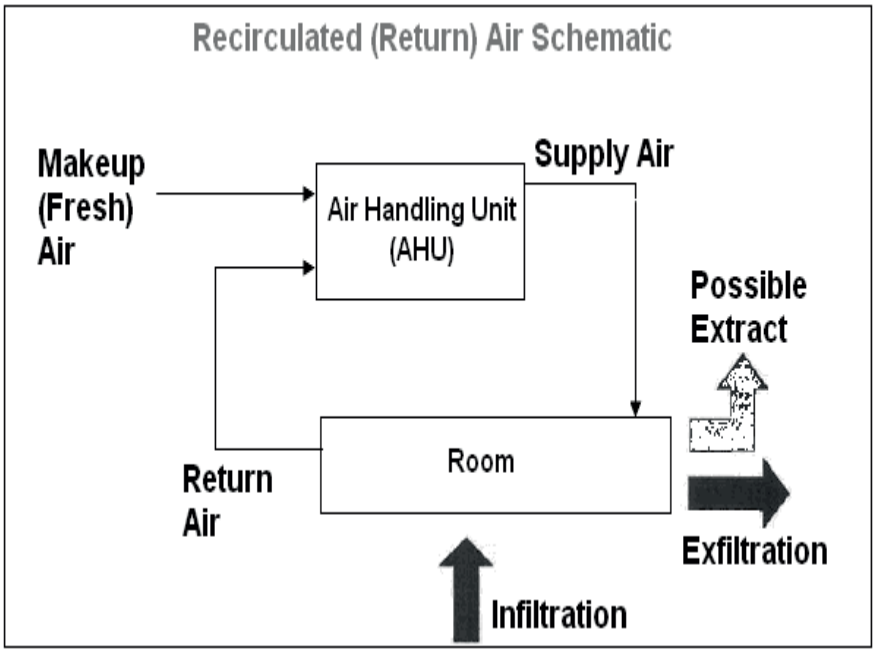
- To provide required Temperature and Relative Humidity for product protection
- To provide required quantity of Filtered Air and maintain Cleanliness
- To maintain differential Pressure
- To provide Personnel comfort

Types of HVAC System

There are two types of HVAC System:

- I. Once through system
- II. Re-circulation system





AHU DEFINITION

Air handling unit (AHU) is the equipment which delivers the designed quantity and quality of air through filters, coils and ducts to respective areas.

TYPES OF AIR HANDLING UNITS:

- SINGLE SKINNED AHU
- DOUBLE SKINNED AHU

SINGLE SKINNED AHU

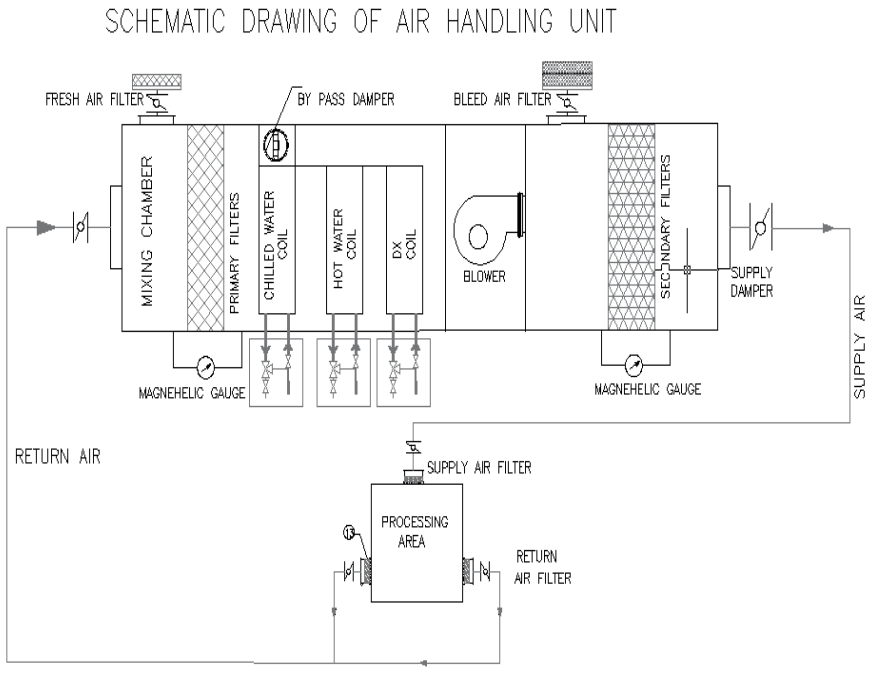
- Single Skin Air Handling Units - for all Ventilation applications.
- As the name suggests, has a single casing made of G.I without insulation.

DOUBLE SKINNED AHU

- Double Skin Air Handling Units - for all Air-conditioning applications
- As the name suggested AHU has an outer casing made of sandwiched panels with polyurethane foam acting as a thermal barrier for better insulation.

COMPONENTS OF AHU

- Filters
- Coil
- Blower
- Dampers
- Ducts
- Diffuser
- Raiser



FILTERS

TYPES OF FILTERS

- PRE FILTER
- MICROVEE FILTER
- HEPA FILTER

Pre Filters

- Also known as rough filters or coil protection filters.
- Filter particles 10 to 20 microns with an efficiency of 80% to 90%. Recommended for comfort applications.

Microvee Filters

- Also known as fine filters or 5 micron / 3 micron filters.
- Filter particles, with an efficiency of 95%. Recommended for industrial applications.

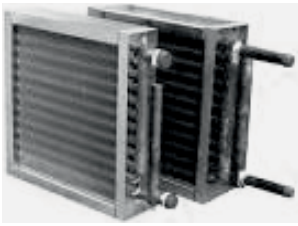
HEPA Filters

- High efficiency particulate Air Filters are also known as Absolute filters, which are the ultimate means of removal of 0.3 micron air borne particles 99.97% and are widely used in clean rooms.

COILS

TYPES OF COIL

- CHILLED WATER COIL
- HOT WATER COIL
- DX COIL



BLOWER

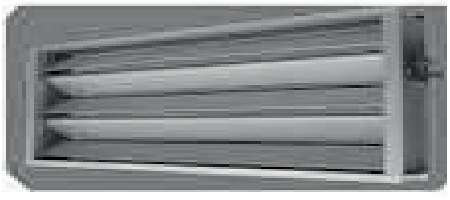
- These Blowers are used to deliver the required airflow with high stati

DAMPER

- Damper classified into two types :
  I. Volume Control Dampers

  II. Fire Dampers

- Volume Control Dampers:
  Dampers are devices incorporated into the system to have a proper control on airflow for better maintenance of conditions and better uniformity.



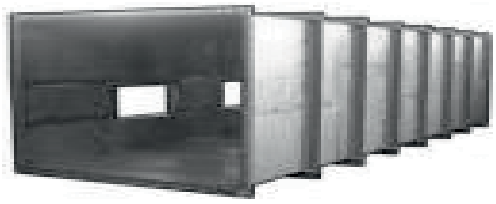
DAMPER

II. Fire dampers:

Fire dampers are passive fire protection products used in heating, ventilation, and air conditioning (HVAC) ducts to prevent the spread of fire inside the ductwork.

DUCTS

- Ducting plays a major role in distribution of conditioned air to the rooms and returns it to the AHU.

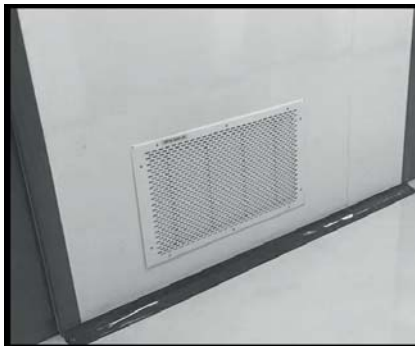


DIFFUSER / GRILL

Sr.No.	TYPES	Function	view
1.	Square	Free four way distribution pattern.	
2.	Rectangular	Free four way distribution system	
3	Circular	360 degree free air distribution patterns.	
4	SS Grill	To protect the manufactured product from contamination.	

RAISERS

- More precisely known as return air risers, which are used to collect the return air in a specific manner to maintain a perfect air flow.
- They find a wide application in Pharmaceuticals and clean room industry where proper class of cleanliness is to be maintained.



AIR LOCK

Airlock helps to protect the Classified areas from the contamination that may occur during the entry and exit of personnel and material.

TYPES OF AIR LOCK

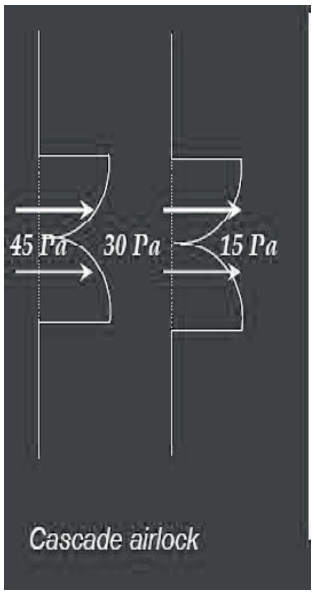
There are three types of Air lock.

- Cascade type air lock
- Bubble type air lock
- Sink type air lock

DEFINITION ABOUT DIFFERENT TYPES OF AIR LOCK

1. Cascade Airlock :

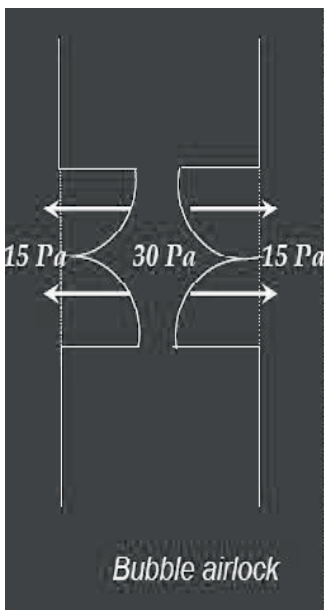
These airlocks are very common having higher pressure on one side and lower pressure on another side. This prevents to enter contaminants from outside to airlock and from airlock to inner side.



DEFINITION ABOUT DIFFERENT TYPES OF AIR LOCK

2. Bubble Airlock :

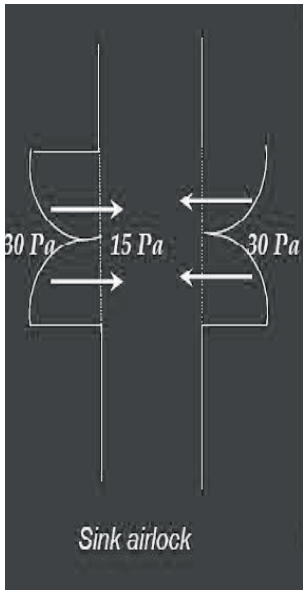
These types of airlocks have higher pressure inside the airlock and lower pressure in both outsides. This prevents the flow of air between two areas through the airlock creating a pressure barrier.



DEFINITION ABOUT DIFFERENT TYPES OF AIR LOCK

3. Sink Airlock :

Airlocks having lower pressure inside the airlock and higher pressure on both sides of the airlock. This airlock pulls from both adjacent areas creating a low pressure barrier.



Qualification and validation of HVAC system

in

Pharmaceutical Industry.

HVAC SYSTEM QUALIFICATION

Definition:

Qualification is the planning, carrying out and recording of tests on equipment and a system, which forms part of the validated process, to demonstrate that it will perform as intended.

-WHO

Why Qualification required in pharma industries?

The purpose of qualification is to ensure that equipment, facilities, and utilities are capable of consistently producing quality products in accordance with regulation and industry standards.

International Standard : ISO 14644

- ISO 14644:2015E details the following, under the general title
- Clean rooms and associated controlled environments :
    - Classification of air cleanliness
    - Monitoring to provide the evidence of clean room performance related to air cleanliness by particle concentration.
    - Test methods
    - Design, construction and start-up
    - Operation
    - Separative devices (clean air hoods, glove boxes, isolators and mini-environments)

Requirements for Qualification:

- **URS** - User Requirement Specification
- **DQ** - Design Qualification
- **IQ** - Installation Qualification
- **OQ** - Operational Qualification
- **PQ** - Performance Qualification

URS

User requirement specification is an document evidence in which user department provides the requirement to the manufacturer regarding the equipment and its usage.

URS Requirement

S.N	Parameters	Requirement Specification
1.	Description	Air Handling Unit that can treat the external atmospheric air, suitable for the conditions specified.
2.	Overview, Purpose, Field Identification, Size / Capacity.	i) The AHU shall cater to which area. ii) AHU Room size iii) Temperature and RH requirement, area classification iv) Capacity to be determine by vendor.
3.	Cleaning requirements	Provision for manual cleaning of filters and other components
4.	Material of construction	AHU , Duct material
	Electrical construction	FLB or NFLB
5.	Operational requirements	AHU operation in Auto / Manual
6.	Utilities	Chilled and hot water requirement, instrument requirement.
7.	Regulatory requirements	cGMP, etc.,
8.	Inspection and testing	FAT / SAT
9.	Validation requirements for PLC installed (If any)	If PLC based system available, need to be validation prior to the operation.
10.	Commissioning and Documentation	DQ, IQ, OQ to be provided by the vendor
11.	Delivery at	Site address

DQ

- Design qualification is the documented check of planning documents and technical specifications for conformity of the design with the process, manufacturing, GMP and regulatory requirements.

- The requirements of the URS should be verified during the design qualification.

IQ

Installation qualification is documented verification that the premises, HVAC system, supporting utilities and equipment have been built and installed in compliance with their approved design specification.

-WHO.

IQ Verification checks

S.No	Components	Specification	Observation
1.	AHU Plenum		
2.	Blower Fan		
3.	Chilled water Coil		
4.	Hot water Coil		
5.	Drain Tray		
6.	Motor		
7.	Filter		
8.	Supply Duct		
9.	Return Duct		
10.	Supply Grill		
11.	Return Grill		
12.	Volume control Damper		
13.	Magnehelic Gauges		
14.	Pressure Gauges		
15.	Temperature Gauges		
16.	Actuators		

OQ

Operational qualification is the documentary evidence to verify that the equipment operates in accordance with its design specifications in its normal operating range and performs as intended throughout all anticipated operating ranges.

-WHO

OQ Verification Checks

S.No	Test	Observation
1.	Switch 'ON' the AHU	
2.	Press emergency push button	
3.	Check the 10 micron differential pressure in magnehelic gauge, i) ON condition. ii) OFF condition	
4.	Check the 3 micron differential pressure in magnehelic gauge, i) ON condition. ii) OFF condition	
5.	Check the chilled water inlet pressure.	
6.	Check the chilled water temperature.	
7.	Check the hot water inlet pressure.	

OQ Verification Checks

S.No	Test	Observation
8.	Check the Hot water temperature.	
9.	Check the AHU sound level	
10.	Check the motor voltage	
11.	Check the motor RPM	
12.	Open door in AHU	

PQ

Performance qualification is the documented verification that the process and or the total process related to the system performs as intended throughout all anticipated operating ranges.

-WHO

PQ

The following test to be performed:-

- Air Velocity and Air Changes test.
- Filter integrity test (PAO).
- Non viable airborne particle count test.
- Temperature and RH test.
- Pressure control test.
- Airborne particle recovery test.
- Air flow path visualization test.
- Micro environmental test.

Air Velocity and number of air changes test

Air Velocity:
Take the calibrated air capture hood and keep it at the bottom of the filter face. Switch ON the air capture hood and wait till the beep sound attains to achieve stabilised reading and note down the CFM.

Air Changes :
Calculate the number of air changes by given formula

$$\text{Number of air changes/hr} = \frac{\text{Total room airflow in Cfm}}{\text{Total volume of the room in cft.}} \times 60$$

The number of air changes calculation shall be as per velocity report.

Acceptance criteria: NLT 25 ACPH

Filter Integrity Test (PAO):

Position the smoke generator and introduce PAO smoke into the air stream, ahead of the HEPA filters and set the instrument at 100% concentration. Scan the downstream side of the filter with an appropriate photometer probe.

- The probe should scan the entire filter face and frame at a position about 1 - inch from the face of the filter.

Acceptance criteria:

Leakage should not be more than 0.01%

Air borne Particle Count Test:

- This test should be carried out at rest condition with no operating personal present, area to be cleaned before start of the test.
- Derive the minimum no. of sampling point locations as per ISO14644-1& 2:2015, below given table,

Area of Clean room (m^2)	Sampling point location
2	1
4	2
6	3
8	4
10	5
24	6
28	7
32	8
36	9
52	10

Air borne Particle Count Test:

Area of Clean room (m^2)	Sampling point location
64	12
68	13
72	14
76	15
104	16
108	17
116	18
148	19
156	20
192	21
232	22
276	22
352	24
436	25
500	26
1000	27
>1000	Equation A

Formula for calculating the area in Sq.mts = Length x Breadth of area

Air borne Particle Count Test:

- While taking the room particle count the isokinetic probe should be positioned at the height of the work activity (30”-40”) above the floor level.
- Calibrated air borne particle counter of 1cfm capacity shall be used.
- After receiving the print (tracing paper) from particle count tester write name of the area and take photo copy immediately.

Selected airborne particulate cleanliness classes for clean rooms as per ISO 14644-1:2015

ISO 14644-1:2015 Classification of air cleanliness by particle concentration						
ISO Class (N)	Maximum allowable concentrations (particles/m^3) for particles equal to and greater than the considered sizes, shown below					
	≥ 0.1µm (m^3)	≥ 0.2µm (m^3)	≥ 0.3µm (m^3)	≥ 0.5µm (m^3)	≥ 1.0µm (m^3)	≥ 5.0µm (m^3)
ISO 1	10[b]	d	d	d	d	e
ISO 2	100	24[b]	10[b]	d	d	e
ISO 3	1.000	237	102	35[b]	d	e
ISO 4	10.000	2.370	1.020	352	83[b]	e
ISO 5	100.000	23.700	10.200	3.520	832	d,e,f
ISO 6	1.000.000	237.000	102.000	35.200	8.320	293
ISO 7	c	c	c	352.000	83.200	2.930
ISO 8	c	c	c	3.520.000	832.000	29.300
ISO 9[g]	c	c	c	35.200.000	8.320.000	293.000

Facility Area Classification

FACILITY	CLASSIFICATION
OSD	Class 1,00,000
Topical and Oral liquids	Class10,000
Injectable	Class 100

Particle count Recovery Test:

- The recovery test is performed to determine whether the installation is capable of returning to a specified cleanliness class with in a finite time after being briefly exposed to a source of airborne particulate challenge.
- EU GMP Annex 1 : 2022 mentions that the particle limits for “At Rest” condition should be achieved within a short period of less than 20 minutes.

Airflow Path Visualization Test:

- The purpose of this test is to confirm the air flow direction or pattern or both with regard to the performance requirements.
- The evidence of the test is produced in the form of photography and videography.
- Fog generated by fogging / smoking machines. (Glycol based foggers being the most preferred)
- The smoke should be very gently introduced at a low velocity directed into and towards the air flow

- Acceptance Criteria:

Air should flow from high pressure zone to low pressure zone

Pressure Difference Monitoring:

- Calibrated pressure magnehelic gauge shall be used for measurement of pressure.
- The test has to be performed for three days Monitoring with regular intervals.

Temperature & RH Test Monitoring:

- Calibrated hygrometer shall be used for measurement of temperature and RH.
- The test has to be performed for three days at regular intervals.

Microbial Environmental Test:

- Individual rooms shall be monitored for environmental compliance by Active sampling using air sampler and Passive sampling using settle plate method with respect to the class of areas.
- Individual rooms shall be monitored continuously for a period of 03 consecutive days.
- **Acceptance Criteria:**

Microbial environmental monitoring	Passive sampling method	Active sampling method
	TAMC- NMT 100 cfu/Plate	TAMC - 200 cfu/m^3

CLEAN ROOM VALIDATION

Definition :

Validation is the process of ensuring that a product, process, or system meets its intended requirements and specifications.

Frequency and schedule of Test

- Required Testing (ISO 14644-2:2015) Schedule of Tests to demonstrate continuing compliance

Test Parameter	Cleanroom Class	Frequency	Type of test
Air Velocity	= ISO 5	6 Months	Compulsory
	> ISO 5	12 Months	
Particle Count Test	= ISO 5	6 Months	
	> ISO 5	12 Months	
Filter integrity	= ISO 5	6 Months	
	> ISO 5	12 Months	

Frequency and schedule of Test

Test Parameter	Frequency	Type of test
Air flow visualization	At commissioning, and thereafter every 4 years, or after any significant change to the air flow system or equipment content.	optional
Recovery		
Pressure Differentials, Temperature, Relative Humidity	Continuously monitoring	Compulsory

Maintenance OF HVAC Systems

Preventive Maintenance:

- Preparation of yearly schedule
- Implementation of monthly preventive maintenance as per check list.
- If spare replacement updated in equipment history card.

PREVENTIVE MAINTENANCE CHECK LIST

S. No	Check List	Frequency	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
AHU														
1	Check the blower and motor base bolts and nuts tightness, if found loose tighten it.	M												
2	Check for belt condition and alignment, if found loose align the same, if damaged replace the same with new one.	M												
3	Check for blower and motor pulley grub screw tightness.	M												
4	Check for leaks in the door panels of AHU, if leaks apply silicon sealant.	M												
5	Clean the cooling and heating coils SS drain tray.	M												
6	Clean the blower, motor and surroundings area.	M												
7	Check the condenser fan, motor bearing and base bolt tightness. (If applicable).	M												
8	Clean the condenser fins. (If applicable).	M												
9	Check chilled water and hot water manifold drain valve condition	Q												
10	Check for abnormal sound from blower shaft bearings, if found replace the bearings.	H												
11	Check the gas pressure. (If applicable).	H												

PREVENTIVE MAINTENANCE CHECK LIST

S.No	Check List	Frequency	Jan.	Feb	Mar	Apr	May	Jun	Jul.	Aug	Sep	Oct	Nov	Dec
12	Clean the cooling coil and hot water coil fins with fins cleaner or water.	M												
ELECTRICAL														
1	Check the motor amps, abnormal noise and motor terminals loose connections if any problems rectify / replace it.	M												
2	Check the earthing connections if any problem rectify it.	M												
3	Check the door interlock proper working condition if any problems rectify / replace it.	M												

Maintenance OF HVAC Systems :

Filter Cleaning:

- Preparation of yearly filter cleaning schedule.
- Perform monthly HVAC filter cleaning activities as per schedule.
- Room return air filter cleaning activity Perform as per product to product change over.

Computer System Validation in Pharmaceutical Industries

by
Mr. T. K. Raghuraman,
Deputy General Manager, QA & QC M/s. Apex Laboratories Pvt Ltd., Chennai

Lecture Delivered during Webinar series conducted by IDMA, TNPKSB

Regulations

- **EU:** GMP Volume 4 Annex 11 - Computerised Systems
- **US FDA:** 21 CFR Part 11 - Electronic Records & Signatures & General Principles of Software Validation
- **PIC/s:** Good Practices For Computerised Systems In Regulated "GxP" Environments
- **WHO:** TRS 1033, Annexure 4 - Guidance on Data integrity
- **INDIA:** Schedule M – Computerized System

Guidelines

- **ISPE:** GAMP
- **ICH:** Q9 Quality Risk Management
- **APIC:** Computer Validation Guide

Why CSV ?

Olden days

Nowadays

Security will be applied, wherever treasure / assets are stored.

This is electronic era

Approach to Validation

- It is essential that the validation is practical and achievable.
- The approach to validation of computer systems should be based on complexity of system design and its use.
- It is important to establish the final objective of validation.
- It is never successful to completely outsource computer validation.

EU Guidelines

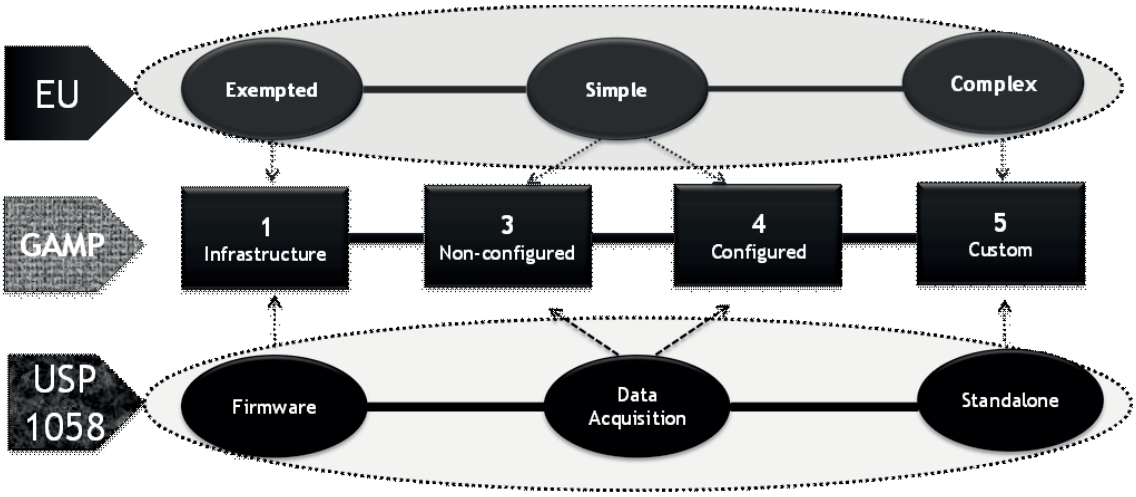
Systems	Definitions	Examples	Action
Exempted	Framework/ layered software	Microscope, Operating system security Software, Word, Excel, database software	None
Simple	Small part of software or Restricted customisation	pH meter, thermo hygrograph/hygrometer, balance, TLC analyser, micro plate counter, etc.	Simplified validation - Calibration - Function control test
Complex	Extended amount of functionality software Extended customisation	LIMS, ERP, eDMS, user-developed Excel spreadsheet, user-developed Access application, HPLC, GC and detection systems (UV, VIS, IR, MS, NMR, etc)	Validation

GAMP Guidelines

Category	Validation Approach
1 Infrastructure Software	●Record version (include service pack). ●Verify Correct Installation
3 Non - Configured	●URS ●Record version and verify installation ●Risk based tests against requirements ●Procedures put in place for maintaining compliance ●Consider auditing supplier for critical and complex applications
4 Configured	●As above, plus… ●Life cycle approach ●Supplier questionnaire – Adequate QMS ●Risk based tests against requirements in a test environment ●Risk based tests against requirements within the business process
5 Custom	●As above, plus… ●Full life cycle documentation ●Design and source code review

GAMP 5 Appendix M4

Software classifications



Key Issues to be Considered

- **Compliance to critical points includes:**
  - Proven fit for purpose
  - Access control /user management
  - Data integrity including: prevention of deletion, poor transcriptions and omission
  - Authorised / unauthorised changes to data and documents
  - Critical Alarms handling (Process)
  - Audit trails
  - Disaster recovery / Back up and retrieval
  - System maintenance and change control
  - Training
- **Evidence of sufficient control of these issues should be demonstrated in the validation documentation**

SOPs and Training

- **The following procedures to be in place:**
  - Inventory handling (System and applications)
  - System / software operation
  - User Security
  - Computer system validation
  - Back up and Restore
  - Disaster recovery
  - Preventive maintenance
  - Change Control
  - Audit trail review
  - Periodic evaluation
  - Data Archiving
  - System retirement
- **Training must be completed prior to PQ**

Responsibility Matrix

- Activities and responsibilities should be assigned, for example by using a matrix, which lists all the deliverables versus contributors for each task:

Contributors/ Deliverables	System owner	QA	Supplier	IT Support
URS	W & R	R & A	Support	W
Functional/Design Specifications	W & R	R & A	Support	W
Validation Plan	W & R	A		W
Qualification protocol	W & R	A		W
Execution	Executor	R & A	Support	Executor
Validation Report	W & R	R & A		R

W: Writing, R: Reviewing, A: Approving

Installation Qualification

- **An IQ is expected to include at least:**
  - Document verification (e.g. specifications, installation documents, drawings, manuals, licenses)
  - Software CD verification
  - Standard Operation Procedure verification
  - Server installation verification (e.g. hardware, operating system, database, software)
  - Client installation verification (e.g. hardware, operating system, database, software)
  - Instrument installation verification (e.g. hardware,)
  - UPS installation verification
  - Interface installation verification
  - User access setup verification

Operational Qualification

- **An OQ is expected to include at least:**
  - Security testing
  - Functional testing of software
  - Functional testing of interfaces
  - Functional testing of instruments through software

Performance Qualification

- **An PQ is expected to include at least:**
    - User Acceptance testing
    - Backup and recovery

Group Discussion…

Shall deletion rights be given to IT administrator?

Maintaining the validation status

- Computer validation is not a one-time event, It needs to be maintained over time.
- The fact is that software applications are being changed, probably more frequently than expected, and the validation status and documentation must be kept synchronized.
- Whenever software is changed, a validation analysis should be conducted.
- It is important to have a fast track for implementation of corrections and patches especially concerning security.

Documentation map

- Validation Project Plan
- Risk Assessment
- URS
- FS, DQ (if required)
- Validation Plan
- Execution Protocol (IQ, OQ, PQ)
- Report
- Traceability Matrix

Example (HPLC system)

- **URS**
  - Hardware requirements (simple)
  - Application requirements (simple)
  - User authority matrix
  - Electronic signature requirements
  - Instrument control requirements
  - Data management
  - Data traceability
  - Data processing and report requirements
  - System Administration
  - Backup and Disaster recovery
- **Validation Plan (Responsibility, List of documents, studies planned)**

Example (HPLC system)

- **Execution Protocol (IQ, OQ, PQ)**
  - Document Verification
  - System hardware configuration
  - System policies
  - Application user level configuration
  - Domain security
  - Data Security in system and application
  - System connectivity
  - Data acquisition, processing and reporting
  - Audit trail verification
  - Backup test

- **Report (List of attachments, conclusion)**
- **Traceability Matrix (Cross reference of URS parameters and relevant execution step number of protocol)**

Example (PLC system)

1. System design
   - Components controlled by PLC
   - List of input components (Sensors, buttons, switches)
   - Matrix of control parameters (Response system vs control parameters)
   - Ex.: conveyor – Bottle jam sensor, Air wash valve – no bottle
2. Hardware verification, software verification,
3. User role matrix
4. HMI function test (test each functions)
5. Interlock tests (List out all interlocks and check they are working)
6. I/O test (List all input & output parameters and confirm with requirements)
7. Create actual product recipe and conduct a trail run
8. Security check & audit log
9. Power loss recovery test

Questions & Answers

- **Is it required to do separate CSV for non-computerized instruments like analytical balance?**
  No. perform the required checks in instrument qualification itself.

- **To what depth CSV to be done?**
  We are not software quality tester. We have to focus on functional testing for our intended use and environment.

- **Are screenshots mandatory?**
  wherever possible keep, but, not necessary for all.

- **If we have 100 user roles in software and should we need to test all for each category (manager, supervisor, executor, admin)?**
  No. Check critical options like deletion. Refer answer for Ques 2.

Questions & Answers

- **Backup is mandatory?**
  Yes, business and quality requirements.

- **Who is responsible for execution ie… IT, User or QA?**
  40%, 40%, 20%

- **Do we need to study any special course?**
  No. Knowledge on computer function, network, instrument operation is sufficient.

- **If a software does not meet security requirements?**
  If possible, upgrade. Or configure security in system OS. Or procedural control.

New terminologies

- **Audit trail** - Record of the actions performed.
- **Hybrid system** - System of both electronic and manual documents.
- **Meta data** - Data of data.
- **Black box** - System whose inner process in unknown.

Recent observations

USFDA Observations

2021 – 84 observations
2022 – 43 observations
2023 – 81 observations

Recent 483

Error notifications are not reviewed and reported.

In Empower application,

33 warnings on “Injection alteration”,
49 logs on “User Abort”,
69 warnings on “File checksum error”,
10 intimation on “Stop flow key pressing”.

Data Integrity - Group Discussion…

- During audit, auditor requested to bring a logbook. Before giving it to auditor, you are just verifying and found chemist signature is missing on last month entry. (chemist is available on that day).

  What will you do?

- ஆடிட்டின் போது , ஆடிட்டர் ஒரு **Log Book** ஐ கொண்டு வருமாறு கேட்டுக்கொண்டார். அதைத் ஆடிட்டரிடம் கொடுப்பதற்கு முன், நீங்கள் ஒருமுறை சரிபார்க்கிறீர்கள்; அதில் போனமாதம், **chemist** கையொப்பம் விடுபட்டுள்ளது. (இப்போது **chemist** அங்கு உள்ளார்).

  என்ன செய்வீர்கள்?

Guidelines

- **US FDA:** Data Integrity and Compliance With Drug CGMP Q & A
- **MHRA:**'GXP' Data Integrity Guidance and Definitions
- **EMA**: Q & A on Data integrity
- **PIC/s:** Good Practices for Data Management and Integrity in Regulated GMP/GDP Environments
- **WHO:** TRS 1033, Annexure 4 - Guidance on Data integrity

Definition

MHRA Regulating Medicines and Medical Devices

Data Integrity is the extent to which all the data are complete, consistent and accurate throughout the data lifecycle.

FDA U.S. FOOD & DRUG ADMINISTRATION

Data Integrity refers to completeness, consistency and accuracy of data. That data should be **ALCOA**.

World Health Organization

The collected data should be **Attributable, Legible, Contemporaneously recorded, Original or a true copy, and Accurate (ALCOA).**

PIC/S

Data Integrity is defined as the extent to which all data are complete, consistent and accurate, throughout the data lifecycle.

Systems of Data Integrity

- Data governance including its life cycle
- Risk management
- Data criticality
- Quality culture
- Importance of controlling records Generation, distribution and control of template records
- Filling out records
- Making corrections on records Verification of records (secondary checks)
- Direct print-outs from electronic systems
- Document retention
- Disposal of original records or true copies
- Specific data integrity considerations for computerised systems
- Qualification and validation of computerised systems
- Data Transfer
- System security for computerised systems
- Audit trails for computerised systems
- Storage, archival and disposal of electronic data

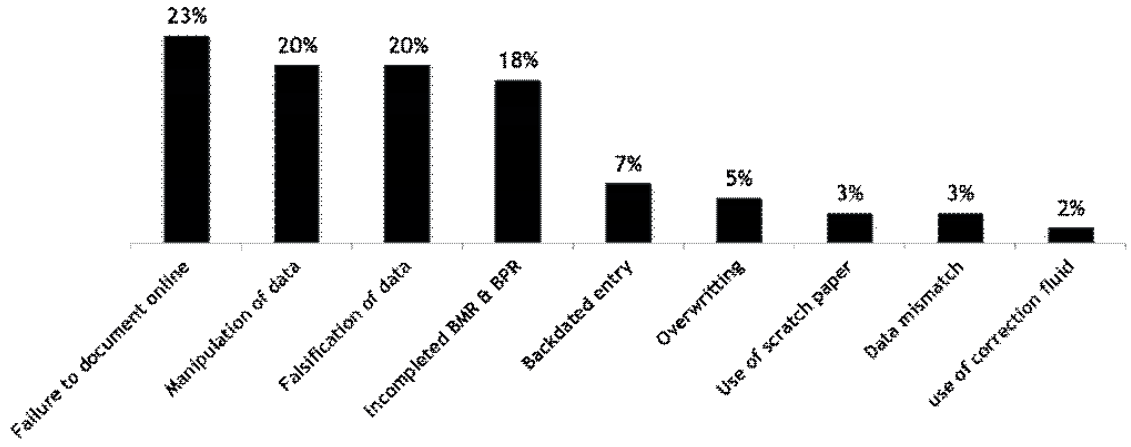
Terminologies used in regulatory audit observations

- Falsification of data
- Alteration of data and events
- Misleading information, statements or facts
- Misrepresentation of what really happened
- Untruthful statements

EU Agency's report – Data integrity failures

- Releasing failing product, as if they had passed
- Testing into compliance
- Not saving electronic or hard copy data that would confirm the failing results.
- Making up microbiological test (EM) results.

10 years trend in India



QC Care – Data Integrity

Cause for laboratory failure

Data Manipulation

- Falsification of documents
- **Discrepancies between electronic data and data reported on paper**
- Re written training records
- Falsified entries
- Unreported / unauthorized trial injections of samples
- Raw data chromatogram files deleted
- **Retesting samples until passing results obtained**

Poor Laboratory Controls

- Failure of Lab controls
- Insufficient management of data, change control and laboratory controls
- No user requirements
- Shared password
- Failure in integrity and security of data
- **Analysts routinely perform "trial" injections of sample aliquots prior to performing the official/reported analysis**
- PC admin account used to **change time back and overwrite failing results**
- No system validation of electronic record generating systems

Incomplete Data Review

- OOS results marked as Passed
- **Weakness of QA department around Data integrity**
- No procedure for audit trail
- Hide non conformities from QA

What leads failure ?

- Lack of controlled access to computer systems
- "Trial" HPLC injections outside a quality structure
- Deleted data
- Not recording activities contemporaneously
- Backdating
- Fabricating data
- Copying existing data as new data
- Discarding or deleting results with no justification and re-running/retesting samples to present better results

Join Pharmacists to Ensure Patient Safety

by

Ms. Saranya Devi. C.S
PSG College of Pharmacy, Coimbatore

Note: This article was awarded 3rd prize in the Essay Competition conducted by our Trust

Prologue:

Patient safety is a healthcare concept that focuses on keeping patients safe during their treatment. As a member of the medical community, pharmacists are essential in protecting patient safety and minimizing medication errors. Pharmacists play a crucial role in ensuring the security of medications at every stage of patient care, and their participation not only found to reduce errors but also improve dispensing manners, and enhance observation of patients.

> **"WHEREEVER THE ART OF MEDICINE IS LOVED, THERE IS ALSO A LOVE OF HUMANITY!"**
> **- Dr. Hippocrates**

Healthcare Provider's Role in Promoting Patient Safety:

Medications are potent tools that, when utilized correctly, can be used to treat, cure diagnose and prevent disease. When taken inappropriately, they have the potential to cause significant harm to the consumers. These unanticipated and undesired effects are known as Adverse Drug Reaction (ADR) or side effects that can occur with any medicine. As members of health care organizations that comprises of legally registered physicians, medical professionals, registered pharmacists, and other health care providers must accept responsibility from preventing ADR. Healthcare providers battle it out to give the best overall patient safety and medications at the most affordable cost.

One of the Pharmacist's main responsibilities is to make sure that patients receive their medications in a safe and effective manner. Pharmacists ensures that patients receive the right medication at the right dose by performing the final check of the prescription and they are obliged to give consumers with the instructions on how to utilize the drug safely and efficiently.

An Overview: The Expanding Function of the Pharmacists:

Pharmacists are essential to promote patient safety since they are medical professionals with a focus on the appropriate and safe administration of drugs. The knowledge that every healthcare professional should have, involves:

- Information on drugs, dosage form, drug interactions and ADR.
- The finished product of medication, Availability & Accessibility
- Health care facilities and services
- Dispensing appropriate medications based on patient age

A specialized pharmacist plays a significant role in fostering an environment of safety within their work areas. On addition, they also play a crucial part in drug safety. They are not only responsible for assuring the drug safety but also in appropriate and effective administration of specialty medications such as large volume parentrals (LPV) and high molecular weight protein and amino acid molecules, as well as guaranteeing the patient receives education on the treatment they are receiving.

General roles of pharmacists in healthcare sector :

Verification of Prescription and patient details	Accurate dispensing of medication to the consumers	Short explanation of utilization of drug
Analyze drug-drug interactions	Explaining the route and time of administration	Analyze adverse drug effects

Medication Inaccuracies:

Any avoidable incident that could result in improper drug administration or patient illness when the medication is under the health care provider's control is considered a “medication error”. One of the most frequent categories of medical errors includes medication error, which can result in severe injury, being hospitalized, or possibly death.

In medicine, the word "Medication Error" refers to a broad range of more specific occurrences that have the potential to cause or result in improper pharmaceutical use or harm to patients. These include inaccurate prescriptions written for patients (i.e., the wrong medication or the right at the wrong dosage), dangerous drug interactions, mistakes made during the preparation or delivery of drugs, and the improper or excessive prescribing of Narcotic drugs. Drug errors can occur in a variety of forms, such as those involving prescription, dose, administration, drug delivery, and its consumption.

My personal effects due to lack of conveying drug information:

As my mother been diagnosed with Rheumatoid Arthritis, she was visiting a specialist for her treatment. That Doctor have advised her to take HQC (Hydroxychloroquine) drug every day and she continued taking the same medicine for years with the knowledge of doctor. She gradually suffered from pain and redness of eyes and her vision for decreased. Since she faced blurred vision problems, she was forced to do eye checkup, and there the ophthalmologist made her realize that her vision has been affected due to the side effect of taking HQC. The main side effect of HQC and QC is irreversible visual loss due to retinal toxicity. Neither the doctor who prescribed this drug nor the pharmacists who dispensed this drug educated her with the information about the side effects of prolong usage of HQC. Because of their carelessness, my mother lost her good vision and she is been pushed to wear specs to read and write. I find this as a biggest mistake from the side of healthcare professionals. Educating about the drug and their side effects to the patients who are consuming them should be followed necessarily.

Pharmacists should go by their Oath – "THE PHARMACIST OATH"::

Every pharmacist takes an Oath and promises to devote their lives to serve people via the profession of pharmacy. Pharmacists should prioritize the welfare of humanity and the alleviation of pain. They are required to respect and safeguard all personal and health information provided to them. They must embrace responsibility for increasing their professional knowledge and self-awareness. If every pharmacist go by this OATH, medication errors will be hindered and anticipated patient care will be attained.

Epilogue:

Patient safety is something every Pharmacist and other healthcare professionals should focus on and they should contribute their utmost effort to prevent patients from any harmful drug interactions and forbid ADR. As pharmacists they hold great responsibility in serving both. Patients rely upon both doctors and pharmacists and if they assure them back with proper service, a safety environment shall be fostered. Thus, the advancement in Pharmacist's role towards public service and patient safety and their profession has been evolved and expanded when compared to ancient traditional pharmacy practices which has been viewed as a positive notion.

"IF YOU TREAT A DISEASE, YOU LOSE. IF YOU TREAT A PERSON, YOUR WIN IS GURANTEED, NO MATTER WHAT THE OUTCOME IS!"

- Patch Adams

INFORMATION

M. Pharm & Pharm. D Scholarships 2023-24 Awardes by TNPSW Trust

Profile of 3rd Rank

PHARMACEUTICS

Name: Mr. Mr. Ashwin. R

Project Title: Treated egg shell as Novel ingredient for Treating Hyper pigmentation issues: Optimization, Formulation development & Characterization

College: JSS College of Pharmacy, Ooty

Guide's Name: Dr. Suresh Kumar. R

PHARMACEUTICAL CHEMISTRY

Name: Ms. G. Vinotha

Project Title: Synthesis, Characterization, Docking Studies and Biological Evaluation of Novel 4-Amino Quinolone Schiff and Mannich Bases.

College: Arulmigu Kalasalingam College of Pharmacy, Srivilliputhur

Guide's Name: Prof. Dr. N. Venkateshan

PHARMACEUTICAL ANALYSIS

Name: Mr. S. Ranjith

Project Title: Determination of Antibiotic Residues in Raw Milk Samples by Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS).

College: C. L. Baid Metha College of Pharmacy, Chennai

Guide's Name: Dr. C. N. Nalini

PHARMACOLOGY

Name: Ms. Saranya. S

Project Title: Effect of Ethanolic extract of Hel iotropium indicum Linn. against Scopolamine – Induced Memory Impairment and Brain Oxidative Stress in Zebra fish.

College: The Erode College of Pharmacy, Erode

Guide's Name: Dr. G. Sumithira

PHARMACOGNOSY

Name: Ms. M. Kaviyarasi

Project Title: Pharmacognostical, Phytochemical Studies and Anti-anaemic Evaluation of Bark of Ixora arborea Roxb

College: College of Pharmacy, Madurai Medical College, Madurai

Guide's Name: Dr. P. Muthusamy

PHARMACY PRACTICE

Name: Mr. Akash Ganga. R

Project Title: Impact of Clinical Pharmacist Intervention in the Nephrology department of Tertiary Care Multi-specialty Teaching Hospital.

College: SRM College of Pharmacy, Chennai

Guide's Name: Dr. M. Jagadeesan

PHARM D

Name: Mr. Sethuraman. K, Ms. Shalini. S, Ms. Sharon Ishwarya Roy

Project Title: A Study on Drug utilization and Drug interaction on Antibiotics in the orthopedic patients

College: College of Pharmacy, SRIPMS, Coimbatore

Guide's Name: Mrs. Merin Levy Philips.

EVENTS

IPA Fellowship Award

Every year, IPA presents the Fellowship award to the members. For 2023, the award was received by our trustee, Mr. R. Narayanaswamy.

Dr. M. Venkateswarlu Memorial Lecture Awardee

Every year, IPA awards the Dr. M. Venkateswarlu Memorial Lecture Award to its members. For 2023, the award was presented by our trustee, Dr. S. Manivannan, and Mr. T. Sathish collected the award on his behalf.

IPA - State Branch of Excellence Award

For the year 2023, the Tamil Nadu State Branch of IPA received the State Branch Excellence Award during the 73rd IPC held in Hyderabad.

Pharma South 9th Edition

IDMA-Tamil Nadu Puduchery Kerala State Board, organized the 9th successful edition of India's flagship Pharma event - Pharmac South 2024, an annual B2B Exhibition cum Conference for both the Pharma and Nutraceutical sector was held on 24th & 25th May 2024 at Chennai. The theme of Pharmac South is to “Discover the present and explore the future of Pharma”.

Over the years, Pharmac South has actively facilitated business between leading contract manufacturers, marketing companies, Allied industries - Pharma Machinery and Packaging, lab Analytical and Pharma ingredients segments. PAN India Exhibitors participated to showcase their unique products for the benefit of their prospective clients.

The unique feature of Pharmac South is the conference organized with Speakers from - Senior Govt officials, leading thought leaders, Pharma stalwarts, professionals from Marketing, Motivational, MSME and regulatory areas.

Pharmac south 2024 was a resounding success, attracting more than 100 plus Leading Exhibitors from across the country with Footfalls of about 7000 plus visitors.

The Inauguration was done by the Chief guest **Thiru. Gagandeep Singh Bedi** (IAS, Additional chief Secretary to Govt, Health and Family Welfare Department , Govt of Tamil Nadu .

Mr. J. Jayaseelan , chairman - IDMA(TNPKSB) in his welcome address said" Pharmac south provides a unique platform to understand the industry trends, dialogue with key technical and regulator personnel along with associated stakeholders ,to compare notes with major suppliers of products and services in the Pharmaceutical industry.

IDMA past National president & Chairman, Pharmexil **Dr. S.V. Veeraamani** added the turnover of Indian pharma industry has grown exponentially from Rs.10 Crore (about US$ 2 Million)in 1948 to about 1,00,000 crores (US$ 21 Billion) today, a growth rate of over 15% . IDMA has been in the forefront actively supporting Ministry of Health & Family welfare in compiling the Indian Pharmacopenia for many years. IDMA Exports were Rs.50,000 crores(over US $10 Billion) last year growing at 22% .

Shri. M. N. Sridhar , JDDC & Controlling Authority (i/c) Tamilnadu & **Dr. K.M. Srinivasan** Deputy Drug Controller India CDSCO , South Zone also participated in the Inaugural function.

Shri. Daara B. Patel , Secretary General , IDMA Mumbai , highlighted on the active role being played by National IDMA for the growth and welfare of Pharma Industry .

Shri S. Sivanandhan Hon Secretary IDMA Tamil Nadu Puduchery Kerala State Board, the Pharmac South committee chairman & the core committee team –Shri T. Sathish, Vice Chairman IDMA Tamil Nadu Puduchery Kerala State Board, **Shri S.Sridharan** and Shri K Makesh in association with Orbit Exhibitions Pvt Ltd Mumbai conducted this event with great professionalism and finesse.

The regulatory conclave was spearheaded by **Shri. S.M. Mudda,** Chairman ,Regulatory Affairs Committee, IDMA & Managing Director ,Misom Labs Malta.

His Holiness **Shri Assanji** (world renowned non-religious contemporary spiritual teacher) delivered -A speech on SUCCESS UNSTOPPABLE"!! Untold secrets about Health Happiness & Abundance. His teachings and techniques were scientific and designed to instantly free a person of all misguiding belief systems, negativity and conditioned habits that limit one from achieving success and from enjoying life to its fullest.

MSME Conclave included scope for Pharma industries to collaborate with NIPER by **Dr. V. Ravichandiran,** Director NIPER, Kolkata. Support for collaborative research, Development / Evaluation Value Addition & NIPER Research facility were the key areas discussed.

With the support of Pharmexcil (Pharmaceuticals Export Promotion Council of India) participants could explore vast export opportunities .The event was further strengthened by The Indian Pharmaceutical Association, Tamil Nadu Pharmaceutical Sciences Welfare Trust and The Pharmaceutical Manufacturer's Association of Tamil Nadu & Pharma bodies like the Pharmacy Council of India & Indian Pharmacy Graduates Association.

On the closing day, Mr. S.Sivanandhan, Hon.Secretary, IDMA (TnPKSB) announced Pharmac south 2025 to be held on **4th and 5th July 2025.**

NOTIFICATION

IMP-12/1/2024-eoffice

Government of India
Directorate General of Health Services Central
Drugs Standard Control Organization
(Import & Registration Division)

FDA Bhawan, Kotla Road,
New Delhi-110002
Dated: 30 APR 2024

To
All States/UT Drugs Controllers

Subject: NOC's for Manufacture of Unapproved/Banned/New Drugs Solely for Export Purpose -Reg

NOC's for manufacture of unapproved/banned/new drugs solely for export purpose are granted as per the Guidance Document issued by CDSCO.

The above activity was delegated to State licensing Authorities w.e.f. 20th August, 2018 vide letter of F.No.7-5/2018/Misc./03 4(NOC) dated 2nd August, 2018

Now, it has been decided with the approval of Hon'ble HFM vide Ministry F. No. X.11035/210/2018-DR (Pt) dated 21st June, 2023 that Industry must be facilitated to file fresh applications for NOC for manufacture of unapproved/approved new drug/banned drugs solely for export purpose from15thMay, 2024 on online mode through CDSCO Zonal Offices. Accordingly, power delegated to State/UT Licensing Authority stands withdrawn w.e.f. 15 th May, 2024 and such NOC's shall be granted by the Head of respective CDSCO Zonal office w.e.f.15thMay 2024. Further All State/UT Drugs Controllers are required to handover all NOC's issued from 20th August, 2018 to14thMay, 2024 to respective Zonal Offices of CDSCO.

All manufacturers may be informed that they are required to obtain NOC from respective Zonal Offices of CDSCO through online mode (SUGAM Portal) w.e.f.15th May 2024 before issuing Manufacturing License from SLA for manufacture of Unapproved/Banned/New Drugs for export purpose.

Sh. Ranga Chandrashekar Rao Joint Drugs Controller (India) will be Nodal and designated person at CDSCO, HQ for said activity.

Yours faithfully

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

File No.: MED/48/2024-eoffice
Central Drugs Standard Control Organisation
Government of India
Ministry of Health and Family Welfare

FDA Bhawan, New Delhi
Dated 29 MAY 2024

CIRCULAR

Subject: Testing and evaluation of Medical Devices(MD)/ In vitro diagnostics(IVDs) by Medical Devices Testing Laboratories in the country - Reg.

In order to ensure the quality, safety and performance of Medical Devices(MD)/ In vitro diagnostics (IVDs), the Ministry of Health and Family Welfare, Government of India has granted registration of Laboratory for carrying out Test or Evaluation of a Medical Device on behalf of a manufacturer, under Chapter X of Medical Device Rules 2017 to strengthen the testing facility in the country

It is pertinent to mention that consequent to the implementation of MDR 2017 with effect from 01/01/2018, the Drug Rules 1945 are no longer applicable for MDs/IVDs. Also, the product standards of Medical Devices as prescribed under Rule 7 of the Medical Device Rules (MDR) are mandatory as under.

"(1) The medical device shall conform to the standards laid down by the Bureau of Indian Standards established under section 3 of the Bureau of Indian Standards Act, 1985 or as may be notified by the Ministry of Health and Family Welfare in the Central Government, from time to time.
(2) Where no relevant Standard of any medical device has been laid down under sub-rule (1), such device shall conform to the standard laid down by the International Organisation for Standardisation (ISO) or the International Electro Technical Commission (IEC), or by any other pharmacopoeial standards.
(3) In case of the standards which have not been specified under sub-rule (1) and sub-rule (2), the device shall conform to the validated manufacturer's standards."

It has been observed that the Medical Devices which has BIS standards available, the testing of such devices are not being carried out as per BIS standards.

In view of the above, it may be ensured that the samples of the medical devices shall comply to the BIS standards for its quality and performance and accordingly the medical devices shall be tested with respect to the requirements as prescribed in the BIS standards. If no BIS standard is available, then only other standards as mentioned in Rule 7 of the MDR may be applied.

This is for strict compliance.

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

To
All Medical Devices Testing Laboratories registered with CDSCO
Copy to:
All Stakeholders through website.
All Medical Device and In vitro diagnostics Associations in India

F. No. FDC/7/2023-eoffice
Government of India
Directorate General of Health Services
Central Drugs Standard Control Organization
(FDC Division)

FDA Bhawan,
Kotla Road, New Delhi.

Date: 16 MAY 2024

To,

All State/UTs Drugs Controller,

Subject: DTAB Sub-Committee to examine the proposal to regulate antibiotic and its irrational use -Reg.

This is with reference to the meeting of the expert group held on 25.04.2023 at ICMR HQ, New Delhi on pathway for strategic access to new antibiotics and regulation against excessive and irrational use of antibiotic in India. One of the recommendations of the expert group was to take steps that inappropriate combinations being sold currently should be banned immediately and steps should be taken that the inappropriate combinations do not find their way to India markets in future.

Subsequently, a meeting was held under chairmanship of Dr. Atul Goel, DGHS on 16.10.2023 to discuss how to regulate antibiotics overuse and irrational use. The committee has decided that CDSCO will be responsible for 6 monthly review of various fixed drug combinations of antibiotics marketed in various states.

Further, the proposal was placed in the 90th DTAB meeting held on 25.01.2024 wherein the committee deliberated the matter and a sub-committee constituted under chairmanship of Dr. D.S Arya to examine the matter in detail and give their recommendation vide O.M no F.No. 15-05/2024-DC dated 08.04.2024.

In this regard, the first meeting of Sub-Committee was held on 01.05.2024 through Webex wherein the following actions were recommended:

1) Request SLAs to provide the list of antibiotic combinations licensed by them for manufacturing and marketing in their respective states.
2) Request SLAs to monitor the availability of unapproved antibiotic combinations if any, moving in the market under their jurisdiction and intimate CDSCO on priority.

In view of above, you are requested to provide the list of antibiotic combinations licensed by you till date within 2 weeks. You are also requested to monitor the availability of unapproved antibiotic combinations if any moving in the market under your jurisdiction and take necessary action under the provisions of Drugs and Cosmetics Act & Rules and intimate to CDSCO from time to time on priority.

Yours faithfully,

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

Copy forwarded to:
1. All zonal, sub zonal and port offices of CDSCO
2. PPS to DGHS, MoHFW, Nirman Bhawan, New Delhi.
3. Under Secretary, Drugs, Ministry of Health and Family welfare, Nirman Bhawan, New Delhi.

F. No. 12-07/18-DC
Government of India
Directorate General of Health Services
Central Drugs Standard Control Organization
(New Drugs Division)

FDA Bhawan, Kotla Road,
New Delhi 110002,
Dated: 16 MAY 2024

To

All State/UTs Drugs Controller

Subject: Withdrawal of indication for Olaparib Tablets 100mg and 150mg in the treatment of patient with gBRCA mutation and advanced ovarian cancer who have been treated with three or more prior lines of chemotherapy- reg.

The Olaparib Tablets 100mg/150mg was initially approved by this office in 13.08.2018 for following indications:

Ovarian cancer:

- For the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer, who are in a complete or partial response to platinum-based chemotherapy.

- For the treatment of adult patients with deleterious or suspected deleterious germline BRCA-mutated (gBRCAm) advanced ovarian cancer who have been treated with three or more prior lines of chemotherapy.

Breast cancer:

- In patients with deleterious or suspected deleterious gBRCAm, human epidermal growth factor receptor 2 (HER2)-negative metastatic breast cancer who have previously been treated with chemotherapy in the neoadjuvant, adjuvant or metastatic setting. Patients with hormone receptor (HR)-positive breast cancer should have been treated with a prior endocrine therapy or be considered inappropriate for endocrine treatment.

The firm M/s. Astrazeneca Pharma India limited has submitted application to this directorate for the withdrawal of indications for Olaparib Tablets 100mg and 150mg in the treatment of patient with gBRCA mutation and advanced ovarian cancer who have been treated with three or more prior lines of chemotherapy. Based on post hoc subgroup analysis indicating a potential detrimental effect on overall survival (OS) for Olaparib compared to the chemotherapy control arm in the subgroup of patients who had received three or more prior lines of chemotherapy.

The matter has been reviewed in consultation with SEC (Oncology) experts in the 06th/24 meeting held on 19.03.2024 & 20.03.2024 at CDSCO (HQ), New Delhi.

The firm presented the clinical evidence for the withdrawal of indication of Olaparib 100mg and 150mg tablets in the treatment of patient with gBRCA mutation and advanced ovarian cancer who have been treated with three or more prior lines of chemotherapy and accordingly, the firm has been directed to withdraw the said indication and revise the package insert.

In view of the above circumstances, you are requested to direct all the manufacturers of said drug under your jurisdiction to withdraw marketing of the product Olaparib Tablets 100mg and 150mg approved by your office for the treatment of patients with gBRCA mutation and advanced ovarian cancer who have been treated with three or more prior lines of chemotherapy indication and submit the revised package insert. The drug may continue to be marketed for other approved indications.

Yours faithfully,

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

Copy to: -

1. All Zonal/Sub Zonal offices of CDSCO
2. Indian Drug/Pharmaceuticals Association Forum
3. Website of CDSCO

NEWS

Changes in Law Will Just Make Medicines More Expensive, Not Better

A good health system requires a constant supply of quality affordable medicines. Medicines constitute nearly 50 per cent of the health costs incurred by people. The high costs of medicines are primarily due to patenting. This can be overcome by allowing the competition which generic pharmaceutical companies provide. The Indian generic industry has been the provider of essential quality medicines at affordable prices all over the world. However, the newly amended patent rules could change the ecosystem. Indian patent rules were amended earlier this year, making it difficult to file opposition to patents at the pre-grant stage, thus allowing easy patenting and increasing drug prices.

The Indian Patent Law does have provisions to oppose the patenting of medicines. A successful opposition means that generic companies can produce the same drug. This allows for competition, the key to lowering prices. The opposition can also be registered to a proposed patent, and after it has been granted.

By the turn of the century, India could provide affordable and quality drugs because of the change in the Patent Act in the early 1970s. The law allowed protection only to the process through which a medicine was made, but not the product itself. This spurred the development of the generic industry, making India a net exporter of drugs by the late 1980s and the leading generic manufacturer by the 1990s.

However, there were headwinds in the form of the TRIPS Agreement of 1995 which mandated the re-introduction of product patents. Patents are to be granted for products which are both novel and inventive. However, in 2005, when amendments to the Patent Act had to be made following the TRIPS agreement and had to be introduced to the agreement, it was noticed that nearly 76 per cent of the drugs patented in the US and Europe were in only new forms — popularly known as me-too drugs. They did not have any significant increase in the therapeutic benefit. To ensure that India does not slip back, in 2005, all political parties and civil society came together to introduce an amendment to the Patent Act – Section 3(d). This was to make sure that an old drug in a new form would not be patented unless its therapeutic efficacy was significantly greater. This was upheld by the Madras High Court in the iconic Novartis case.

India also amended its patent law to take advantage of the flexibilities of the TRIPS Agreement. One of them pertained to opposition to patent applications at all stages – pre-grant and post-grant. It also allowed the revocation of patents and filing counterclaims. Rules were framed to facilitate these changes. It also allowed the government to issue licenses to other companies without the consent of the patent holder. The TRIPS Agreement allows such flexibility in patent laws. The Indian Patent Act stipulates that whenever reasonable requirements of the public are not met or a drug is not available at

a reasonably affordable price, the government, at the instance of a generic company or any interested person, can issue a license to a firm to produce the drug. This can be done without consulting the patent holder.

These rules are now being sought to be altered because of pressure from pharma majors – largely Western and Japanese companies. The repeal of Section 3(d) has been a demand in the negotiations to Free Trade Agreements with the US, UK, and the EU.

Most pre-grant oppositions (PGOs) to patents today come from patients' groups or civil society organisations. Generic companies are hesitant to file PGOs as they will not allow them to get a license from the Western or Japanese pharma company in case they get a patent.

Until the Rules were amended earlier this year, the patent controller would send the PGO to the applicant who would file a reply. The opponent to the patent was then allowed to file a rejoinder. The patent controller would then hear the PGO and arrive at a decision on the patent.

After the amendment to the patent rules, the patent controller is first to decide if the PGO is maintainable. The official can dismiss it without even hearing the opponent to the patent. This power is not only against the provisions of the Patent Act but allows arbitrary ercise of power.

In the past opposition by patients or patient organisations has scuttled numerous patents which are frivolous and have no therapeutic benefit. Data shows that PGOs reduce the likelihood of frivolous patents. The amendments will only help non-deserving patents, stymie competition and drive the prices of drugs up.

The opponent to the patent now has to pay fees which was not the case earlier. This is a financial burden for patients and civil society organisations and could discourage them from filing PGOs.

The new rules also alter the relations between the patent holder and the patent controller in another way. After a patent is granted, the patent holder is supposed to “work the patent” — produce the drugs in India. According to the old rules, the controller had to be given details about the production process every year. After the amendments, this information will be provided on a three-yearly basis. The non-working of the patent is one of the basis for seeking a compulsory license. The fact that data will not be available to the Patent Controller, and hence the public, will make compulsory licensing difficult.

The amended rules will prolong the life of drugs on account of frivolous patenting, increase their prices, and make lives difficult for patients.

Source: *The Indian Express,* 22nd April 2024

Druggist Association Opposes Centre's Move to Sell Over-the-Counter Medicines Without License

The Central Government's proposal to permit the sale of Over-The-Counter (OTC) drugs without a license in India is a cause of deep concern warned the All India Organization of Chemists and Druggists (AIOCD).

AIOCD president, JS Shinde, said that such a move would contravene existing drug laws, pharmacy regulations, and pertinent legal frameworks, including directives from the Supreme Court.

Allowing OTC drug sales without proper regulation poses serious threats, including drug abuse, increased risk of adverse drug reaction, delayed access to healthcare, possible comprise in storage of medicines etc.

"Besides this, the absence of pharmacist consultation services, proliferation of counterfeit drugs, delayed access to healthcare services and inadequate pharmacovigilance measures are also cause of concern," said AICOD general secretary Rajiv Singhal.

The group has also urged the government to consider the multifaceted implications of this proposal, emphasising that unregulated availability of medications in general and grocery stores does not serve the best interests of society.

"With a membership comprising 12.40 lac chemists across the nation, AIOCD firmly opposes any measure that undermines the integrity of the healthcare system. The organisation stresses the importance of consulting all relevant stakeholders, including AIOCD, in the formulation of regulations pertaining to this matter," the group said in its memorandum submitted to the Health Ministry.

OTC treats common, self-treated medical problems and symptoms like colds, mild discomfort, allergies, and other benign health issues. The Union Government has proposed to bring OTC medications into India through an amendment to the Drugs and Cosmetics Regulations and permit their retail market sales without the need for a prescription. A list of OTC medicines which are permitted to be sold in shops will be authorised by the Drug Technical Advisory Board (DTAB) and could include drugs like — antifungal creams, cough syrup, laxatives etc.

Source: *The Hindu,* 27th April 2024

How is India Streamlining the Pharma Sector? | Explained

The story so far: India's drug regulator, the Central Drugs Standard Control Organisation (CDSCO), has withdrawn powers delegated to State licensing authorities to issue NOCs (no objection certificates) for manufacture of unapproved, banned or new drugs for export purposes. This latest announcement covering drugs for export comes at a time when India has been under scrutiny for allegations of supplying substandard drugs causing health concerns in several countries. The CDSCO is now the sole authority for issuing manufacturing licences for drugs meant for export.

What is India's role in the pharma market?

India ranks third worldwide as a producer of drugs and pharmaceuticals by volume, exporting to around 200 countries/territories. The Indian pharmaceutical industry supplies 62% of the global demand for vaccines and is a leading supplier of DPT (diphtheria, pertussis and tetanus), BCG (Bacillus Calmette-Guérin, used primarily against tuberculosis), and measles vaccines. At least 70% of WHO's vaccines (as per the essential immunisation schedule) are sourced from India, the Centre had noted in a submission in Parliament.

What will be the impact?

India is a key player in the international generic medicine market and any change in policy has a direct impact on manufacturers and importers, say industry insiders. The centralising of the licensing authority is significant, they point out, because according to a study conducted by the Department of Pharmaceuticals, India needs to get ready to take advantage of drug sales worth $251 billion going off-patent this coming decade.

The study notes: “In the years between 2022 and 2030, the pharmaceutical sector in India will undergo landmark changes as several drugs are expected to go off-patent and provide an opportunity for the entry of generic products. Expiry of patents is very promising for the Indian generic drug market as it is expected to expand and grow further with inclusion of these new drugs. With ongoing developments, India has started focusing on self-reliance at a large scale. Hence, it is imperative to identify these drugs beforehand, draft and implement strategies which help in their timely entry into the market by promoting generic drug manufacturing.”

What are the challenges?

India is dealing with several challenges, including tackling intellectual property rights, lack of research and development etc. The study points out that understanding the political, economic, sociocultural, technological, environmental, and legal factors is vital for assessing the opportunities and challenges in the pharmaceutical market in India. “The industry must adapt to changes in these external factors, navigate regulatory requirements, leverage technology advancements, and align their strategies with the evolving needs of the

pharmaceutical industry to succeed in the global market," it noted. Speaking about the change, Raheel Shah, business development director, BDR Pharmaceuticals, says the move is welcome as the centralisation of NOCs will formalise the Indian pharma industry. "This will result in the efficiency of the overall process along with bolstering pharma exports to key international markets. It will help to bring uniformity in protocols, achieve the target of reaching $450 billion by 2047," he adds.

What about the quality of manufacturing?

An article in the British Medical Journal titled, 'Indian government cracks down on 18 drug companies for poor quality manufacturing', noted that the Indian government had cancelled the licences of over 10 pharmaceutical companies as part of a crackdown on poor quality manufacturing. The action last March came after an inspection of 76 drug firms across 20 States. "The government is also understood to have given notices to a further 26 companies for not complying with good manufacturing processes. The Indian pharmaceutical industry has an estimated 10,500 companies, with drug exports having more than doubled in the past decade. But the industry has faced a series of scandals of late, including a World Health Organization investigation into four contaminated cough syrups that caused acute kidney injuries and were linked to the deaths of 66 children in the Republic of the Gambia last year," it added.

In what seems like an effort to keep a strict watch, the latest order by CDSCO states that pharmaceutical companies will have to get their NOCs from the zonal offices of CDSCO online before applying for manufacturing licences from their respective State/UT drug regulators. The Drugs Controller General of India, Rajeev Singh Raghuvanshi, said the decision was taken to facilitate the application process. In 2018, the CDSCO had permitted State and UTs' drug licensing authorities to grant permissions to export some specific drugs. As per the new order, local regulators will have to hand over the details of all the approvals they have given from August 2018 to May 2024 to CDSCO.

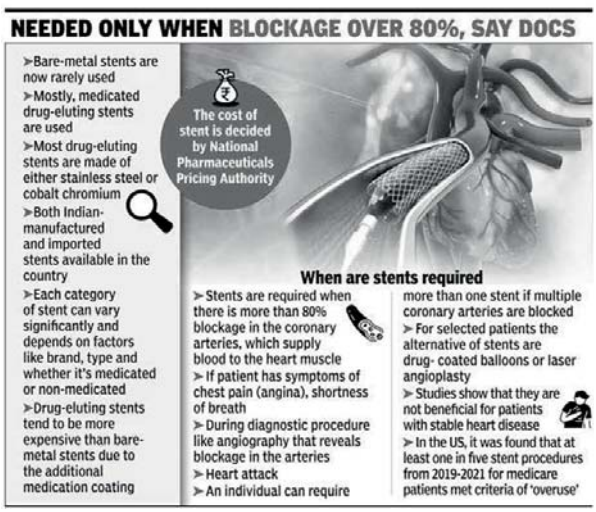
The centralisation of powers hasn't come as an overnight development, says an industry expert. The Central government's advisory group on drugs had earlier this year noted that getting NOCs from local drug regulators for pharmaceutical products is a tedious process, leading to delays. Says Harish K. Jain, president, Federation of Pharma Entrepreneurs: "We don't anticipate any major impact as far as costing or delays with this latest move. Export of goods is on the Union List. Also, the central authority was always the Central government; the power to hand out licences for export of drugs was delegated to States a few years ago."

Source: *The Hindu,* 13th May 2024

Why Overuse of Stents in Cardiac Patients Needs to be Arrested

The arrest of nearly a dozen people, including two senior cardiologists, working in Ram Manohar Lohia Hospital for allegedly taking bribes to promote stents and other medical products of a particular company, has again brought the critical issue of overuse of stents to treat cardiac patients to the fore. While police investigation is under way, studies from across the globe indicate that a significant number of doctors are prescribing stenting unnecessarily.

A US study has revealed that five stents were placed in every fifth patient with stable coronary artery disease. The study, conducted between 2019 and 2021, revealed that 2,29,000 unnecessary stents were placed in patients.



While no similar study has been conducted in India, many doctors admit that a similar 'overkill' occurs in the country as well. And most of the time, it is for the purpose of making money by inflating patients' hospital and treatment bills. According to doctors, cardiac stents are vital but are required only when there is more than 80% blockage in the coronary arteries supplying blood to the heart muscles. Blockage can lead to symptoms such as chest pain (angina) or cause a heart attack.

The National Pharmaceuticals Pricing Authority has fixed the ceiling price for coronary stents. Stents are free for poor patients and those covered under the Ayushman Bharat Yojana, CGHS scheme and Delhi Arogya Kosh.

Dr S Ramakrishnan, cardiology professor, AIIMS, was unequivocal that if a cardiac condition could be managed medically, no stent ought to be used. “Stents are indicated only If a patient does not get relief from medicines. If you use a stent when the blockage is not significant, or if it is in a non-critical artery, that is misuse and unethical,” he declared. He said that stents should be used in acute heart attack cases, considering the use of stents as life-saving and effective in reducing symptoms.

Dr Ashwani Mehta, senior cardiology consultant, Sir Ganga Ram Hospital, similarly said, “In 99% of balloon angioplasty cases, a stent is placed to prevent the artery from re-narrowing. In some cases, other than heart attacks, however, angioplasty can be delayed and managed with medications.”

The different types of stents include bare-metal stents (BMS) and drug-eluting stents (DES). BMS have a metal mesh and provide structural support to keep the artery open. Dr Pradeep Kumar Nayak, director, interventional cardiology, Dharamshila Narayana Hospital, said, “At our hospital, we don't use BMS. But DES, which are coated with medication, helps prevent the artery from becoming blocked again after the stent is placed. The cost of stents can vary depending on factors such as the type, brand and the requirement of our facilities,” said Nayak.

Discussing alternatives to stents, Dr Praveen Chandra, chairman of cardiology, Medanta Medicity, said there were drug-coated balloons or laser-assisted angioplasty. These alternatives are particularly suitable for patients with long (more than 25mm) and diffuse blockages, thin arteries (which are common in Indian diabetic patients), and in cases of stent failure (when a stented blood vessel becomes blocked). “Such alternatives are preferable for young patients because if a stent is placed at an early age, it will remain inside the body for the patient's entire life and can have its own effects,” said Chandra, adding that the longer the stent stayed in the body, the higher the chances of re-blockage.

Elaborating on this, Chandra said, “Drug-coated balloons represent a new concept of stentless angioplasty, where the arteries remain natural, and there is a smaller need to use double blood thinners. This approach keeps the arteries ready for a future bypass if needed. Laser-assisted angioplasty is also stentless and prevents re-blockages.”

Source: *The Times of India,* 11th May 2024.

Study Indicates Rise in Antimicrobial Resistance in Tamil Nadu's Poultry Sector

Recent research by Toxics Link and World Animal Protection has identified Tamil Nadu's poultry sector as an emerging hotspot for Antimicrobial Resistance (AMR). The study involved collecting 14 samples from various poultry farms across the state, revealing that 11 samples contained high levels of Antimicrobial Resistance Genes (ARGs).

The research highlights a concerning trend of indiscriminate antibiotic use among poultry farmers, driven by a lack of awareness and understanding of the consequences. Despite the Bureau of Indian Standards' recommendations against the use of Antibiotic Growth Promoters in poultry feeds, these substances remain available in the market and are still being utilized by farmers.

Furthermore, the study noted that Colistin, a critical antibiotic designated for treating multidrug-resistant infections and banned by the Union Ministry of Health in 2019 for use in food-producing animals, continues to be sold through online platforms.

ARGs are genetic elements that enable bacteria, viruses, fungi, and parasites to withstand antimicrobial treatments. While ARGs occur naturally, their prevalence has been exacerbated by human activities, particularly the overuse and misuse of antimicrobials in various sectors. This has led to a rise in diseases such as pneumonia, gonorrhoea, post-operative infections, HIV, tuberculosis, and malaria becoming increasingly difficult to treat.

India accounts for 3% of the global consumption of antimicrobials in food animals, with one of the highest rates of antimicrobial use in the livestock sector worldwide.

Vijay Pal Singh, Principal Technical Officer at CSIR-IGIB, emphasized the significance of the findings: "The current study provides evidence of antibiotic use in poultry and its role in increasing trends of antimicrobial resistance."

Satish Sinha, Associate Director of Toxics Link, stressed the urgent need for action: "It's crucial for the country to identify potential hotspots, establish monitoring and surveillance systems, and enforce restrictions on antibiotic use across all sectors."

Source: *The Times of India,* 13th May 2024

DCGI Calls for Strict Reporting of Side-Effects Related to Medical Devices

The Drugs Controller General of India (DCGI) has called for timely reporting of adverse events related to medical devices and directed all medical device licence holders and manufacturers to report any adverse events related to life-saving medical equipment on the government's Materiovigilance Programme of India (MvPI) platform stating that the move is vital to mitigate risks and safeguard public health.

In its circular issued this week the top drug regulator said that the post-market surveillance (PMS) of medical devices is one of the important aspects to ensure safety and performance of the medical devices.

"PMS supports identifying and addressing any potential risk or adverse event associated with the medical device. Timely reporting of the adverse events allows for the identification of unidentifiable risks, analysing frequency of already identified risks and enabling the manufacturers and regulatory authorities to take appropriate measures to mitigate risks and safeguard public health," it said.

The MvPI was launched by the Health Ministry with the objective to improve Indian patient safety by monitoring, recording and analysing the root cause of adverse events or risks associated with the use of medical devices including in-vitro diagnostics by healthcare professionals or patients/users

and suggesting regulatory bodies for appropriate action with the sole intention of improving patient safety.

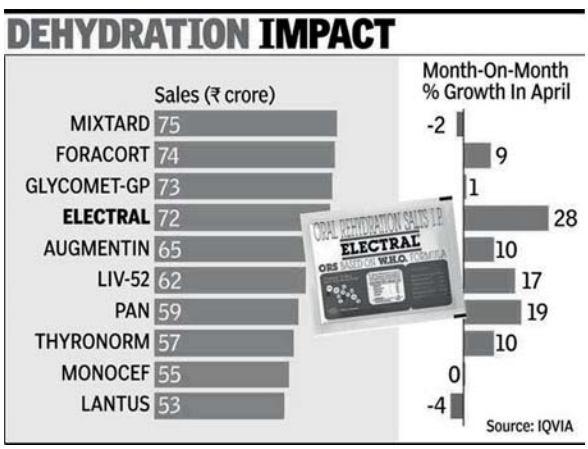
"MvpI is an important program for reporting of adverse events, coordinated analysis etc related to the medical devices including in-vitro diagnostic devices, therefore it is suggested that all the license holder should also use the MvPI platform for reporting of any adverse events/serious adverse events associated with the devices," the communication said.

Currently in India medical devices including In-vitro diagnostic medical devices have come under the regulation under the Drugs and Cosmetics Act, 1940 and Medical Devices Rules, 2017. A license/approval is required for the import/manufacture for marketing of the devices in the country.

Source: *The Hindu,* 18th May 2024

Electral Sales Jump 26% as Heatwaves Take Toll

Dehydration seems to have troubled us the most in April with the onset of dry and scorching heat. Sales of widely-sold oral electrolyte Electral jumped over 26% year-on-year in April, while its month-on-month growth was the highest among top 10 rankers, data culled from market research firm IQVIA said. The month-on-month growth for Electral stood at 28%, with sales of Rs 72 crore in the domestic pharma retail market. The growth catapulted the brand to move up from 20th slot in March to fourth rank in April.



Among therapies, cardiac, gastroenterology and dermatology managed to shake off the sluggishness in the domestic pharma retail market, sources told TOI. The market valued over Rs 19,500 crore in April, bounced back with a 9% growth year-on-year. Poor sales of respiratory and anti-infectives had pulled down the market in March to a flat growth, with reduction in winter chill.

Other growth drivers for the month include gastroenterology medicines, Pan and Pan D, which increased by 19% and 17% respectively, liver therapies, Liv-52 by 17%, andUdiliv28%. Antidiabetic therapy Mixtard topped the list, netting sales of Rs 75 crore during April, followed by respiratory medication Foracort (Rs 74 crore) and antidiabetic pill Glycomet-GP (Rs 73 crore). Among the players, Sun Pharma, Mankind, Torrent and Intas registered a strong growth month-on-month. Mumbai-based Sun Pharma maintained the top position in the market with market share of 8%.

Further, during the month, acute therapy - mainly painkillers and anti-infectives - has shown a growth of 6%. As against this, chronic medication - prescribed for long-term ailments - has grown more than double at 13%. For past six months, chronic has outperformed acute therapy.

The month proved to be healthy for both MNCs and domestic companies, with both posting growth of 8% each. On a MAT (moving annual total) basis, the pharma retail market grew over 7% at Rs 2.2 lakh crore.

Meanwhile, EBITDA margins of companies are expected to improve from FY25, driven by cost rationalisation and benefits of operating leverage on account of higher volumes. Those with a significant presence in the API (active pharmaceutical ingredient) segment are likely to see revenue growth of 10%-11% y-o-y with operating margins of 17-20% through FY25-26, India Ratings and Research said in a note.

Source: *The Times of India,* 18th May 2024

Centre's Lens on Unapproved Antibiotic Combos, Asks States to Monitor Availability

Centre has asked drug controllers of all states and UTs to share a list of antibiotic combinations licensed by them for manufacturing and marketing in their respective jurisdictions. It has also asked states/UTs to monitor the availability of unapproved antibiotic combinations, if any, present in markets under their jurisdiction and take action, reported.

In 2018, Central Drugs Standard Control Organisation (CDSCO) had banned 26 antibiotic combinations. However, a follow-up study published in the Journal of Pharmaceutical Policy and Practice in 2022 showed that a significant number of such antibiotics remained available in the market. Also, the study found, sales of antibiotic combinations containing chemical compounds belonging to the same drug classes as the banned drugs increased after the ban. Sales of similar non-banned formulations also went up.

Some pharma companies promoted products containing new non-antimicrobial components to the banned combination to dodge the govt order, therefore nullifying any attempts to reduce antibiotic resistance caused by the consumption of such drugs. An antibiotic combination refers to fixed dose combination medicine comprising two or more antibiotics in a fixed ratio of doses and available in a single dosage form.

"Although antimicrobial FDCs (fixed-dose combinations) have been critical in improving clinical outcomes among patients with certain infections such as tuberculosis and HIV, use of such FDCs for routine bacterial infections is inappropriate as it drives AMR (antimicrobial resistance) by selecting co-resistant microorganisms. Thus, their indiscriminate use is widely discouraged, including in World Health Organisation's AWaRe framework of antimicrobial

prescribing," the study said.

It added that many FDCs marketed in India were never approved by CDSCO, their approval comes from state-level regulatory bodies that, at times, lacked sufficient technical expertise to make such decisions.

Source: *The Times of India,* 21st May 2024

TN PTA Demands Inclusion of AIOCD as Member to the Subcommittee Formed to Classify OTC Drugs

The Tamil Nadu Pharma Traders Association (TN PTA), the splinter group of the TN CDA, has demanded to the Union Health Ministry to include the all India pharma trade body, AIOCD, as a member to the sub-committee constituted by the CDSCO recently to classify OTC drugs. TN PTA, in its state committee held at Perambalur near Chennai, has passed one resolution in this regard.

Presently, apart from the drug controllers of Jharkhand and Karnataka, all members of the subcommittee formed by the CDSCO are medical doctors of different ranks. There is no member to represent the public or the stakeholders of medicines.

The eight-member sub-committee is headed by Dr Anupam Prakash, Director and Professor of Medicine, Lady Hardinge Medical College, Delhi, with Dr Umesh D Suranagi, Associate Professor of Medicine, Director General of Health Services (DGHS); Dr Ratan Kumar Gupta, Department of Paediatrics, Vardhman Mahavir Medical College & Safdarjung Hospital, Delhi, Dr Bikash Medhi, Professor, Department of Pharmacology, Post Graduate Institute of Medical Education & Research (PGIMER), Chandigarh; Dr Abhishek Agarwal, Professor, Department of Medicine, SMS Medical College, Jaipur; one representative from Indian Council of Medical Research (ICMR), and Drugs Controllers of Jharkhand and Karnataka, as members.

The TN PTA has forwarded the resolution to the Union ministry of chemicals and fertilizers, ministry of health and also to the Prime Minister of India. President of the association, T Natarajan said he will forward the copy of the resolution to the DCGI also.

Another resolution passed by the TN PTA is with regard to electricity charges for wholesale and retail drug business. The association has observed that the National Pharmaceutical Pricing Authority (NPPA) is trying to lower the drug prices, but they are not considering the expenses of the traders. Both the wholesalers and the retailers have to use coolers to keep the drugs in their true potency and it requires huge electricity charges. So, the traders must be helped with by providing household domestic charges. The copies of the resolution were sent to the central and state governments.

The fourth resolution passed by the association was for a local issue based on pharmacy education in Chennai. The CL Baidu Mehta College of Pharmacy is an institution under the management of TN CDA Education Trust. TN PTA has raised one demand through their resolution that fifty percent of the total seats for the D Pharm course must be reserved for the children of the pharma traders. The committee has engaged T Natarajan and the Advisor of the association, Mannargudi Ramachandran, to discuss the matter with Trichy Manohar, president of the TNCDA.

While speaking to Pharmabiz, the advisor of the TN PTA, Mannargudi Ramachandran said all the resolutions were passed unanimously and one resolution was for inviting the attention of the drug control department. According to him, the traders request the DCA to limit the issue of sale licences for pharmacies with a ratio of 1 licence for 500 families in urban areas, and 1:1000 in rural areas.

Meanwhile, T Natarajan said he plans to visit AIOCD office in Mumbai along with Ramachandran to invite the national president JS Shinde and the secretary general Rajiv Singhal to Chennai. A special general body will be called to felicitate the national leaders in the state capital. JS Shinde had earlier told Pharmabiz that he was interested to meet the pharma traders of Tamil Nadu.

Source: *Pharmabiz ,* 23rd May 2024

Pharma Sector Targets Latin American Mkt for Exports

After the US, Europe and Africa, the Indian pharmaceutical industry is looking to tap the Latin American market for exports. Currently, the Latin American region accounts for only 7% of the total $27.8 billion drug and pharmaceutical exports from India.

Pharmaceuticals Export Promotion Council of India (Pharmexcil) chairman S V Veeramani told TOI, “Geographically, the US is the largest importer for us and the same trend will continue. We are targeting Latin America as there is a lot of scope. Presently, they are not buying much from India,” he said.

Veeramani was speaking on the sidelines of the 9th edition of 'Pharmac South 2024', a pharmaceutical expo organised in Chennai on Friday. India's global drug and pharmaceutical exports will rise by 10% in FY25 over last FY and exceed the $30 billion mark, he added.

While India's exports to North America stood at $10 billion, it was just $2 billion for Latin America. Meanwhile, J Jayaseelan, chairman, Indian Drug Manufacturers' Association, Tamil Nadu, Puducherry and Kerala said, steps must be taken to establish the National Institute of Pharmaceutical Education and Research (NIPER) in Tamil Nadu.

Source: *The Times of India,* 25th May 2024

Weight Loss Drugs up Abdominal Paralysis Risk: Study

Medications like Wegovy and Ozempic, effective for rapid weight reduction, may come with the risk of uncommon yet serious side effects, including abdominal paralysis, a condition characterised by delayed stomach emptying, a new US study has suggested.

Abdominal paralysis can cause unintended weight loss, malnutrition and other complications that may require medical or surgical intervention.

The study, results of which has been published only in abstract form, found people who took Wegovy and Ozempic, also referred to as GLP-1 agonist drugs, were 30% more at risk of developing abdominal paralysis compared to those who did not. Glucagon-like peptide-1 receptor agonists (GLP-1RAs), also known as GLP-1 agonists, are a class of medications used to treat Type 2 diabetes and obesity.The study, presented at a medical conference - Digestive Disease Week 2024 - in Washington on Saturday, is based on an analysis of the records of more than three lakh persons with diabetes and obesity of which 1.65 lakh were prescribed GLP-1 agonists that are known to slow stomach emptying and stimulate insulin production among other things.

Dr Prateek Sharma, professor of medicine at the University of Kansas, who led the study, told TOI that abdominal paralysis is a rare side-effect of these drugs but given the high usage of GLP-1 drugs, or weight-loss drugs as it is commonly referred to, it's important too warn people about it. "These drugs are new and while the positive effects are well-established and talked about, we are yet to discover the full extent of its long-term side-effects and that's why I feel people who are taking them should be careful," he said.

Wegovy and Ozempic are not legally available in India. However, reports suggest that these drugs are being sourced by many through the grey market at premium. Recently, a Denmark-based company called Novo Nordisk has launched 'Rybelsus' which has semaglutide - the main ingredient of Ozempic - in tablet form in India. It has been approved for diabetes management but, doctors say, the drug is also being used 'off-label' for weight loss.

Wegovy and Ozempic were also initially approved for diabetes management. But when reports emerged that it could help lose 10-15% weight within a year, the US FDA allowed its limited use in people with obesity as well. Soon, the drug group took the world by storm as people, including celebrities such as Elon Musk and Oprah Winfrey, said they were using it.

Dr Anoop Misra, chairman, Fortis C-Doc, said Rybelsus is quite expensive with one month's prescription amount costing over

"Given the popularity of these drugs, it is likely that we may have easy availability of the drug in near future and that too at lesser costs which is good as these drugs have proven to be effective in managing blood sugar, reducing weight, and even in managing chronic kidney disease. But the medical community as well as the public needs to be aware of its side-effects," he said.

According to Dr Randhir Sud, chairman of the department of digestive and hepatobiliary sciences at Medanta hospital, drugs like Wegovy and Ozempic work by slowing the stomach movement and thus reducing appetite. "Users can feel nausea and vomiting when they start taking the drug but in most cases these side-effects are likely to subside. I haven't come across any case of abdominal paralysis yet but these are early days of its usage in India," he said.

In the US study, Sharma and his colleagues used a large database to analyze healthcare records of over 120 million patients, focusing on those with diabetes and obesity. They compared patients taking GLP-1 drugs to a control group, matching them by demographics and health factors. Over one year, they found that 32% of GLP-1 users experienced gastrointestinal issues like nausea, GERD, and stomach paralysis. While GLP-1 users had more GI-related procedures, they had slightly fewer ER visits and hospital admissions. This suggests that while GLP-1 drugs increase GI side effects, they don't lead to more severe health crises requiring emergency care or hospitalisation, the Kansas University professor said.

We aren't saying that one shouldn't use them. But our research clearly underscores the need for medical monitoring of gastro-intestinal side-effects such as abdominal paralysis that can impact quality of life," he added.

Source: *The Times of India,* 27th May 2024

Pharma Exports to Grow at A Faster Clip, Touch $31 Billion in FY25

India's pharmaceutical exports are expected to grow over 11% and touch record $31 billion in FY25 on the back of multiple factors, especially a shortage of drugs in the key U.S. market, a top official of the exporters body under the Commerce Ministry said

For the fiscal ended March 2024, pharma exports, a mainstay in the country's global trade, rose 9.6% to $27.8 billion. The growth came amid numerous global challenges, Pharmaceuticals Export Promotion Council of India Director General Ravi Uday Bhaskar said.

More than 50% of the exports last fiscal were to highly regulated markets such as North America and Europe. “Pharmaceutical exports to the U.S. increased 15% to more than $8 billion, while the exports to the U.K. were 21%

higher at $783 million demonstrating the robust growth of the Indian pharmaceutical industry even in challenging situations," he told PharmaLytica expo and conference that got underway in Hyderabad.

As long as India continued to manufacture quality drugs at affordable prices the industry will remain unmatched, he said. Geo-political tensions, economic slowdown and logistical challenges apart, Indian pharma industry faced heat last fiscal over quality issues.

Talking to The Hindu, Mr.Bhaskar said the shortage of generic prescription drugs in the U.S. is expected to increase in the backdrop of some units there shutting down. Likewise, the demand in shipments to Africa is expected to enhance as non-governmental organisations that had shifted their focus to Covid had reverted to supply of free drugs.

Pharma exports to Africa, which had declined 5% in FY23, ended 8% higher last fiscal. Barring CIS countries, pharma exports to all other markets were higher year on year in FY24. As a pointer to the road ahead, the exports in April 2024 rose more than 7%.

Source: *The Hindu,* 30th May 2024

CDSCO Panel Gives Nod for Continuation of Phase-II Clinical Trial of SII's Dengue Vaccine

An expert committee under the Central Drug Regulatory Authority has recommended continuation of phase-II clinical trial of the Serum Institute of India (SII)'s vaccine against dengue after noting the promising results of the phase-I interim clinical trial. The Serum Institute conducted the phase-I, double-blind, randomised, placebo-controlled trial on 60 healthy individuals aged 18 to 45 years in Australia to assess safety and immunogenicity of the tetravalent live attenuated dengue vaccine.

A tetravalent live attenuated dengue vaccine was manufactured in India after receipt of vaccine strains from NIAID, NIH, USA.

"A single dose of dengue vaccine was safe and well tolerated in adults. The vaccine was highly immunogenic with trivalent or tetravalent seroconversion and seropositivity in most of the participants," stated the study results published in Vaccine, a journal by Elsevier, last year in August.

In light of recommendation of the subject expert committee dated July 18, 2023, the SII presented phase-I interim clinical trial report of Dengue Tetravalent Vaccine (Live, Attenuated) which was discussed by the panel on May 31.

"After detailed deliberation, the committee noted the results of Phase I interim clinical trial and recommended for continuation of Phase II clinical trial as per approved protocol," the SEC recommendations stated.

Source: *The Economic Times,* 6th June 2024

Bengaluru Co, Global Initiative to Take New Compound Against Superbugs to Patients

The Global Antibiotic Research & Development Partnership (GARDP), and Bengaluru-based Bugworks Research Inc, are collaborating to co-develop a promising new antibiotic compound — "BWC0977" — with broad-spectrum antibiotic activity against multidrug-resistant bacteria that cause life-threatening infections.

As per the agreement, GARDP will provide up to $20 million to Bugworks in technical and financial support for the pharmaceutical and clinical co-development of BWC0977. In return, Bugworks has granted GARDP manufacturing and commercialisation rights for the compound in 146 nations, almost all of which are low-or middle-income countries (LMICs). "...BWC0977 has shown potent activity against two 'critical priority' superbugs (drug resistant pathogens) identified by the WHO – carbapenem-resistant Acinetobacter baumannii and Klebsiella pneumoniae – which are increasingly untreatable and accounted for over 20% of antimicrobial resistance (AMR)-associated deaths in 2019 according to the global research on AMR study," the release read. Manica Balasegaram, GARDP's executive director said "BWC0977" stands out for its novelty and potential to address unmet public health needs against priority pathogens where few treatments exist.

Anand Anandkumar, co-founder and CEO, Bugworks, which incubated at the Centre for Cellular and Molecular Platforms (C-CAMP) in Bengaluru, said: "An overarching goal of this partnership is to enable access to this compound simultaneously in Western countries and in LMICs with high AMR burden. The GARDP-Bugworks collaboration builds on more than $12.4 million in prior funding from CARB-X to advance BWC0977 through early-stage research and initial clinical testing.

The release, issued by C-CAMP, reads: "The development of BWC0977 reflects the bolstering of the global health ecosystem to respond to the AMR crisis. CARB-X has provided critical support for the pre-clinical development and first-in-human (phase 1) clinical study of this compound. GARDP will now collaborate with Bugworks to further develop BWC0977 and, upon approval, enable global access."

Source: *The Times of India,* 12th June 2024

Patent Filings Credit Bharat Biotech as 'Inventor' of Covaxin, Omit ICMR

India's first indigenously developed coronavirus vaccine, Covaxin, was a joint collaboration between the Indian Council of Medical Research (ICMR) and the Hyderabad-based Bharat Biotech International Limited (BBIL) with intellectual property (IP) rights jointly shared between the two organisations. That is what the public record states. However, filings by the BBIL at patent offices in India, the United States and Europe suggest that only its scientists and personnel are credited as 'inventors' of the vaccine with no mention of ICMR scientists.

The Hindu has viewed documents detailing these patent applications. If BBIL personnel, credited in applications as Deepak Kumar and Krishna Murthy Ella — Chairman and Founder, BBIL— are indeed the only inventors, it contradicts a statement by the Union Health Ministry, the nodal Ministry of the ICMR, in the Rajya Sabha, which claimed that the IP rights are "jointly owned".

In response to a question in the Rajya Sabha on July 2021 by Congress president Mallikarjun Kharge, who demanded details of the agreement between the ICMR and the BBIL for the development of Covaxin, the then Minister of State (Health Ministry) Bharati Pravin Pawar laid out a detailed response.

The Minister's statement said the ICMR would provide a "well characterised" virus strain for vaccine development, the BBIL would develop the final vaccine formulation and, be given a "non-exclusive" licence granted to commercialise the product within two years. It was explicitly mentioned that the "..intellectual property over the product would be jointly owned by the ICMR and the BBIL." The ICMR would also receive as royalty 5% of net sales to be remitted half-yearly.

The ICMR said that while it had not funded the BBIL for Covaxin development, one of its institutes — the ICMR-National Institute of Virology (NIV), Pune — had spent "funds for Covaxin development".

It also funded phase-3 clinical trials of Covaxin at 25 locations, involving 25,800 participants. All in all, the ICMR spent ₹35 crore for developing Covaxin. As of January 2022 — as per an update by the government to the Rajya Sabha — the ICMR received ₹171 crore as royalty for Covaxin.

Ms. Pawar's response to Parliament, however, did not elaborate on the sharing of patent rights. The BBIL, which has over the years had several research collaborations with public research bodies such as the Council of Scientific and Industrial Research (CSIR) and the ICMR itself, has listed scientists from all institutions as 'inventors' in patent applications.

A BBIL spokesperson told The Hindu that the patent filed by Bharat Biotech was only for "process development" and specific to the making of the vaccine. It also covered the use

of an adjuvant (an ingredient used in vaccines to elicit a stronger response) that was licensed from the Kansas-based ViroVax and added to Covaxin.

India's patent laws allow both product and process patents. Product patents grant an inventor a monopoly over, say, a drug. Process patents bar competitors from making a similar drug using the same sequence of steps. “Bharat Biotech is innovator of the process developed after procuring strain from the NIV through an agreed consideration between both the parties. Moreover, the NIV was also responsible for testing for other variants. It is to be noted that while ICMR/NIV owns the animal challenge (clinical trials on animals) studies, Bharat Biotech owns the process development and new adjuvant added to the vaccine.

”In the case of the CSIR, product development involved funding from both the CSIR and the BBIL and hence merited co-inventorship during patent applications, the spokesperson's email suggested. The BBIL did not clarify on who owned the rights to the human clinical trial data — information that is usually not disclosed by pharmaceutical companies.

Close involvement of ICMR.

The ICMR's close involvement in all aspects of Covaxin development is well known, particularly — as former chief Dr. Balram Bhargava has described in his book, Going Viral: The Making of Covaxin, how ICMR scientists isolated the Sars-Cov2 strain from Italian tourists in March 2020, gave it to Bharat Biotech which developed a batch of vaccine candidates by April 30 that were then used to conduct pre-clinical animal studies on rats, hamsters, monkeys and following encouraging results, trials on humans. All of the resulting publications that describe the results of these trials — some published in leading journals such as TheLancet — list both ICMR scientists as well as scientists from the BBIL as co-authors in the study.

An independent expert said collaborating entities usually clearly spell out how IPR and patenting rights from a resulting invention would be shared in a memorandum of understanding (MoU). “There could be multiple kinds of agreements and only a perusal of the MoU can clarify on such matters,” an IPR lawyer, who declined to be identified as he consulted both of these organisations, told The Hindu. The ICMR has previously declined Right to Information requests by activists and media on the terms of this MoU citing “third party confidentiality”.

“This raises some important questions. If intellectual property is jointly owned, then patent applications require that all the inventors be mentioned. In the United States, for instance, not mentioning all inventors can be strong grounds for the rejection of patents,” Dr. Zakir Thomas, who was previously been involved in intellectual property development at the CSIR, told The Hindu.

Source: *The Hindu,* 21st June 2024

Cancer Drugs to be Cheaper in Kerala

The State government has announced a key intervention in the pharma market to make expensive cancer drugs and immunosuppressant drugs available at zero-profit price to consumers, to bring down the out-of-pocket expenditure on health in the State.

Kerala has the highest per capita out-of-pocket expenditure on health in the country at ₹7,206, according to the last National Health Accounts (2019-20).

The State intends to make available 800 drugs, including cancer drugs and immunosuppressants, at the original prices fixed by drug firms. The medicines would be purchased in bulk by Kerala Medical Services Corporation Ltd. and sold through the network of 74 Karunya fair price stores across the State. These drugs would be made available through special "profit-free" counters in Karunya shops.

The new initiative is expected to be kicked off in July.

Already, some 7,000 drugs are sold at rates much lower than the market price through Karunya outlets. The "profit-free" counters will be set up in the prime Karunya outlets in all districts. Additional staff would be deployed to handle the new counters, the statement issued by the Health Minister said.

The statement said that the new initiative was part of the several interventions taken up by the State government to provide affordable and quality cancer care to people.

Steps have been taken to run cancer screening clinics as well as cancer preventive clinics at least one day a week in all hospitals; cancer treatment facilities have been augmented at Regional Cancer Centre and Malabar Cancer Centre; plans are afoot to introduce HPV vaccination against cervical cancer amongst Plus One and Plus Two-level girls and facilities for mammogram, biopsy and pap smear have been made available at at least one district/taluk hospital in every district, the statement said.

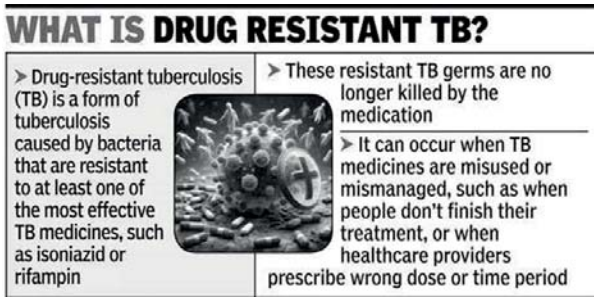
Source: *The Hindu,* 28th June 2024

Concern Over Shortage of TB Meds, Foreign Language Labels

If you have TB, you may have to learn Russian or Spanish. Medication instructions printed on the free drugs distributed in govt hospitals in many parts of the state are only in Russian and Spanish, despite being a part of govt of India supply chain. Additionally, medication shortages force alternate-day dosing, raising concern among doctors about drug resistance.

The instructions on the tablet sleeve state that drugs must not be stored at temperatures above 25°C, while day temperatures in most parts of the state exceed

this limit. Experts said there is no guarantee of the quality of medicine when you don't follow the storage instructions.



Patients who are diagnosed with tuberculosis (other than drug resistant forms) are prescribed with daily regimen of fixed dose combinations. In the intensive phase of eight weeks they are given isoniazid, rifampicin, pyrazinamide and ethambutol. In the continuation phase, patients are asked to stop pyrazinamide and continue with the other drugs for 16 weeks. While hospital administrators from various GHs, including those in Chennai, said they have alerted the state TB division and health officials about drug shortage, govt doctors said they have no choice but to advise their patients to buy their medications from retail medical shops to avoid complications.

Doctors in private sector concur. On Wednesday, a patient given free TB drugs at the Gingee GH showed her medications to infectious diseases expert Dr Subramaniam Swaminathan, who works at Gleneagles Health City. "Name, formulations and instructions were all in a foreign language although the medicine was made in Jammu and Kashmir. If the medicine loses potency because of improper storage, the patient may not benefit from it," he said. "If they skip medicines, it can cause drug resistance. This will make treatment complex and expensive for patients. Worse, these patients can also spread drug-resistant TB to other patients," he said.

Health department officials said drugs for TB are procured by the govt of India and distributed free of cost to patients. Following the acute shortage, the state TB division alerted the TN Medical Services Corporation, which purchases drugs and equipment for all govt hospitals. "Hospitals have also been allowed to make purchases locally," said a senior official at the DMS.

Meanwhile, officials at the Medical Services Corporation said orders have been placed for three-drug combinations and tendering process for four-drug combinations has begun. "We are expecting the three-drug combination drugs to come in a couple of weeks. We will be placing orders for four-drug combinations in a month after completing the tendering process," said TNMSC MD M Arvind.

Source: *The Times of India,* 4th July 2024

Indian Drugmakers Seek Govt Tax Reliefs, Incentives to Spur Innovation

India's pharmaceutical companies are hoping for tax incentives and financial assistance for research on innovative drugs as Prime Minister Narendra Modi's government readies a federal finance budget likely to be presented in July.

The upcoming budget would be Mr. Modi's first major policy announcement in his third term as Prime Minister.

Indian drug manufacturers must focus on developing complex drugs beyond the usual generic variety if the country is to continue being renown for being the 'pharmacy of the world' for its affordable medicines, experts say.

"If the Indian government can give some income tax exemptions for 5-10 years for any new molecule developed in India...that can pull innovation to grassroot level.. companies will start investing in innovation," Bharat Biotech's Chairman Krishna Ella told Reuters on the sidelines of an event in Hyderabad on Friday.

Bharat Biotech developed India's first indigenous COVID-19 vaccine, Covaxin.

India, whose pharmaceutical market is expected to be valued at $130 billion by the end of the decade, is the world's third largest manufacturer of drugs by volume after the United States and China and is a hub of generic drug manufacturers.

Generic drugs are cheaper versions of brand-name drugs.

In March, research firm Bernstein said that India needs to create a domestic market where innovative drugs can be profitable at the right price.

"Spending millions on clinical trials with no pricing power is not a business they (pharma companies) want to be in," Bernstein said in an open letter to the Prime Minister.

The firm also said insurance coverage for novel drugs and harmonising regulatory standards for manufacturing and clinical trials will be required for fostering innovation.

India has offered incentives since 2020 to spur the manufacturing of a broad range of products from drones to drugs in the country. But manufacturers of novel drugs are not eligible for the incentives yet.

"I think government is evaluating on how their existing scheme is working...but industry is expecting a policy from the government to boost research and development in companies," HIV drugs maker Hetero Drugs' Chairman Partha Saradhi Reddy told Reuters.

India's export sales, which dominate the U.S. generics market, is expected to double to $55 billion by 2030, according to a government-backed trade body Pharmaceuticals Export Promotion Council of India (Pharmexcil).

"And if you want to have this flag going high in the entire globe and again...I think probably we have to look a little bit out of the box," Raja Bhanu, director general of Pharmexcil, said.

Source: *The Hindu,* 6th July 2024

MP Calls for Action Against Firms Involved in Unethical Practices in Clinical Trials

Member of Parliament (Rajya Sabha) Kanimozhi N.V.N. Somu urged the Union government to take stringent action on all those involved in unethical practices in clinical trials.

Citing an issue raised by the Ethical Committee of National Institute of Virology about the rising cases of dubious drug trials in India, she said it would have serious repercussions on the whole healthcare sector. This also raised questions about monitoring and quality control of clinical studies in the country, she said in the Rajya Sabha. Dr. Kanimozhi noted that recently, the Drug Controller General of India received an appeal to investigate the critical gaps in clinical trials by a pharma company, to develop a biosimilar product for treatment of breast cancer.

All clinical trials have to be registered with the Central Trial Registry of India for a company to conduct trials, she said, adding that the most important factor in such trials is the genuineness of the original product which is considered the gold standard. Any doubt about the authenticity of the gold standard is bound to give misgivings about the integrity of the whole trial and the effectiveness of the biosimilar copy being tested.

She said that there was an allegation of trials being conducted four months before the procurement of the gold standard drug from the original manufacturer.

She pointed out that the same pharma company had made a substantially large contribution through electoral bonds. Data showed that 35 pharma companies in India have contributed nearly ₹1,000 crore to political parties (mostly to the party in power in both Centre and States) through electoral bonds. Of these, at least seven companies were being investigated for poor quality drugs when they purchased the bonds.

She urged the Union government not to play with the lives of innocent people by supporting and facilitating those who conduct dubious unethical drug trials in the country.

Source: *The Hindu,* 22nd July 2024

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