ISSUE No. 41

SILVER JUBILEE YEAR 2016

TAMILNADU PHARMACEUTICALS SCIENCES WELFARE TRUST

25 Years

Special Issue : Pharmacovigilance Training Course

Pharma Web

Newsletter of Tamilnadu Pharmaceutical Sciences Welfare Trust

Jan. - Feb. - Mar. 2019

Delvin Formulations

Destiny for Innovation

Moving Globally

- R & D and Manufacturing of API
- R & D and Manufacturing of Formulations
- International Marketing
- Domestic Marketing
- Medical Devices
- Surgicals

Our Group of Companies

NURAY CHEMICALS PVT. LTD.	Sai Mirra Innopharm Pvt. Ltd.	Delvin Formulations	Numen Healthcare Pvt. Ltd. (Singapore)	Delvin Klarvoyant Biogenics Pvt. Ltd.	Delvin Surgicals
R & D and Manufacturing of API	R & D and Manufacturing of Formulations	Domestic Marketing	International Marketing	Medical Devices	Surgicals

info@delvin.in | www.delvin.in

Tamilnadu Pharmaceutical Sciences Welfare Trust

Pharma Web

Newsletter of Tamilnadu Pharmaceutical Sciences Welfare Trust

ISSUE : 41 Jan. - Feb. - Mar. 2019

CONTENTS **Page No.**

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

EDITORIAL

Dear Readers,

Pharma Web is happy to inform all its readers that **Mr. J. Jayaseelan**, Joint Secretary of our Trust has been elected as President of Tamilnadu Pharmacy Council.

We wish to inform our readers, that The Pharma Knowledge and Training Institute of the Trust has conducted the Pharmacovigilance programme to final year students of Pharm D / M. Pharm Pharmacology in February 2019. The programme was supported by **Dr. V. Kalaiselvan**, Principal Scientific Officer, IPC, Ghaziabad.

The following lectures delivered by the faculty during the program and the highlights of the program are featured in this issue.

- Management, Understanding and Reporting to Ensure Better Patient Care - **Dr. Saibal Das and Dr. Kirubakaran R**, Department of Clinical Pharmacology, JIPMER, Puducherry
- Pharmacovigilance – A Holistic Perspective - **Dr. J. Vijay Venkatraman**, Managing Director & CEO, OviyaMedSafe, Coimbatore
- Pharmacovigilance and GMP Regulatory compliance for Pharmaceuticals as per D & C Act and Rules - **Dr. P. Manavalan**, Assistant Drugs Controller (India), CDSCO, Sea Port, Chennai
- Pharmacovigilance Practice in Indian Pharmaceutical Industries: Current Status and Way Forward - **Mr. Balakumar Mahalingam**, Drug Inspector, CDSCO, South Zone, Chennai
- ICSRs and PSURs Format and Reporting - **Dr. V. Kalaiselvan**, Principal Scientific Officer, Indian Pharmacopoeia Commission, Ghaziabad

Gazette Notifications pertaining to the amendment of Drugs & Cosmetics Act & Rules, important circulars issued by DCGI, and Important news items connected to our Pharma profession (which appeared in various National News papers) are the others forming part of the issue.

We are very much thankful to M/s. Fourrts (India) Laboratories Pvt. Ltd., M/s. Delvin Formulations Pvt Ltd., M/s. Medopharm, M/s. Tablets (India) Ltd., M/s. Sri Ramachnadra College of Pharmacy, Porur, Chennai, for their continuous support by giving advertisements, in order to sustain the cost of publishing this newsletter.

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

The 41st issue of Pharma Web Newsletter Jan – Mar 2019 is being dedicated to the Pharmacovigilance program conducted by our Trust

With Best Regards,
R. NARAYANASWAMY
Chief Editor

PHARMA KNOWLEDGE AND TRAINING INSTITUTE (FINISHING SCHOOL)

Pharmacovigilance Training Course

"Pharma Knowledge and Training Institute (PKTI) – Finishing School" has conducted its 2nd Pharmacovigilance Training course on 22nd & 23rd February 2019 in coordination with Indian Pharmacopoeia Commission, Ghaziabad under the guidance of Dr. V. Kalaiselvan, to update the knowledge of Pharm D / M. Pharm students.

The trainees were final year students of Pharm D / M. Pharm Pharmacology from SRM University, Sri Ramachandra University, Vels University, C. L. Baid Metha College of Pharmacy, PSG College of Pharmacy, Coimbatore, JSS College of Pharmacy, Swamy Vivekanandha College, Sri Padmavathy School of Pharmacy. A total of 55 students were trained in this programme. A formal inauguration of this programme was held on 22nd February 2019. Prof. K. Chinnaswamy, President, Tamilnadu Pharmacy Council, inaugurated the programme. Mrs. Shanthy Gunesekaran, DDC(I), CDSCO, South Zone, Chennai and Mr. J. Jayaseelan, MD Delvin Group of companies & Chairman, IPA Industrial Pharmacy division were guest of honour.

Details of the Program

Day 1: 22nd February (Friday)

Topic	Speaker / Faculty
Module 1: Management, understanding and reporting to ensure better patent care – Demonstrating with few case studies	**Dr. Saibal Das & Dr. Kirubakaran R** JIPMER, Puducherry
Module 2: Scope and challenges of the pharmacists in Pharmacovigilance – Demonstrating with few case studies	**Dr. Pratibha Nadig,** Vydehi Institute of Medical Sciences & Researach Centre, Bengaluru
Module 3: Pharmacovigilance in requirements – special emphasis to developed/developing countries	**Dr. J. Vijay Venkatraman** Oviya MedSafe Pvt Ltd, Coimbatore

Day 2: 23rd February (Saturday)

Topic	Speaker / Faculty
Module 5: Pharmacovigilance and GMP regulatory compliance for pharmaceuticals as per Drugs & Cosmetics Act 1940 and Rules 1945 there under	**Dr. P. Manavalan,** Assistant Drugs Controller, CDSCO, Chennai
Module 4: Understanding the global PV tools and its applications – such as Med Watch, yell card etc	**Dr. Vikas M. Vaishnavi** Novartis, Hyderabad
Module 6: Pharmacovigilance Practice in Indian Pharmaceutical Industries: Current status and way forward	**Mr. Bala Kumar,** CDSCO, Chennai
Module 7: Understanding the format and reporting ICSRs and PSURs – Special emphasis to Indian context	**Dr. V. Kalaiselvan,** IPC, Ghaziabad
Module 8: ICSRs and PSURs – A case study	**Dr. V. Kalaiselvan,** IPC, Ghaziabad **Dr. N. Senthil Prabhu & Dr. N. Surendra Reddy,** Accenture, Chennai

The valedictory function was held on 23rd February 2019. Mr. S. V Veerramani, CMD M/s. Fourrts (India) Labs Pvt, Chennai, was the Chief guest for the function. Dr. V. Kalaiselvan, Principal Scientific officer, IPC, Ghaziabad, was the guest of honour.

The training programme was concluded with the issue of certificate to the trainees. The students who attended the programme have given the feedback that the programme is well organised and given them more information about pharmacovigilance which have not been taught in their curriculum. They stressed that such program should be held more often and also a similar programme may be held at Coimbatore separately.

R. NARAYANASWMAY
Director - PKTI

Address by Prof. K. Chinnaswamy

Address by Mr. J. Jayaseelan

Faculties and Trainees

Lecture by Dr. Saibal Das

Lecture by Dr. Kirubakaran R

Lecture by Dr. Pratibha Nadig

Lecture by Dr. J. Vijay Venkatraman

Lecture by Dr. R. Manavalan

Lecture by Dr. Vikas M. Vaishnavi

Felicitation to Mr. Balakumar Mahalingam

Lecture by Dr. V. Kalaiselvan

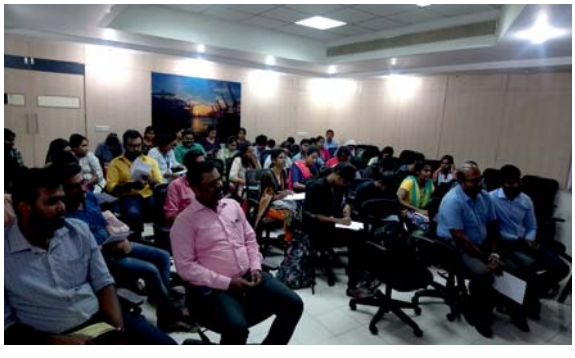
Lecture by Dr. N. Senthil Prabhu

Address by Mr. R. Narayanaswamy

Address by Mr. S. V. Veerramani

Certificate Distribution

Certificate Distribution



Faculties and Trainees

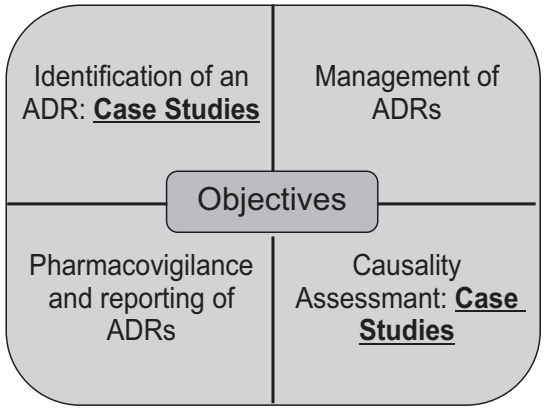
Group Photo

ARTICLES

MANAGEMENT, UNDERSTANDING AND REPORTING TO ENSURE BETTER PATIENT CARE

by

Dr. Saibal Das and Dr. Kirubakaran R,
Department of Clinical Pharmacology, JIPMER, Puducherry
(Lecture delivered during Pharmacovigilance Training Course conducted by Trust – 22nd & 23rd February 2019)



Introduction

Incidence

ADR in hospitalized patients: 6.7 % (range 1.2–24.1%)

Fatal ADRs 0.32% (0.1–0.85%)

Inability to detect ADR leads to inappropriate management resulting in increased

Complications | Hospital stay | Cost

Essential to establish causal relationship between the drug and ADR

Case studies

A 30 year old male patient diagnosed with gastric ulcer was prescribed

1. T. pantoprazole 40 mg BD

Next day morning at 9.30 AM patient met with an accident and sustained head injury.

Comments:

A 30 year old male patient diagnosed with essential hypertension was prescribed

1. T. PRAZOSIN (minipress) 1 mg B.D
2. T. HYDROCHLOROTHIAZIDE 25 mg O.D

After the first dose patient complaining about dizziness while getting up from toilet seat.

Comments:.

A 30 year old male patient diagnosed with essential hypertension and was prescribed

1. T. PRAZOSIN (minipress) 1 mg B.D
2. T. HYDROCHLOROTHIAZIDE 25 mg O.D

The patient is admitted in EMS with hypotension, drowsiness and plasma Prazosin levels 10 times above normal range.

Patient had past h/o of suicidal attempts

Comments:

Organizations involved

- WHO – World Health Organization
- CIOMS – Council of International Organizations of Medical Sciences
- ICH – International Conference on Harmonisation

Pharmacovigilance

Pharmacovigilance is "the science and activities relating to detection, assessment, understanding and prevention of adverse effect or any other drug related problems."

(WHO 2002)

Adverse event

Medical occurrence temporally associated with the use of a medicinal product, but not necessarily causally related

Adverse reaction

- WHO, (1972)
- A response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modifications of physiological function

Unexpected adverse reaction

Not consistent with applicable product information or characteristics of drug.

Side effect

Unintended effect occurring at normal dose related to the pharmacological properties

Serious adverse event or reaction

Any untoward medical occurrence that at any dose;

- Results in death
- Life threatening
- Requires inpatient hospitalization or prolongation of existing hospitalization
- Results in persistent of significant disability or incapacity

Poisoning / Toxicity

At higher doses above the recommended pharmacological doses

Types of ADRs

Type A – Augmented eg. postural hypotension, hypoglycemia, hypokalemia

Type B – Bizarre eg. Idiosyncratic reactions

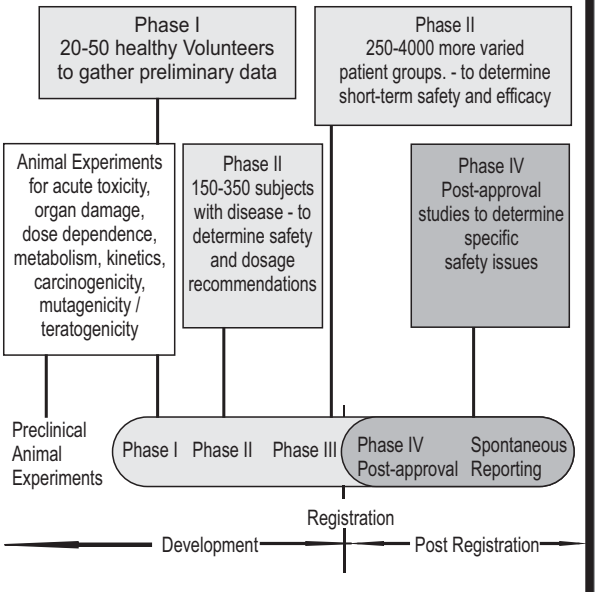
Type C – Chronic eg.analgesic nephropathy, dyskinesias with levo dopa

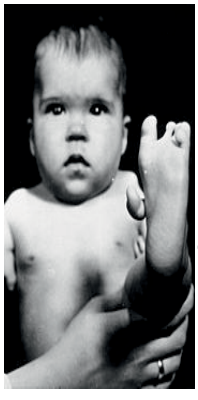
Type D – Delayed eg. Carcinogenesis, teratogenesis

Type E – End of dose response eg. Rebound hypertension

Type F – Failure of therapy

Why pharmacovigilance?





THALIDOMIDE AND CONGENITAL ABNORMALITIES

SIR,—Congenital abnormalities are present in approximately 1·5% of babies. In recent months I have observed that the incidence of multiple severe abnormalities in babies delivered of women who were given the drug thalidomide (' Distaval ') during pregnancy, as an antiemetic or as a sedative, to be almost 20%.

These abnormalities are present in structures developed from mesenchyme—i.e., the bones and musculature of the gut. Bony development seems to be affected in a very striking manner, resulting in polydactyly, syndactyly, and failure of development of long bones (abnormally short femora and radii).

Have any of your readers seen similar abnormalities in babies delivered of women who have taken this drug during pregnancy?

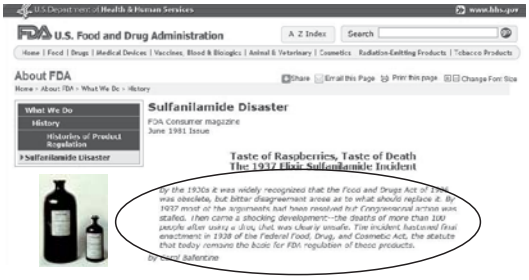
Waverley, New South Wales. W. G. MCBRIDE.

*** In our issue of Dec. 2 we included a statement from the Distillers Company (Biochemicals) Ltd. referring to " reports from two overseas sources possibly associating thalidomide (' Distaval ') with harmful effects on the fœtus in early pregnancy ". Pending further investigation, the company decided to withdraw from the market all its preparations containing thalidomide.—ED.L.

McBride WG (1962). Thalidomide and congenital abnormalities. Lancet 2:1358.

Why pharmacovigilance?

- Clinical trials cannot detect all ADRs and are conducted in a controlled manner
- Long term effects, rare ADRs
- Collecting ADR information in a systematic manner and analysis of data is essential for continued safe use of medicine



Drugs Banned in India

Due to adverse drug reactions (ADRs):

- Rofecoxib
- Valdecoxib
- Cisapride
- Rosiglitazone
- Rimonabant
- Tegaserod
- Phenformin

Pharmacovigilance in India

National Pharmacovigilance Programme (2004)

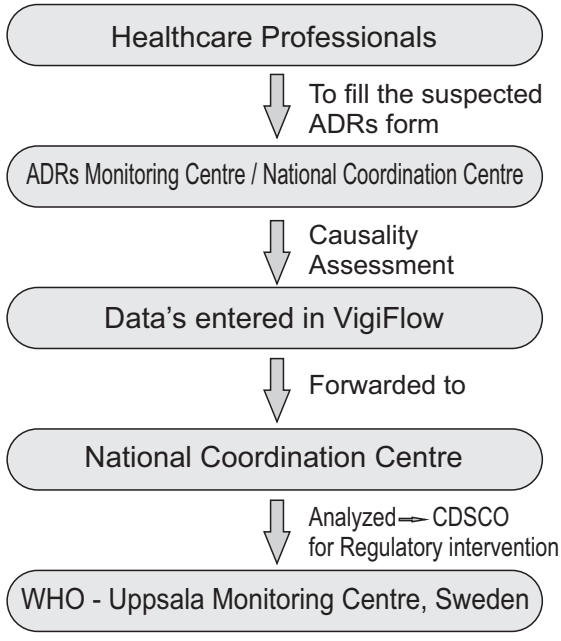
- Sponsored by WHO & World Bank
- Zonal centers (2)
- Regional centers (5)
- peripheral centers (20)
- program was closed

2009

2010

RESTARTED (PVPI)

- IPC, Ghaziabad, NCC
- 250+ ADR monitoring centers (AMC)



the UPPSALA MONITORING CENTRE

WHO – UMC at Uppsala, Sweden

Who can Report ADRs to AMC?

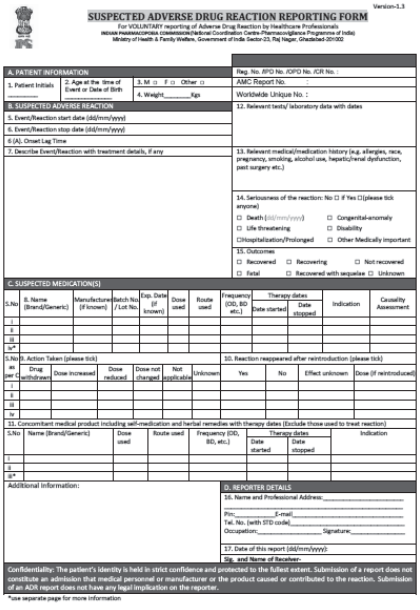
- Doctors
- Nurses
- Pharmacists
- Interns
- Patients

What to report – WHO / PVPi recommendations

Every single problem related to the use of a drug, because probably nobody else is collecting such information

- All suspected adverse reactions
- ADRs associated with contrast media in radiology, vaccines, diagnostics, drugs used in traditional medicine, herbal remedies, cosmetics, medical devices and equipment
- Lack of efficacy and suspected pharmaceutical defects
- Counterfeit pharmaceuticals
- Development of resistanced

Red Forms



SUSPECTED ADVERSE DRUG REACTION REPORTING FORM

Version-1.3

For VOLUNTARY reporting of Adverse Drug Reaction by Healthcare Professionals
INDIAN PHARMACOPOEIA COMMISSION/National Coordination Centre-Pharmacovigilance Programme of India)
Ministry of Health & Family Welfare, Government of India: Sector-23, Raj Nagar, Ghaziabad-201002

A. PATIENT INFORMATION

Reg. No. IRPD No. /OPD No. /CR No. :

1. Patient Initials _____ | 2. Age at the time of Event or Date of Birth _____ | 3. M ☐ F ☐ Other ☐ | 4. Weight_____Kgs

AMC Report No. :

Worldwide Unique No. :

B. SUSPECTED ADVERSE REACTION

5. Event/Reaction start date (dd/mm/yyyy)

6. Event/Reaction stop date (dd/mm/yyyy)

6 (A). Onset Lag Time

7. Describe Event/Reaction with treatment details, if any

12. Relevant tests/ laboratory data with dates

13. Relevant medical/medication history (e.g. allergies, race, pregnancy, smoking, alcohol use, hepatic/renal dysfunction, past surgery etc.)

14. Seriousness of the reaction: No ☐ if Yes ☐(please tick anyone)

☐ Death (dd/mm/yyyy) ☐ Congenital-anomaly
☐ Life threatening ☐ Disability
☐Hospitalization/Prolonged ☐ Other Medically Important

15. Outcomes

☐ Recovered ☐ Recovering ☐ Not recovered
☐ Fatal ☐ Recovered with sequelae ☐ Unknown

C. SUSPECTED MEDICATION(S)

S.No	8. Name (Brand/Generic)	Manufacturer (if known)	Batch No. / Lot No.	Exp. Date (if known)	Dose used	Route used	Frequency (OD, BD etc.)	Therapy dates: Date started	Therapy dates: Date stopped	Indication	Causality Assessment
i											
ii											
iii											
iv*											

S.No	9. Action Taken (please tick)					10. Reaction reappeared after reintroduction (please tick)			
	Drug withdrawn	Dose increased	Dose reduced	Dose not changed	Not applicable	Unknown	Yes	No	Effect unknown	Dose (if reintroduced)
i										
ii										
iii										
iv										

11. Concomitant medical product including self-medication and herbal remedies with therapy dates (Exclude those used to treat reaction)

S.No	Name (Brand/Generic)	Dose used	Route used	Frequency (OD, BD, etc.)	Therapy dates: Date started	Therapy dates: Date stopped	Indication
i							
ii							
iii*							

Additional Information:

D. REPORTER DETAILS

16. Name and Professional Address:_____
_____
Pin:_____E-mail:_____
Tel. No. (with STD code)_____
Occupation:_____Signature:_____

17. Date of this report (dd/mm/yyyy):

Sig. and Name of Receiver-

Confidentiality: The patient's identity is held in strict confidence and protected to the fullest extent. Submission of a report does not constitute an admission that medical personnel or manufacturer or the product caused or contributed to the reaction. Submission of an ADR report does not have any legal implication on the reporter.

*use separate page for more information

Red Forms

National Coordination Centre for Pharmacovigilance Programme of India
Ministry of Health & Family Welfare, Government of India
Sector-23, Raj Nagar, Ghaziabad-201002
Tel.: 0120-2783400, 2783401, 2783392, Fax: 0120-2783311
www.ipc.nic.in

ADVICE ABOUT REPORTING

A. What to report?

- Report serious adverse drug reactions. A reaction is serious when the patient outcome is:
  - Death
  - Life-threatening
  - Hospitalization (initial or prolonged)
  - Disability (significant, persistent or permanent)
  - Congenital anomaly
  - Required intervention to prevent permanent impairment or damage
- Report non-serious, known or unknown, frequent or rare adverse drug reactions due to Medicines, Vaccines and Herbal products etc.

Note- Adverse Event Following Immunization can also be reported in Serious AEFI case Notification Form available on http://www.ipc.gov.in)

B. Who can report?

- All healthcare professionals (Clinicians, Dentists, Pharmacists and Nurses etc) can report adverse drug reactions

C. Where to report?

- Duly filled inSuspected Adverse Drug Reaction Reporting Form can be sent to the nearest Adverse Drug Reaction Monitoring Centre (AMC) or directly to the National Coordination Centre (NCC) for PvPI.
- Call on Helpline (Toll Free) 1800 180 3024 to report ADRs or directly mail this filled form to pvpi@ipcindia.net or pvpi.ipcindia@gmail.com
- A list of nationwide AMCs is available at: http://www.ipc.gov.in, http://www.ipc.gov.in/PvPI/pv_home.html

D. What happens to the submitted information?

- Information provided in this form is handled in strict confidence. The causality assessment is carried out at AMCs by using WHO-UMC scale. The analyzed forms are forwarded to the NCC through ADR database. Finally the data is analyzed and forwarded to the Global Pharmacovigilance Database managed by WHO Uppsala Monitoring Centre in Sweden.
- The reports are periodically reviewed by the NCC-PvPI. The information generated on the basis of these reports helps in continuous assessment of the benefit-risk ratio of medicines.
- The Signal Review Panel of PvPI to review the data and suggest any interventions that may be required.

E. Mandatory fields for suspected ADR reporting form

- Patient Initials, age at onset of reaction, reaction term(s), date of onset of reaction, suspected medication(s) and reporter information.

For ADRs Reporting

- **E-mail:**pvpi@ipcindia.net **or** pvpi.ipcindia@gmail.com
- ***PvPI Helpline (Toll Free):****1800 180 3024(9:00 AM to 5:30 PM, Monday-Friday)*
- ***ADR Mobile App: "ADR PvPI"***

Google Play

IPC

Filling WHO forms

Version 1.3

SUSPECTED ADVERSE DRUG REACTION REPORTING FORM

For VOLUNTARY reporting of Adverse Drug Reaction by Healthcare Professionals
INDIAN PHARMACOPOEIA COMMISSION(National Coordination Centre-Pharmacovigilance Programme of India)
Ministry of Health & Family Welfare, Government of India Sector-23, Raj Nagar, Ghaziabad-201002

A. PATIENT INFORMATION			Reg. No. /IPD No. /OPD No. /CR No. :
1. Patient Initials	2. Age at the time of Event or Date of Birth	3. M ☐ F ☐ Other ☐	AMC Report No. :
		4. Weight_____Kgs	Worldwide Unique No. :
B. SUSPECTED ADVERSE REACTION			12. Relevant tests/ laboratory data with dates
5. Event/Reaction start date (dd/mm/yyyy)			
6. Event/Reaction stop date (dd/mm/yyyy)			
6 (A). Onset Lag Time			
7. Describe Event/Reaction with treatment details, if any			13. Relevant medical/medication history (e.g. allergies, race, pregnancy, smoking, alcohol use, hepatic/renal dysfunction, past surgery etc.)
			14. Seriousness of the reaction: No ☐ if Yes ☐(please tick anyone) ☐ Death (dd/mm/yyyy) ☐ Congenital-anomaly ☐ Life threatening ☐ Disability ☐Hospitalization/Prolonged ☐ Other Medically important
			15. Outcomes ☐ Recovered ☐ Recovering ☐ Not recovered ☐ Fatal ☐ Recovered with sequelae ☐ Unknown

C. SUSPECTED MEDICATION(S)

S.No	8. Name (Brand/Generic)	Manufacturer (if known)	Batch No. / Lot No.	Exp. Date (if known)	Dose used	Route used	Frequency (OD, BD etc.)	Therapy dates: Date started	Therapy dates: Date stopped	Indication	Causality Assessment
i											
ii											
iii											
iv*											

S.No as per C	9. Action Taken (please tick): Drug withdrawn	Dose increased	Dose reduced	Dose not changed	Not applicable	Unknown	10. Reaction reappeared after reintroduction (please tick): Yes	No	Effect unknown	Dose (if reintroduced)
i										
ii										
iii										
iv										

11. Concomitant medical product including self-medication and herbal remedies with therapy dates (Exclude those used to treat reaction)

S.No	Name (Brand/Generic)	Dose used	Route used	Frequency (OD, BD, etc.)	Therapy dates: Date started	Therapy dates: Date stopped	Indication
i							
ii							
iii*							

Additional Information:

D. REPORTER DETAILS

16. Name and Professional Address:_____
_____
Pin:_____E-mail_____
Tel. No. (with STD code)_____
Occupation:_____ Signature:_____

17. Date of this report (dd/mm/yyyy):

Sig. and Name of Receiver-

Tamil form for consumers

Version 1.0
பதிப்பு 1.0

MEDICINES SIDE EFFECT REPORTING FORM (FOR CONSUMERS)

மருந்துகளின் பக்க விளைவுகள் குறித்து புகார் அளிப்பதற்கான படிவம் (நுகர்வோர்களுக்கானது)

Indian Pharmacopoeia Commission, National Coordination Centre- Pharmacovigilance Programme of India,
Ministry of Health & Family Welfare, Government of India.
இந்திய மருந்தியல் ஆணையம், தேசிய ஒருங்கிணைப்பு மையம் - இந்திய மருந்தியல்சார் புலனாய்வுத் திட்டம்,
சுகாதாரம் & குடும்ப நல அமைச்சகம், இந்திய அரசு.

1. Patient Details/ நோயாளியின் விவரங்கள்

Patient Initials/நோயாளியின் முதலெழுத்துக்கள்:	Gender/ பால (v): Male/ஆண ☐ Female/பெண ☐ Other/ பிறர ☐	Age (Year or Month)/ வயது (ஆண்டு அல்லது மாதம்):

2. Health Information/ உடல்நலம் பற்றிய தகவல்

a. Reason(s) for taking medicine(s) (Disease/Symptoms)/ மருந்து(கள்) உட்கொள்வதற்கான காரணங்கள் (நோய் ரு அறிகுறிகள்):

b. Medicines Advised by/ மருந்துகளை உட்கொள்ள பரிந்துரைத்தவர் (v): Doctor/ டாக்டர ☐ Pharmacist/ மருந்தாளுனர ☐ Friends/Relatives/ நண்பர்/உறவினர்கள ☐
Self (Past disease experienced/No past disease experienced)/ சுயமாக (முன்னர் ஏற்பட்ட நோயின் அனுபவம் / நோய் முன்னர் ஏற்பட்ட அனுபவம் இல்லை) ☐

3. Details of Person Reporting the Side Effect/ பக்க விளைவுகள் குறித்து புகார் அளிக்கும் நபரின் விவரங்கள்

a. Name (Optional)/ பெயர் (விருப்பப்பட்டால்):

b. Address/ முகவர்:

Telephone No./ தொலைபேசி எண்:	Email/ இ-மெயில்:

4. Details of Medicine Taking/Taken/ எடுத்துக் கொள்ளும் / எடுத்துக் கொண்ட மருந்தின் விவரங்கள்

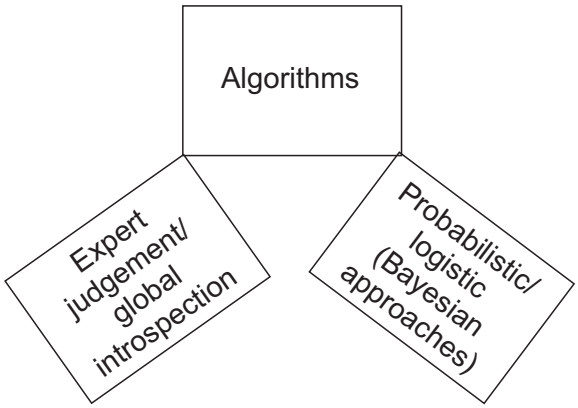
Name of Medicines/ மருந்துகளின் பெயர்கள்	Quantity of Medicines taken (e.g. 250 mg, Two times a day)/ எடுத்துக் கொண்ட மருந்துகளின் அளவு(எ.டு. 250மிகி, ஒரு நாளைக்கு இரு முறை)	Expiry Date of Medicines மருந்துகளின் காலாவதி தேதி	Date of Start of Medicines/ மருந்துகளை உட்கொள்ள தொடங்கிய தேதி	Date of Stop of Medicines/ மருந்துகளை நிறுத்திய தேதி

Causality assessment

Causality assessment is the evaluation of the likelihood that a particular treatment is the cause of an observed adverse event.

It assesses relationship between drug treatment & occurrence of adverse event.

Methods of Causality Assessment

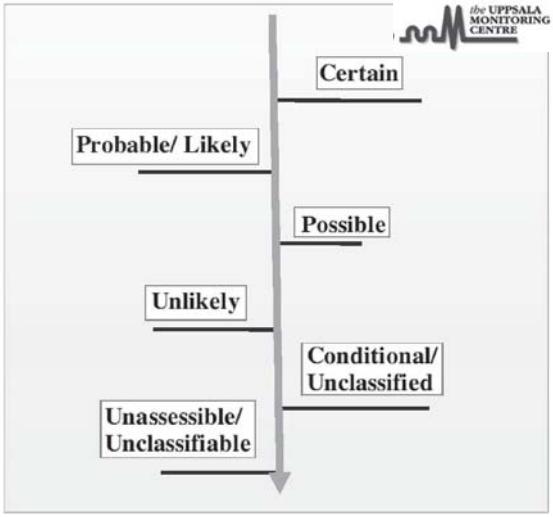


Causality assessment methods

- **Expert judgement**
  – Swedish method and WHOUMC
- **Algorithm based**
  – Naranjo, Karch and Lasagna, French, Kramer, Begaud, Jone, Maria and Victorino, RousselUclaf causality assessment method (RUCAM)
- **Probabilistic or Bayesian approach**
  – Australian, Bayesian Adverse Reactions Diagnostic Instrument (BARDI), MacBARDI and the recently developed updated Logistic method

Scale 1: WHO CAUSALITY ASSESSMENT OF SUSPECTED ADVERSE DRUG REACTIONS

(The Uppsala Monitoring centre 2002)



Certain

A Clinical event, including laboratory test abnormality, was occurring in a plausible time relationship to drug administration, and which cannot be explained by concurrent disease or other drugs or chemicals. The response to withdrawal of the drug (dechallenge) should be clinically plausible. The event must be definitive pharmacologically or phenomenologically, using a satisfactory rechallenge procedure in necessary.

IN SHORT

Significant temporal association+

Dechallenge information+

Rechallenge Information+/-

Probable

A Clinical event, including laboratory test abnormality, with a reasonable time sequence to administration of the drug, unlikely to be attributed to concurrent disease or other drugs or chemicals, and which follows a clinically responsible response on withdrawal (dechallenge). Rechallenge information is not required to fulfill this definition

IN SHORT

Rechallenge information is not available (-)

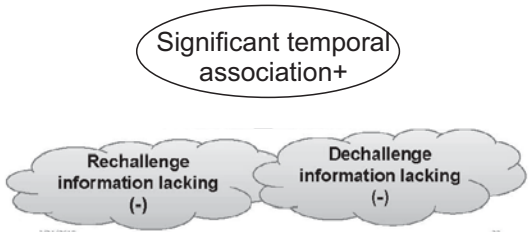
Significant temporal association+

Dechallenge information+

Possible

A Clinical event, including laboratory test abnormality, with a reasonable time sequence to administration of the drug, but which could also be explained by concurrent disease or other drug or chemicals. Information on drug withdrawal may be lacking or unclear.

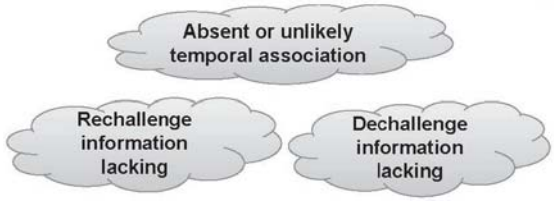
IN SHORT



Unlikely

A Clinical event, including laboratory test abnormality, with a temporal relationship to drug administration which makes a causal relationship improbable, and in which other drugs, chemicals or underlying disease provide plausible explanations.

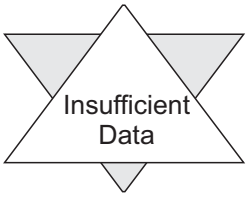
IN SHORT



Conditional / Unclassified

A Clinical event, including laboratory test abnormality, reported as an adverse reaction, about which more data is essential for a proper assessment or the additional data are under examination.

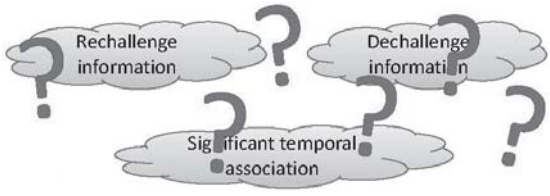
IN SHORT



Unassessible / Unclassifiable

A report suggesting an adverse reaction, which cannot be judged because information is insufficient or contradictory, and which cannot be supplemented or verified

IN SHORT



Algorithams

NARANJO'S ALGORITHM

To assess the adverse drug reaction, please answer the following questionnaire and give the pertinent score

	Yes	No	Do not know	Score
Are there previous conclusive reports on this reaction?	+1	0	0	
Did the adverse event occur after the suspected drug was administered?	+2	−1	0	
Did the adverse reaction improve when the drug was discontinued or a specific antagonist was administered?	+1	0	0	
Did the adverse reaction reappear when the drug was re-administered?	+2	−1	0	
Are there alternative causes (other than the drug) that could have on their own caused the reaction?	−1	+2	0	
Did the reaction reappear when a placebo was given?	−1	+1	0	
Was the drug detected in the blood (or other fluids) in concentrations known to be toxic?	+1	0	0	
Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	+1	0	0	
Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	+1	0	0	
Was the adverse event confirmed by any objective evidence?	+1	0	0	
Total				

The ADR is assigned to a probability category from the total score as follows: 'Definite' if the overall score is 9 or greater, 'probable' for a score of 5-8, 'possible' for 1-4 and 'doubtful' if the score is 0, The Naranjo criteria do not take into account drug-drug interactions, Drugs are evaluated individually for causality, and points deducted if another factor may have resulted in the adverse event, thereby, weakening the causal association

Bayesian Adverse Reactions Diagnostic Instrument (BARDI)

can be implemented as spreadsheet programme	provides feedback following new evidence of ADR	Apt descriptions from literature are listed to asess pprior probability
considers elements to distinguish potential causes	evaluates more than 2 possible causes at the same time	allows for rapid calculation & interaction during the process
	requires expertise to operate	

Probabilistic / logistic methods (Bayesian approaches)

Prior probability calculated from epidemiological information

↓

Posterior probability combines this background information with evidence in individual case

↓

open-ended without limit for details to be assessed

↓

Provides scope for simultaneous assessment of multiple causes

	Statistical weights
1) Time to onset	
Incompatible	- 5
Not suggestive	- 0.48647
Unknown or not available	0
Compatible	+ 0.72218
Highly suggestive	+ 0.79190
2) Dechallenge	
Against the role of the drug	- 1.32394
Non-conclusive or not available	0
Suggestive	+ 0.45961
3) Rechallenge	
Negative	- 0.97045
Not attempted or not conclusive	0
Positive	+ 0.1911
4) Search for other aetiology	
Another cause highly probable	- 2.74122
Required and not investigated or/and another possible cause	- 1.04487
Not required and/or not applicable	0
Another cause ruled out	+0.16723
5) Risk factor(s) for drug reaction	
Ruled out or absent	0
Well validated and present	+ 1.18048
6) Reaction at site of application or plasma concentration known as toxic or validated laboratory test	
Unrelated or not available	
Present or/and positive	0 + 1.25352
7) Previous information on the drug and symptomatology	
Reaction not previously reported and type B	- 0.42331
Not available0	0
Not well known or previously published once or twice	+ 0.02686
Well known and labelled reaction	+ 0.36131

Special scales for DILI

- Roussel Uclaf Causality Assessment Method (RUCAM) in Drug Induced Liver Injury
- M & V Causality Assessment Scale
- DDW – J scale

RUCAM Causality Assessment

Drug: _____ Initial ALT: _____ Initial Alk P: _____ R ratio = [ALT/ULN] ÷ [Alk P/ULN] = _____ ÷ _____ = _____

The R ratio determines whether the injury is hepatocellular (R > 5.0), cholestatic (R < 2.0), or mixed (R = 2.0 – 5.0)

	Hepatocellular Type		Cholestatic or Mixed Type		Assessment
1. Time to onset					
	Initial Treatment	**Subsequent Treatment**	**Initial Treatment**	**Subsequent Treatment**	**Score** (check one only)
o From the beginning of the drug:					
• Suggestive	5 – 90 days	1 – 15 days	5 – 90 days	1 – 90 days	☐ +2
• Compatible	< 5 or > 90 days	> 15 days	< 5 or > 90 days	> 90 days	☐ +1
o From cessation of the drug:					
• Compatible	≤ 15 days	≤ 15 days	≤ 30 days	≤ 30 days	☐ +1
Note: If reaction begins before starting the medication or >15 days after stopping (hepatocellular), or >30 days after stopping (cholestatic), the injury should be considered unrelated and the RUCAM cannot be calculated.					
2. Course	**Change in ALT between peak value and ULN**		**Change in Alk P (or total bilirubin) between peak value and ULN**		**Score** (check one only)
After stopping the drug:					
• Highly suggestive	Decrease ≥ 50% within 8 days		Not applicable		☐ +3
• Suggestive	Decrease ≥ 50% within 30 days		Decrease ≥ 50% within 180 days		☐ +2
• Compatible	Not applicable		Decrease < 50% within 180 days		☐ +1
• Inconclusive	No information or decrease ≥ 50% after 30 days		Persistence or increase or no information		☐ 0
• Against the role of the drug	Decrease < 50% after 30 days OR Recurrent increase		Not applicable		☐ -2
o **If the drug is continued:**					
• Inconclusive	All situations		All situations		☐ 0
3. Risk Factors:	**Ethanol**		**Ethanol or Pregnancy (either)**		**Score** (check one for each)
o Alcohol or Pregnancy	Presence Absence		Presence Absence		☐ +1 ☐ 0
o Age	Age of the patient ≥ 55 years Age of the patient < 55 years		Age of the patient ≥ 55 years Age of the patient < 55 years		☐ +1 ☐ 0

4. Concomitant drug(s):	Score (check one only)
o None or no information or concomitant drug with incompatible time to onset	☐ 0
o Concomitant drug with suggestive or compatible time to onset	☐ -1
o Concomitant drug known to be hepatoxic with a suggestive time to onset	☐ -2
o Concomitant drug with clear evidence for its role (positive rechallenge or clear link to injury and typical signature)	☐ -3

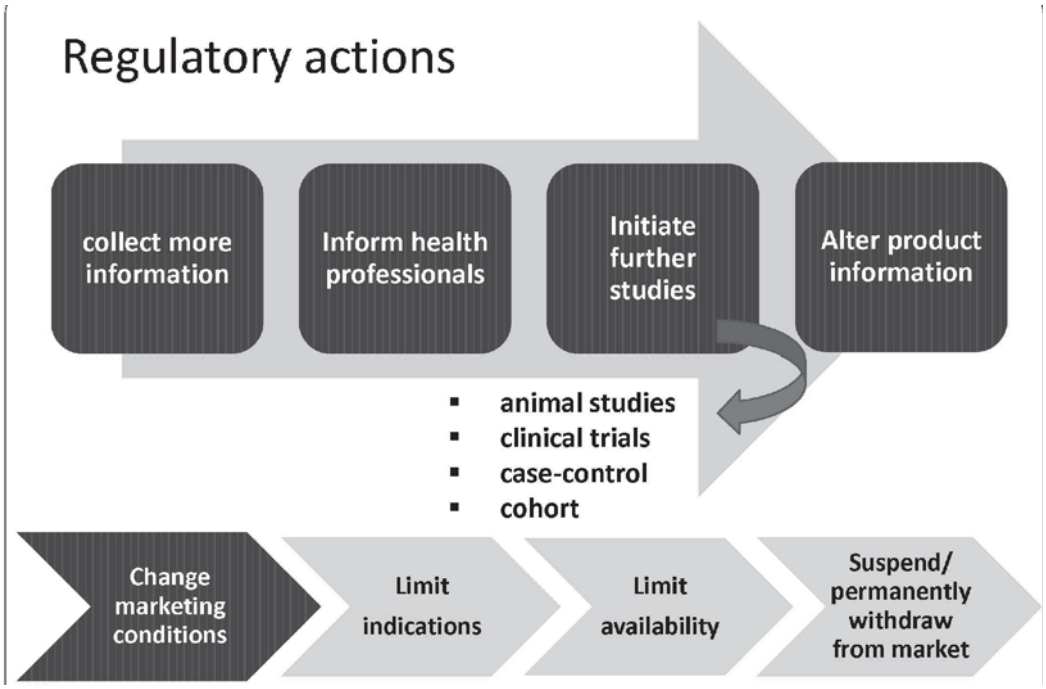
5. Exclusion of other causes of liver injury:		Score (check one only)
Group I (6 causes): o **Acute viral hepatitis due to HAV** (IgM anti-HAV), or o **HBV** (HBsAg and/or IgM anti-HBc), or o **HCV** (anti HCV and/or HCV RNA with appropriate clinical history) o **Biliary obstruction** (By imaging) o **Alcoholism** (History of excessive intake and AST/ALT ≥ 2) o **Recent history of hypotension, shock or ischemia** (within 2 weeks of onset)	o All causes in Group I and II ruled out	☐ +2
	o The 6 causes of Group I ruled out	☐ +1
	o Five or 4 causes of Group I ruled out	☐ 0
	o Less than 4 causes of Group 1 ruled out	☐ -2
Group II (2 categories of causes): o Complications of underlying disease(s) such as autoimmune hepatitis, sepsis, chronic hepatitis B or C, primary biliary cirrhosis or sclerosing cholangitis; or o Clinical features or serologic and virologic tests indicating acute CMV, EBV, or HSV.	o Non drug cause highly probable	☐ -3

6. Previous information on hepatotoxicity of the drug:	Score (check one only)
o Reaction labeled in the product characteristics	☐ +2
o Reaction published but unlabeled	☐ +1
o Reaction unknown	☐ 0

7. Response to readministration:			Score (check one only)
o Positive	Doubling of ALT with drug alone	Doubling of Alk P (or bilirubin) with drug alone	☐ +3
o Compatible	Doubling of the ALT with the suspect drug combined with another drug which had been given at the time of onset of the initial injury	Doubling of the Alk P (or bilirubin) with the suspect drug combined with another drug which had been given at the time of onset of the initial injury	☐ +1
o Negative	Increase of ALT but less than ULN with drug alone	Increase of Alk P (or bilirubin) but less than ULN with drug alone	☐ -2
o Not done or not interpretable	Other situations	Other situations	☐ 0
		TOTAL (add the checked figures)	

Abbreviations used: ALT, alanine aminotransferase; Alk P, alkaline phosphatase; ULN, upper limit of the normal range of values
Modified from: Danan G and Benichou C. J Clin Epidemiol 1993; 46: 1323-30.

M & V Causality Assessment Scale	
I. Temporal Relationship Between Drug Intake and the Onset of Clinical Picture	
A. Time from drug intake until the onset of the first clinical or laboratory manifestations	Score
a. 4 days to 8 weeks (or less than 4 days in cases of reexposure)	3
b. Less than 4 days or more than 8 weeks	1
B. Time from withdrawal of the drug until the onset of manifestations	
a. 0 to 7 days	3
b. 8 to 15 days	0
c. More than 15 days*	-3
C. Time from withdrawal of the drug until normalization of laboratory values**	
a. Less than 6 months (cholestatic or mixed patterns) or 2 months (hepatocellular)	3
b. More than 6 months (cholestatic or mixed patterns) or 2 months (hepatocellular)	0
II. Exclusion of Alternative Causes	
Viral hepatitis (HAV, HBV, HCV, CMV, EBV), alcoholic liver disease, biliary tree obstruction, pre-existing liver disease, other (pregnancy, acute hypotension)***	
o Complete exclusion	3
o Partial exclusion	0
o Possible alternative cause detected	-1
o Probable alternative cause detected	-3
III. Extrahepatic Manifestations	
Rash, fever, arthralgias, eosinophilia (>6%), cytopenia	
o 4 or more	3
o 2 or 3	2
o 1	1
o None	0
IV. Intentional or Accidental Reexposure to the Drug	
o Positive rechallenge test	3
o Negative or absent rechallenge test	0
V. Previous Report in the Literature of Cases of DILI Associated with Drug	
o Yes	2
o No (drugs marketed for up to 5 years)	0
o No (drugs marketed for more than 5 years)	-3



INDIAN PHARMACOPOEIA COMMISSION

National Coordination Centre- Pharmacovigilance Programme of India (PvPI)

MINISTRY OF HEALTH & FAMILY WELFARE, GOVERNMENT OF INDIA

SECTOR-23, RAJ NAGAR, GHAZIABAD- 201 002.

Tel No: 0120- 2783392, 2783400, 2783401, Fax: 0120-2783311

e-mail: pvpi@ipcindia.net, pvpi.ipc@gov.in, Web: www.ipc.gov.in

File No: IPC/NCC-PvPI/SRP/2017-18 **Date: 14/07/2017**

PvPI Recommendations to CDSCO for Regulatory Actions

The India specific drug safety signals/drug alerts/others are identified from the reported ADRs by the Signal Review Panel (SRP) of Pharmacovigilance Programme of India (PvPI) and recommended to Central Drugs Standard Control Organisation (CDSCO) for the appropriate regulatory actions as follows:

S.No	Suspected drugs	Adverse drug reactions	Recommendations	Action taken by CDSCO
1	Carbamazepine	Stevens Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN)	For Drug Safety Label Change – Patient may be screened for HLA-B*1502 prior to initiating the carbamazepine	Issued an order to all MAHs to comply the same

INDIAN PHARMACOPOEIA COMMISSION

National Coordination Centre- Pharmacovigilance Programme of India (PvPI)

MINISTRY OF HEALTH & FAMILY WELFARE, GOVERNMENT OF INDIA
SECTOR-23, RAJ NAGAR, GHAZIABAD- 201 002.

Tel No: 0120- 2783392, 2783400, 2783401, Fax: 0120-2783311
e-mail: pvpi@ipcindia.net, pvpi.ipc@gov.in, Web: www.ipc.gov.in

File No: IPC/NCC-PvPI/SRP/2017-18 **Date: 14/07/2017**

2	Mannitol	Hypokalaemia	To include in Prescribing Information	In process
3	Piperacillin and Tazobactam	Hypokalaemia, Bronchospasm	To include in Prescribing Information	Issued an order to all MAHs to comply the same
4	Rota Vaccine	Intussusception	To include in Prescribing Information	In process
5	Ranitidine	Cardiac Arrest	To include in Prescribing Information	In process
6	Anti-Rabies Vaccine	Erythema Multiforme	To include in Prescribing Information	Issued an order to all MAHs to comply the same
7	Pulmonary Surfactant	Pulmonary Haemorrhage	To include in Prescribing Information	In process
8	Ceftriaxone	Stevens Johnson syndrome	To include in Prescribing Information	In process
9	Lamotrigine	Stevens Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN)	To include in Prescribing Information	In process
10	Betamethasone	Photosensitivity Reaction	To include in Prescribing Information	In process

Case studies

1. A 48 year male was started on tab. aspirin 75mg/day after the attack of myocardial infarction. 3 months after taking the drug he complained of epigastric pain. Assess the causality.

2. A 60 year old hypertensive and diabetic was on tab. enalapril 10mg b.d. He developed dry cough after 2 months of taking the drug. It was replaced with tab. losartan 50 mg o.d. The cough subsided. Assess the causality of this scenario.

3. A 25 year old female diagnosed to have SLE was started on prednisolone 10 mg BD. The baseline creatinine was 1.2 and after 2 days the creatinine increased to 2.

Case studies

4. A 31 year old male k/c/o BPAD with mania on valproate 600 mg /day started one week back, developed papular rash. Drug was stopped and the rashes disappeared next day.

A 48 year male was started on tab. aspirin 75mg/day after the attack of myocardial infarction. 3 months after taking the drug he complained of epigastric pain. Assess the causality.

1. Temporal association
2. Dechallenge – No data
3. Rechallenge – No data
4. Can be explained by disease = MI atypically can
present with epigastric pain
5. Known phenomenon = yes

Possible

A 60 year old hypertensive and diabetic was on tab. enalapril 10mg b.d. He developed dry cough after 2 months of taking the drug. It was replaced with tab. losartan 50 mg o.d. The cough subsided. Assess the causality of this scenario.

Assessment criteria*

- ✓ Event or laboratory test abnormality, with plausible time relationship to drug intake
- ✓ Cannot be explained by disease or other drugs
- ✓ Response to withdrawal plausible (pharmacologically, pathologically)
- ✓ Event definitive pharmacologically or phenomenologically (i.e. an objective and specific medical disorder or a recognised pharmacological phenomenon)
- Rechallenge satisfactory, if necessary

Certain

A 25 year old female diagnosed to have SLE was started on prednisolone 10 mg BD. The baseline creatinine was 1.2 and after 2 days the creatinine increased to 2

1. Temporal association – unlikely to cause renal dysfunction within 2 days of treatment
2. Dechallenge – No data
3. Rechallenge – No data
4. Can be explained by disease = Yes
5. Pharmacologically explained?= no

Unikely

A 31 year old male k/c/o BPAD with mania on valproate 600 mg /day started one week back, developed papular rash. Drug was stopped and the rashes disappeared next day.

1. Temporal association
2. Dechallenge – Yes
3. Rechallenge – No data
4. Can be explained by disease = No
5. Known phenomenon = No

Unikely

Table. The Naranjo Algorithm

To assess the adverse drug reaction, please answer the following and give pertinent score.				
Question	Yes	No	Do Not Know	Score
1. Are there previous conclusive reports on this reaction?	+1	0	0	1
2. Did the adverse event appear after the suspected drug was administered?	+2	-1	0	2
3. Did the adverse reaction improve when the drug was discontinued or a specific antagonist was administered?	+1	0	0	0
4. Did the adverse reaction reappear when the drug was readministered?	+2	-1	0	0
5. Are there alternative causes (other than the drug) that could on their own have caused the reaction?	-1	+2	0	0
6. Did the reaction reappear when a placebo was given?	-1	+1	0	0
7. Was the drug detected in the blood (or other fluids) in concentrations known to be toxic?	+1	0	0	0
8. Was the reaction more severe when the dose was increased, or less severe when the dose was decreased?	+1	0	0	0
9. Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	+1	0	0	0
10. Was the adverse event confirmed by any objective evidence?	+1	0	0	0

Naranjo scores of 9 or 10 indicate that an event was "definitely" an ADR; scores of 5-8 rate the likelihood as "probable"; scores of 1-4 are "possible"; and scores of less than 1 are "doubtful."

Comparison of causality assessment by different scales

International Journal of Clinical Pharmacy (2018) 40:903–910
https://doi.org/10.1007/s11096-018-0694-9

RESEARCH ARTICLE

Comparison of different methods for causality assessment of adverse drug reactions

Sapan Kumar Behera[1] · Saibal Das[1] · Alphienes Stanley Xavier[1] · Srinivas Velupula[1,2] · Selvarajan Sandhiya[1]

Received: 23 December 2017 / Accepted: 12 July 2018 / Published online: 26 July 2018

Clin Drug Investig
https://doi.org/10.1007/s40261-017-0601-5

ORIGINAL RESEARCH ARTICLE

Agreement Among Different Scales for Causality Assessment in Drug-Induced Liver Injury

Saibal Das[1] · Sapan K. Behera[1] · Alphienes S. Xavier[1] · Srinivas Velupula[1] · Steven A. Dkhar[1] · Sandhiya Selvarajan[1]

YELLOW FORMS

ADVERSE DRUG REACTION MONITORING CENTRE
(CDSCO, Ministry of Health & Family Welfare, Govt. of India)
DEPARTMENT OF PHARMACOLOGY, JIPMER PUDUCHERRY - 605 006.
Ph: 2277362, 2296359 Email : adr@jipmer.edu.in, adrjipmer@gmail.com

NOTIFICATION OF SUSPECTED ADVERSE DRUG REACTION FORM

Patient name: ..... Age: ..... Sex: .....
I.P / O.P No: ..... Unit / Dept: .....

Suspected drug(s): .....
Diagnosis for use: .....
Drug started on: ..... Drug stopped on: ..... Date of reaction: .....
Brief description of reaction: .....
.....
.....

Name of the Doctor / Reporter: .....
Signature: ..... Date: .....

Please return this to the Adverse Drug Reaction Monitoring Centre, Department of Pharmacology, JIPMER, Puducherry-6 (Phone: 2277362, 2296359) so that a Clinical Pharmacologist can investigate and document the suspected adverse drug reaction as soon as possible.

PHARMACOVIGILANCE - A HOLISTIC PERSPECTIVE

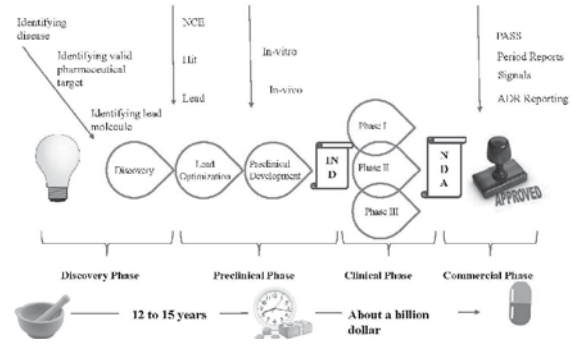
by

Dr. J Vijay Venkatraman,
Managing Director & CEO, Oviya MedSafe, Coimbatore
(Lecture delivered during Pharmacovigilance Training Course conducted by Trust – 22nd & 23rd February 2019)

Drugs as a concept

- A drug is any substance (other than food that provides nutritional support) that, when inhaled, injected, smoked, consumed, absorbed via a patch on the skin, or dissolved under the tongue causes a physiological change in the body
- In pharmacology, a pharmaceutical drug, also called a medication or medicine, is a chemical substance used to treat, cure, prevent, or diagnose a disease or to promote well-being

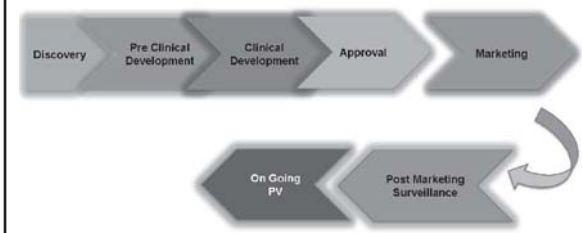
Drug Development: The Roadmap



What is a clinical trial?

A clinical trial is a research study in human volunteers to evaluate the effectiveness and safety of medications or medical devices by monitoring their effects.

Where PV starts?



Historical Background

The concept of pharmacovigilanceis more than 150 years old, and lack of awareness has termed it infancy.

The first known case:

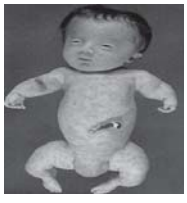
- 1848: Hannah Greener died in course of routine anaesthesiawith chloroform
- 1893: Lancet'iinitiated foundation of a commission and starting collection of notifications about side effects

Sulphanilamide tragedy

- Elixir sulfanilamide was an improperly prepared sulfanilamide with diethylene glycol medicine that caused mass poisoning in the US in 1937. It caused the deaths of more than 100 people.
- 1938 Food, Drug, and Cosmetic Act, which required companies to perform animal safety tests.

The breakthrough case: Thalidomide Tragedy

- Thalidomide was sold from 1956 to 1962 in almost 50 countries.
- Sleeping pills, sedative effect.
- Around 1960 Dr William McBride discovered that the drug also alleviated morning sickness and can be prescribed to pregnant women, as an antiemetic.
- In 1961 Dr William McBride himself started associated the drug with severe malformations in the babies he delivered.

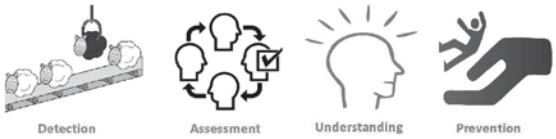


Direct results of thalidomide incident

- USA: 1962 amendment to Federal Food, drug & Cosmetic Act -required both safety & efficacy data
- UK: 1964 Yellow card scheme
- WHO: 1968 Programme for International Drug Monitoring
- Kefauver-Harris Drug Amendments Act in 1962

Thalidomide is FDA-approved for two uses today -the treatment of inflammation associated with Hansen's disease (leprosy) and as a chemotherapeutic agent for patients with multiple myeloma.

What is Pharmacovigilance?



of adverse effects
or
any other drug-related problems

Pharmakon (Greek) - Drug Vigilare (Latin) - To keep watch

Why do we need Pharmacovigilance?

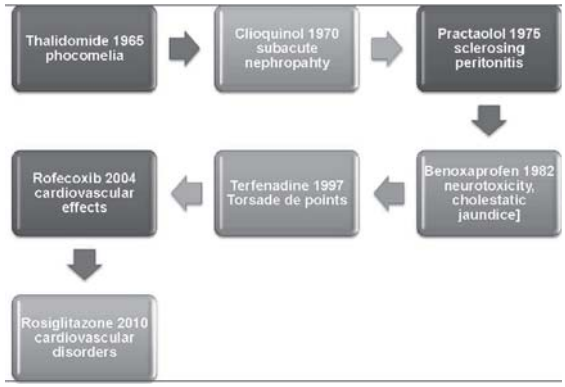
Humanitarian concern

- Insufficient evidence of safety from clinical trials
- Tests in animals are insufficient to predict human safety
- Safety profile in special groups

Limitations in Clinical Trials

	Clinical trials	Clinical practice
Number of patients	Hundreds (rarely thousands)	Thousands to million
Duration	Months	Years
Population	Pregnant, children, elderly excluded	All
Concomitant medications	Avoided	Usually present
Dose	Fixed	Variable (compliance)
Conditions	Rigorous; more information	Flexible; less information

Drug Withdrawals



Scope of PV

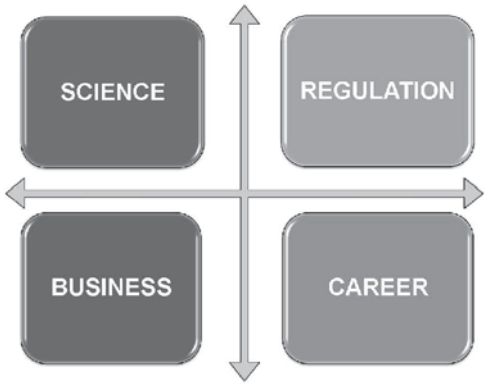
To improve patient care and safety in relation to medicines and all medical &para-medical interventions

To improve public health and safety in relation to the use of medicines

To contribute to the assessment of benefit, harm, effectiveness and risk of medicines

To promote understanding, clinical training & effective communication to health professionals and the public

PV Constellate



PV as SCIENCE

- Pharmacological science
- Part of academic syllabi
- Theoretical foundation for PV professionals
- Helps HCPs to understand adverse effects and educate patients

PV as REGULATION

- Regulation is based on science
- Regulation is required to ensure patient safety
- Industry is mandated by regulation to monitor the safety of their products
- Compliance is mandatory to maintain brand equity
- Non-compliance linked to penalty and disrepute

PV as BUSINESS

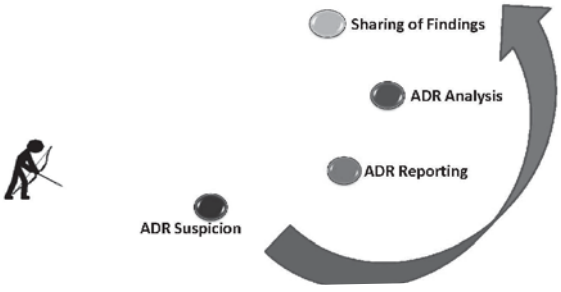
- Industry views PV as cost center
- Opportunity for third party service provider
- PV consultancy and audits
- India –global leader in outsourcing services
- Brings down cost and brings in global talent

PV as CAREER

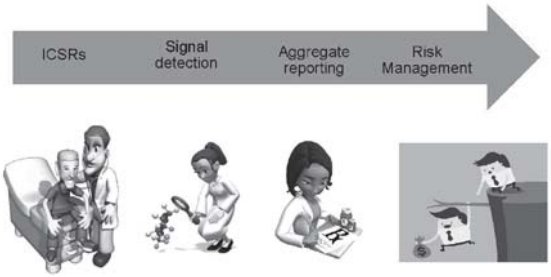
- Indian pharma with PV operations in India
- PV department of Indian affiliate of foreign pharma
- PV service providers in India
- As PV consultants and auditors
- PvPI / CDSCO and other government institutions

Pharmacovigilance stakeholders

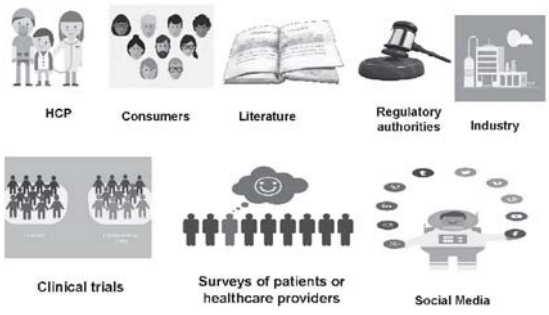
This is how PV works…



Process of Pharmacovigilance – In Industry



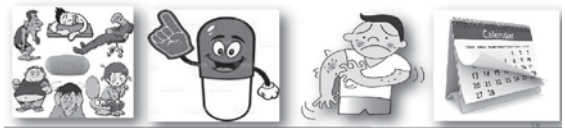
Collection of Safety Information



Individual Case Safety Report

What is an ICSR?

Format and content for the reporting of one or more several suspected adverse reactions in relation to a medical product that occur in a single patient at a specific point of time.



Signal Detection

Reported information on a possible causal relationship between an adverse event and a drug, the relationship being unknown or incompletely documented previously

Traditionally, Signals are detected through the assessment of ICSRs in an individual or cumulative manner.

Aggregate Reports -Overview

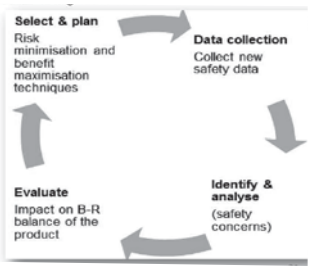
- Plays a key role in the safety assessment of drugs
- Provides a broader view of the safety profile of a drug
- Compilation of safety datafor a drug over a prolonged period of time.
- Submitted to drug regulatory agencies

Aggregate Reports -Overview

- Developmental Safety Update Report (DSUR)
- Periodic Benefit-Risk Evaluation Reports (PBRER)
- Periodic Safety Update Reports (PSUR)
- Periodic Adverse Drug Experience Reports (PADER)

Risk Management

- Performed for assessing a product's benefit-risk balance
- Developing/implementing tools to minimise risk while preserving benefits
- Evaluating tools' effectiveness and reassessing benefit-risk balance

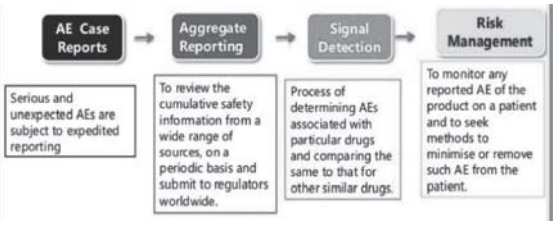


Communication of Safety Information

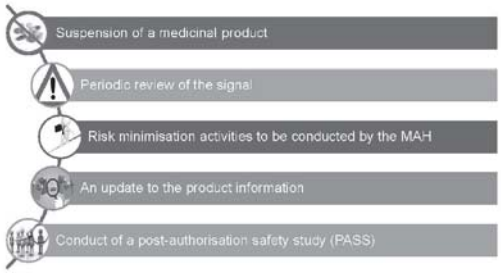
Interactive exchange of information and opinions concerning risk and risk-related factors among regulatory authority, HCP and consumers.

Targeted communication
SmPC/PIL, Physician information, Patient alert card, Treatment initiation and continuation forms and Website information for patients, are examples
General communication
Press release, Q&A documents and National bulletins

Summary of PV Process



Action taken –By Regulatory authority



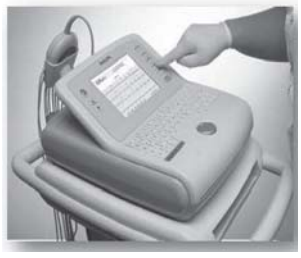
Haemovigilance

Haemovigilance is a set of surveillance procedures covering the whole transfusion chain from the collection of blood and its components to the follow up of its recipiets.

This Haemovigilance Programme is being seen in the wider context of 'Biovigilance'.

Materiovigilance

It enables dangerous devices to be withdrawn from the market and to eliminate faults in medical devices with the intention of constantly improving the quality of devices.



Vaccine Vigilance

Reporting Adverse Events Following Immunization (AEFI). AEFI surveillance monitors immunization safety, detects and responds to adverse events; corrects unsafe immunization practices etc

Cosmetovigilance

Collection, evaluation and monitoring of spontaneous reports of undesirable events observed during or after normal or reasonably foreseeable use of a cosmetic poduct.

Veterinary Vigilance

Science connected to the monitoring, assessment, detection, understanding and prevention of unrecognised adverse effects or changes in the patterns of adverse effects of veterinary medicines.

Take Home Message

Pharmacovigilance can….

- Improve patient care and safety
- Improve public health and safety
- To contribute assessment of benefit, harm, effectiveness and risk of medicines

Dying from a disease is sometimes unavoidable; but dying from a medicine is unacceptable.

CONTACT US

INDIA

Oviya MedSafe Pvt Ltd
2nd Floor, KTVR Gardens
220a-3, Marudha Konar Road
Velandipalayam
Coimbatore - 641 025
Tamil Nadu, India
Tel: +91-422-2444442

UNITED KINGDOM

Oviya MedSafe UK Ltd
Suite LP25393
20-22, Wenlock Road
London
N1 7GU
United Kingdom
Tel: +44-8452-733839

E-Mail: info@oviyamedsafe.com
Web: www.oviyamedsafe.com

Stay connected:

www.linkedin.com/company/oviya-medsafe
www.twitter.com/OviyaMedSafe
www.facebook.com/OviyaMedSafe

Editorial Policy and Disclaimer

The objective of this newsletter is to impart news to the readers and the newsletter is circulated free of cost. Description or reference to any information or publication does not implement endorsement by us.

Every effort has been made to ensure the timeliness and accuracy of information presented in this newsletter. The authors, editors and publisher will not in any way be held responsible for the timeliness of information, errors, omissions and inaccuracies in this publication. Users are advised to recheck the information with original resource material before applying to patient care or other purposes.

This issue of Pharma Web is also available online at the Trust website : www.pictrust.com

PHARMACOVIGILANCE AND GMP REGULATORY COMPLIANCE FOR PHARMACEUTICALS AS PER D & C ACT AND RULES

by

Dr. P. Manavalan,
Assistant Drugs Controller (India), CDSCO, Sea Port, Chennai
(Lecture delivered during Pharmacovigilance Training Course conducted by Trust – 22nd & 23rd February 2019)

Overview

- Responsibility of CDSCO
- Post Marketing Surveillance
- Legal Provisions
- Pharmacovigilance Guidance Document for MAHs
  - Overview
  - Modules
- Regulatory Process
- Challenges for Pharmacovigilance
- Way Forward

VISION

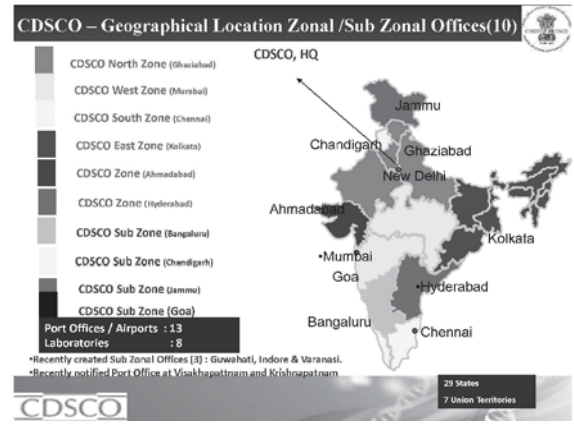
To protect and promote public health in India

CDSCO

MISSION

To safeguard and enhance the public health by assuring the safety, efficacy and quality of drugs, cosmetics and medical devices.

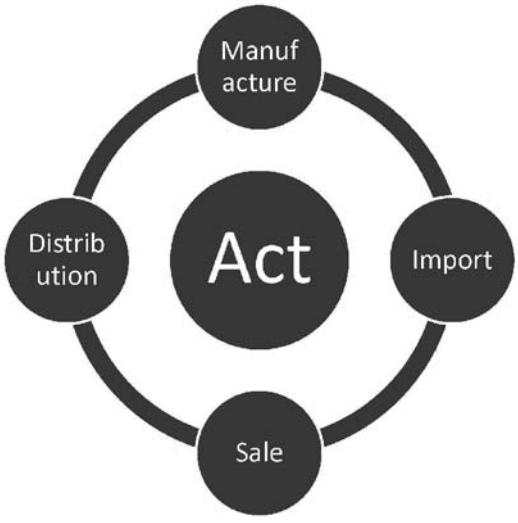
CDSCO



Drugs & Cosmetics Act, 1940

- Drugs fall under the **Concurrent list** of the Constitution
- The Act is a **Central Act**, enforced by both Central and State Govt.
- Extended to Whole of India
- Central Government:
  Central Drugs Standard Control Organization(CDSCO)
- State Governments:
  State Drug Licensing Authorities

What is regulated under the Act



Administration of Act

Advisory
- Drugs Technical Advisory Board
- Drugs Consultative Committee

Executive
- Licensing Authority
- Controlling Authority
- Drugs Inspector

Analytical
- Central Drugs Laboratories
- Drugs Control Laboratories in States
- Government Analyst

Drugs and Cosmetics Act and Rules

Central Responsibilities
- New Drug Approvals/Medical Devices
- Import of Drugs/Medical Devices
- Clinical Trails
- Standards for Drugs
- Amendments to Act and Rules
- Pharmacovigillance

State Responsibilities
- License for Manufacture, Sale and Distribution
- Monitoring quality of Drugs and Cosmetics
- Investigations and Prosecutions

- Regulators are an essential part of the health workforce
- Effective regulatory systems are an essential component of health systems.
- Contribute to better public health outcomes.
- Inefficient regulatory systems themselves can be a barrier to access safe, effective and quality medical products.

Pharmacovigilance

Pharmaco + Vigilance
Pharmaco = Medicine
Vigilance = To Watch

- Alert
- watchfulness
- Wakefulness

Pharmacovigilance

- Pharmacovigilance has become an essential component of drug regulation. PvPI plays an important role for taking regulatory decision by NRA.
- PvPI regularly provides information for taking appropriate decision.

Pharmacovigilance

- Based on the recommendations of such systems few drugs have been banned/modification of Prescribing Information by the NRA.
- Recently conducted NRA assessment reveals that the PvPI is fully functional and awarded maturity level IV status i.e proactive well-resourced regulatory system with continually improving functions are implemented.

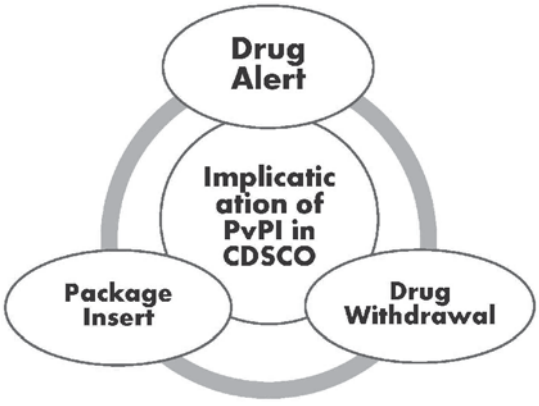
Post Marketing Surveillance

Post Marketing Surveillance of a Pharmaceutical Product entails:

- Post Licensure Safety Evaluation by Marketing Authorisation holder through
  - Submission of Periodic Safety Update Reports
  - Active/Passive Surveillance
  - Structured Phase IV trial
  - Observational Study
- Pharmacovigilance Programme of India through approx. 250 ADR monitoring Centres located in medical colleges and hospitals
- Quality Monitoring of the marketed product by MA holder and Regulatory system

- CDSCO is responsible to take appropriate regulatory decision and actions on the basis of recommendations of NCC-PvPI at IPC Ghaziabad and AEFI programme of Immunization division of Ministry of Health and Family Welfare, New Delhi.
- CDSCO is responsible to take regulatory decision on the basis of analysis of the PMS, PSUR, AEFI data done by expert committee of CDSCO (HQ) alongwith PvPI and AEFI division.

Pharmacovigilance



Legal Provisions


Legal Provisions

REGD. NO. D. L.-33004/99

भारत का राजपत्र
The Gazette of India

EXTRAORDINARY

PUBLISHED BY AUTHORITY

NEW DELHI, TUESDAY, MARCH 6, 2018/ PHALGUNA 15, 1939

2. In the Drugs and Cosmetics Rules, 1945, in Schedule Y,-

(A) for paragraph "(2) **Post Marketing Surveillance"** and clause (i) relating thereto, as published in Part II, Section 3, Sub-section (i) of the Gazette of India, Notification G.S.R. 32 (E) dated 20th January, 2005, at page 63, the following shall be substituted, namely:-

"**4. Post Marketing Surveillance.-**

(i) The applicant shall have a pharmacovigilance system in place for collecting, processing and forwarding the report to the licensing authority for information on adverse drug reactions emerging from the use of the drug manufactured or marketed by the applicant in the country.

(ia) The system shall be managed by qualified and trained personnel and the officer in-charge of collection and processing of data shall be a medical officer or a pharmacist trained in collection and analysis of adverse drug reaction reports.

(ib) Subsequent to approval of the product, new drug shall be closely monitored for its clinical safety once it is marketed.

CDSCO

Legal Provisions

For Post Licensure Safety Evaluation as per Drugs and Cosmetics Act 1940 and Rules 1945 for New Drugs

- Amendment by Gazette notification vide GSR no. 287 (E) dated 08th March 2016 and as per Para 3(4) of Schedule Y of Drugs & Cosmetics Rules-1945.

Post Marketing Surveillance-

- Applicant should have a Pharmacovigilance system in place for collecting, processing and forwarding the report to the licensing authority for information on adverse drug reactions emerging from the use of the drugs manufactured or marketed by the applicant in the country.

Legal Provisions

- The system shall be managed by qualified and trained personnel and the officer in-charge of collection and processing of data shall be a medical officer or a pharmacist trained in collection and analysis of adverse drug reaction reports.
- Subsequent to approval of the product, new drug shall be closely monitored for its clinical safety once it is marketed.
- The applicant shall furnish Periodic Safety Update Reports (PSURs) in order to-

(a) report all relevant new information from appropriate sources;

Legal Provisions

(b) relate the data to patient exposure;

(c) summarise the market authorisation status in different countries and any significant variations related to safety; and

(d) Indicate whether changes shall be made to product information in order to optimize the use of product

- Ordinarily all dosage forms and formulations as well as indications for new drugs should be covered in one PSUR.
- Within single PSUR, separate presentation of data for different dosage forms, indications or separate population need to be given
- All relevant clinical and non-clinical safety data should cover only the period of the report (interval data).

Legal Provisions

Conditions for PSUR submission in Marketing Authorization Permission

- As per conditions 5 and 6 in Form 45 (permission for import of new drugs) and Form 46 (permission for manufacture of new drug)

Condition no.05

"The applicant shall submit PSUR every six months for the first two years. For subsequent two years, the PSUR shall be submitted annually."

Condition no. 06

- "All reported adverse event shall be intimated to Drugs Controller, India and Licensing Authority and regulatory conditions resulting from their review should be complied with.

Legal Provisions

Timelines for PSUR

- PSURs due for a period must be submitted within 30 calendar days of the last day of the reporting period.
- If marketing of the new drug is delayed by the applicant after obtaining approval to market, such data will have to be provided on the deferred basis beginning from the time the new drug is marketed.
- LicensingAuthority may extend the total duration of submission of PSURs, if it is considered necessary in the interest of public health.

Legal Provisions

Conditions of Import for Reporting ADR

- As per condition 4 in Form 41 (Registration Certificate for import of Drugs into India)
- The manufacturer or his authorized agent in India shall inform the licensing authority in the event of any administrative action taken due to adverse reaction, viz. market withdrawal, regulatory restrictions, or cancellation of authorization, and/or not of standard quality report of any drug pertaining to this Registration Certificate declared by the Regulatory Authority of the country of origin or by any Regulatory Authority of any other country, where the drug is marketed/sold or distributed.

Legal Provisions

Conditions of Import for Reporting ADR

Condition 4 in Form 41

- The dispatch and marketing of the drug in such cases shall be stopped immediately, and the licensing authority shall be informed immediately.
- Further action in respect of such stopped marketing of drug shall be followed as per the direction of the licensing authority.

Legal Provisions

- In such cases, action equivalent to that taken with reference to the concerned drug in the country of origin or in the country of marketing shall be followed in India also, in consultation with the licensing authority.
- The licensing authority may, however, direct any further modification to this course of action, including the withdrawal of the drug from Indian market within 48 hours time period

Legal Provisions

Legal provisions for SAE Reporting

- As per Para 3(4) of Schedule Y of Drugs & Cosmetics Rules1945.

All cases involving serious unexpected adverse reactions must be reported to the licensing authority within 15 days of initial receipt of the information by the applicant.

- As per Para 28.2 of Schedule M of Drugs and Cosmetics Rules 1945.

Reports of serious adverse drug reactions resulting from the use of a drug along with comments and documents shall be forthwith reported to the concerned licensing authority.

Guidance Documents for Pharmacovigilance

1. Guidance for Industry for Pharmacovigilance requirements of Biological Product - Published in 2015, (revised on 27th January, 2017)
2. Pharmacovigilance Guidance Document for MAHs of Pharmaceutical Products - Effective date - January 2018

Pharmacovigilance Guidance Document for MAHs of Pharmaceutical Products

- Prepared under the aegis of CDSCO by NCC-PvPI provides guidance to all MAHs of pharmaceutical products (Importers and manufacturers) to establish a Pv system with qualified, trained and experienced manpower to collect and collateAEs/ADRs.
- Should conduct decisive causality analysis of the collated AEs/ADRs cases after due investigation, submit to regulatory authority.
- Broadly based on Good Pharmacovigilance Practices (GVP) document of EMA and has six modules as guidance for establishing PV system at MAH organization.

Pharmacovigilance Guidance Document for MAHs of Pharmaceutical Products

Overview of Guidance Document

Module 01: Pharmacovigilance System Master File (PvMF)

Module 02: Collection, Processing & Reporting of ICSRs

Module 03: Preparation & submission of PSUR

Module 04: Quality Management System at MAH's Organization

Module 05: Audit & Inspection of Pv Systems at MAH's Organization

Module 06: Submission of Risk Management Plan

Module 01: Pharmacovigilance System Master File (PvMF)

- Pv System Master File (PvMF) includes maintenance, content and associated submissions regarding Pv to competent authorities at organization of MAH.
- PvMF shall encompass the list of all approved pharmaceutical products along with the marketing status, approval date and date of pharmaceutical product launched in India.
- PvMF shall contain all the information related to MAH's PV system and shall cover the following sections: concerned licensing authority.

1. Pharmacovigilance O fficer In-Charge (PvOI):

In compliance with Schedule –Y of Drugs and Cosmetics Act, 1940 and Rules, 1945, one qualified and trained personnel should be authorized by the company managements as PvOI with responsibilities for collection and processing of AEs/ADRs data following administration ofdrugs.

PvOI should be a medical officer or a pharmacist trained in the collection and analysis of ADR reports.

Responsibilities of PvOI:

- Development of training modules & organizing training of staff of Pv system.
- Identification of PV activities and framing of SOPs, revisions of SOPs.
- Establishment & maintenance of QMS of Pv development.
- PvOI should reside in India and respond to queries of regulatory authority whenever required.
- PvMF should contain contact details, CV and description of responsibilities of PvOI.

2. Pharmacovigilance Organization Structure

Pv organizational structure of the MAH/ CRO's showing the hierarchy of the Pv department, Name and address of Pv site, and delegated activities.

3. Source of Safety Data:

PvOI shall be responsible to collect data, reports, publications related safety of all pharmaceutical products marketed by the MAH.

4. Pharmacovigilance Processes

- Description and flow diagram of the entire Pv process.
- Data handling, records and archives of Pv performance and SOPs for all the processes.
- Location, functionality and operational responsibility for computerized systems and databases for receiving, collating and reporting safety information should be described in PvMF.
- Description of quality management system including document and record control, training and auditing should be documented in PvMF.

5. Pharmacovigilance System Performance:

Key indicators for the performance of Pv system e.g. number and quality of ICSRs, CAPA needs to be identified and measured for annual trendanalysis.

PvMF should contain evidence of the ongoing monitoring of the Pv system performance, including compliance of the main Pv output.

PvMF should contain evidence of the ongoing monitoring of the Pv system performance, including compliance of the main Pv output.

Annexures to the PvMF:

- A list of pharmaceutical products covered by the PvMF, including the name of the pharmaceutical product and active substances.
- A list of all contract agreements covering delegated activities, including the pharmaceutical products and territory concerned.
- A list of tasks delegated by the PvOI for Pv.
- A list of all completed audits and list of audits schedules.

Module 02: Collection, Processing & Reporting of ICSRs

Under reporting of AEs/ADRs is well known problem associated with spontaneous reporting.

Different methods/sources required to be established by MAHs to strengthen spontaneous reporting ofAEs/ADRs

1. Collection of ICSRs

Medical inquiries
"Contact us", emails and website enquiries forms
MAH employees
Contractual Partners
Information on AEs/ADRs from the internet or digital media
Solicited reports
Miscellaneous sources for reporting

2. Literature Monitoring
Scientific and medical Literature

3. Follow up of ICSRs

ICSR Processing:

- **ICSRs receipt:** MAH shall record the date of receipt for each AEs/ ADRs
- **Validation of reports:** All reports of AEs/ADRs shall be validated before reporting them to the NCC-PvPI with Identifiable reporter (source)
  Identifiable patient
  Suspected pharmaceutical product
  AE/ADR
- **Reporting of ICSR**
  All ICSRs received by MAH shall be submitted to NCC-PvPI in E2B, XML format

Essential data elements of ICSR

- **Patient Information**
  Patient initials, age at the time of onset of event or date of birth, sex, weight
- **Suspected reaction**
  Date of reaction started, date of reaction stopped, describereaction
- **Suspected medications:**
  - Details of suspected medications such as brand name, manufacturer batch number, expiry date, authorization holder, dose route, frequency etc.
  - De-Challenge details
  - Action Taken
  - Re-challenge details
  - Concomitant drugs
  - Relevant laboratory data
  - Other relevant history

- **Seriousness of the reaction :**
  Death, Life threatening, Hospitalization / prolonged, Disabling,
  Congenital anomaly, Other medically important conditions
- **Outcomes :**
  Recovered / Resolved, Not Recovered / Not Resolved, Fatal, Recovering, Recovered with sequele.

Reporter:
Name and professional address, Date of report, Reporter qualification

4. Coding:
For the purposes of ICSRs reporting (expedited and periodic) to regulatory authority, MAHs are required to code ADRs using the ADRs' coding dictionary and indication of suspected & concomitant drug using the latest versionof ICD.

5. Reporting Time Frames:

- All serious AEs/ADRs must be reported to the regulatory authority within 15 calendar days of initial receipt of the information by the MAHs.
- All non-serious AEs/ADRs must be reported to the regulatory authority within 30 days of initial receipt by the MAHs

- Lack of efficacy and medication error shall also be reported to regulatory authority.

6. CausalityAssessment

MAHs are required to follow WHO-UMC causality assessment scale for establishing a temporal relationship between the suspected drug andAEs. Causality assessment for new drugs is mandatory by the MAHs.

7. Special Population

Use of a pharmaceutical product during pregnancy or breastfeeding.

Use of a pharmaceutical product in a pediatric or elderly populations.

Reports of such cases should be followed up for complete information and submitted.

Module 03: Preparation & submission of PSUR

Periodic Safety Update Report is document for evaluation of the benefit – risk profile of a pharmaceutical product submitted by the MAH at defined time points as per D & C Act and Rules during post marketingphase.Other relevant history

Structure & Content:

The recommended content of the PSUR should have data as per Schedule Y of D & C Act and Rules , section (4) Post-marketing Surveillance and ICHE2C (R2) guideline.

1. Title Page
2. Introduction
3. Current worldwide marketing authorization status
4. Update of actions taken for safety reasons
5. Changes to Reference safety Like PIL, CCDS & SmPCs
6. Estimated Patient Exposure
    1. Cumulative subject exposure in clinical trials
    2. Cumulative & interval patient exposure from marketing experience in India

    6.3 Cumulative & Interval patient exposure from marketing experience from rest of the world

7. Presentation of Individual Case Histories

1. Line listing of individual cases received from India
2. Line listing of individual cases received from rest of the world.
3. Cumulative summary tabulations of SAEs from clinical trials.
4. Cumulative & interval summary tabulations from Post marketing data sources

8. Studies

1. Summaries of significant findings from clinical trials during the reporting period
2. Findings from non-interventional studies
3. Information from other clinical trial sources

4. Findings from non-clinical studies
5. Findings from literature

9. Other Information:

1. Lack of efficacy in controlled clinical trials
2. Late Breaking Information
3. Overview of signals: New, Ongoing, or Closed

10. Overall Safety Evaluation:

1. Signal & Risk Evaluation
2. Benefit Evaluation
3. Benefit –Risk Analysis Evaluation

11. Conclusions

12. Appendix to the PSUR

This module should provide a conclusion about the implications of any new information that arose during the reporting interval, in terms of the overall benefit risk evaluation, for each approved indications as well as for relevant sub groups as appropriate. Based on the evaluation of cumulative safety data and the benefit risk analysis, the MAH should assess the need for further change to reference information and propose changes as appropriate. Module

Module 04: Quality Management System at MAH's Organization

MAHs organizational structure - organogram describing Pv system as well as appropriate resource management, compliance management and record management.

Salient Features of QMS:

- MAH shall have a sufficient number of competent and appropriately qualified and trained personnel for the performance of Pv activities.
- All personnel involved in the performance of Pv activities shall receive initial and continued training
- Facilities and equipment which are critical for the conduct of Pv should be subject to appropriate checks, qualification and/or validation activities to prove their suitability for the intended purpose.
- Continuous monitoring of Pv data, the examination of options for risk minimization and prevention , appropriate measures are taken by the MAH
- Effective communication with regulatory authority, including communication on new or changed risks, the PvMF, risk management systems, PSURs and CAPAs

- Recording of all Pv information and ensure that it is handled and stored soas to allow accurate reporting, interpretation and verification of that information
- Hard copies should be retained for a minimum of 10 years and soft copies to be stored indefinitely.
- All elements requirements and provisions adopted for the quality system shall be documented in a systematic and orderly manner in the form of written policies and procedures.
- Performance indicators to be used continuously for monitoring and effective performance of Pv activities.

Module 05: Audit & Inspection of Pv Systems at MAH'sOrganization

- Planning, conducting, reporting and follow up of Pv inspections by officials responsible for inspection
- Pv inspections programmes will be implemented, which will include Routine inspections (risk based approach)
  "For Cause" inspections, (triggered, suspected non-compliance or potential risk, impact on specific products)
- Inspections report and findings with classification of report as critical, major and minor.
- Regulatory action will be taken depending on the potential negative public health impact of non compliances.

Module 06: Submission of Risk Management Plan

Overall aim of risk management is to ensure that the benefits of a particular pharmaceutical product exceed the risks by greatest achievable margin for the individual patient and for the target population as a whole.

Objectives of RMP:

- Identify or characterize the safety profile of the pharmaceutical (s) concerned.
- Indicate how to characterize further the safety profile of the pharmaceutical product concerned.
- Document measures to prevent or minimize the risks associated with the pharmaceutical product including assessment of the effectiveness of those interventions.
- Document post-marketing obligations that have been imposed as a condition of the marketing authorization.

RMP is a dynamic, stand alone document which should be updated throughout the life cycle of the pharmaceutical products.

RMP of every product should be approved by the regulatory authority and should be updated as and when required.

Regulatory Process

- Regulatory decisions and actions may include;
  Suspension
  recall,
  update of product package insert,
  withdrawal,
  revocation of marketing authorization etc.
- Regulatory decision are to be communicated by CDSCO to those concerned (State Drugs Regulatory Authority, Manufacturers etc.)

Challenges for pharmacovigilance

- Although a formal adverse event monitoring system for reporting of adverse events was suggested for India in 1986, nothing much happened till 1997 when India joined World Health Organization adverse event monitoring program based in Uppsala, Sweden
- One of the major challenges for pharmacovigilance in India is underreporting of adverse events. Adverse drug events are estimated to be the fourth to sixth largest cause of death in the USA. As against this, in India, drug adverse effects are responsible for only 3.4% of the hospital admissions and 1.8% of deaths.

- These figures are disproportionate with the country's populations and indicate high underreporting of adverse events from all stakeholders. Companies having patient exposure up to millions of doses reporting not a single AE in their PSUR presentation.
- Many of the adverse events reports may not provide adequate information about adverse events (patient initials, age at onset of the reaction, reaction terms, date of onset of reactions, suspected medications, reporter information) and the data are lost unless extensive follow-up is done. Thus, many events may not qualify as adverse events

- Many Indian multinational companies have their subsidiaries located in Europe and USA where there are clear regulatory requirements for reporting of foreign adverse events and adverse events from published literature, but they don't have pharmacovigilance system in India by which they can monitor all adverse events for their marketed drug products.

Wayforward

- Establishing PV system and assigning responsibilities to qualified and trained personnel within the organisation
- To improve reporting of ADRs by manufacturers/marketing authorisation holders to build up India specific database for the marketed drugs specially those with specific safety concerns for which not much data are available in Indian patients in the clinical trial phase or which have been approved due to health emergencies or due to some life threatening conditions
- Collaboration between all the stakeholders for creating a database of adverse events to ensure safe use of medicinal products throughout product life cycle and accessibility to all stakeholders
- Introducing PV inspection
- Collaboration with various PV organisation for enhancing drug safety

OBITUARY

We regret to inform, Mr. Salvador Fernando, passed away on 8th February 2019

He was the founder trustee of our Trust, since 1989. He was an active member of Trust and also actively involved in “Indian Pharmaceutical Congress” held in Chennai.

He was the Chairman of “Indofrench Laboratories Pvt Ltd., and past President of The Pharmaceutical Manufacturers Association of Tamilnadu.

Our condolences to his family members and pray for his soul be rest in peace.

PHARMACOVIGILANCE PRACTICE IN INDIAN PHARMACEUTICAL INDUSTRIES : CURRENT STATUS AND WAY FORWARD

by

Mr. Balakumar Mahalingam,
Drug Inspector, CDSCO, South Zone, Chennai
(Lecture delivered during Pharmacovigilance Training Course conducted by Trust – 22nd & 23rd February 2019)

Outline of presentation

- Implementation of PVPI in India
- Employment opportunity for Pharma graduates
- Safety & efficacy of Drugs
- How PVPI drive drugs regulations

Implementation of PVPI in India

- CDSCO, is the NRA for medicinal products, Cosmetics& MD
- CDSCO – nodal agency, discharges the regulatory functions to ensure safety, efficacy and quality of "Drugs"
- Schedule –Y of D&C Rules 1945,Para (4) specifies Post Marketing Surveillance;

- GSR Notification no. 287(E), dated 08.03.16
  - "applicant shall have a pharmacovigilance system in place for collecting, processing and Forwarding the report to the LA for information on ADR emerging from the use of the drugs manufactured or marketed by the applicant
- PVP managed by qualified and trained personnel

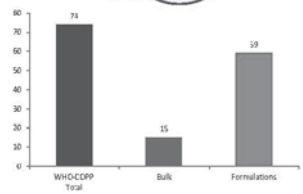
Employment opportunity for Pharma graduates

If 2 Pharma graduates employed in each firm 3000+ new jobs will be created

WHO GMP Certified Manufacturing Units for Certificate of Pharmaceutical Products (COPP) in various States of India*

Sr. No.	State	Total no. of WHO GMP Certified Manufacturers
1.	Andhra Pradesh	35
2.	Assam	01
3.	Delhi (GCT)	08
4.	Goa	38
5.	Gujarat	153
6.	Haryana	40
7.	Himachal Pradesh	115
8.	Jammu and Kashmir	15
9.	Karnataka	82
10.	Kerala	10
11.	Madhya Pradesh	37
12.	Maharashtra	309
13.	Odisha(Orissa)	01
14.	Puducherry	16
15.	Punjab	11
16.	Rajasthan	19
17.	Sikkim	13
18.	Tamil Nadu	74
19.	Telangana	52
20.	Uttar Pradesh	10
21.	Uttarakhand	104
22.	West Bengal	07
	Total	1229

* List as received from the States / UTs through Zonal / Sub-Zonal Offices of CDSCO as on February 2017.



10	Firm conducted stability study at Log term 30°C/65RH Accelerated 37°C/65RH for all the product. However it does not complies with Sch Y or Zone IVb. The same was asked the firm. Firm stated that now firm initiated 30°C/75%RH	Major
11	As per GSR 287(E) Dated 08-03-2016 Mandatory provision for new drugs permission holders to have Pharmacovigilance system in their organization. (CDSCO Notice dated 27-07-2017 File no D.21013/76/2017-DC) FDC drug permission was issued to the firm from FDC division CDSCO- HQ on 17-07-2015. Firm advised to implement Pharmacovigilance system	Minor
12	As per FDC drug permission dated 17-07-2015 condition no 3 firm needs to revise the foil and carton (incorporating 1mm red colour line) for all the product Condition no 4. PSUR needs to be submitted to O/o DCGI	Minor
13	Log for forced evaporator (solid waste disposal) not maintained	Minor
14	Firm did not conducted vendor audit their own, they are using vendor audit report of parent company (M/s Tablets India Ltd)	Minor

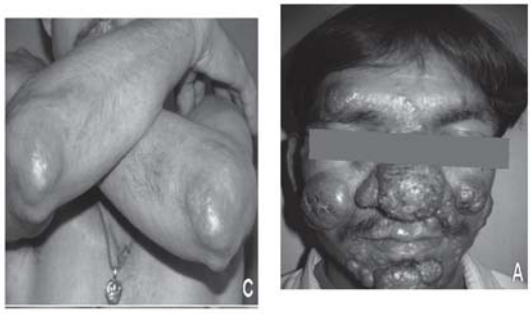
As per Condition no.5 of Form 45/46 PSUR needs to submit

Every 6 months for first 2 yrs for subsequent 2 yrs by annual

Sch M para 28.2 reports of ADRs resulting from use of drugs along with comments reported to concerned LA

Safety & efficacy of Drugs – with special reference to Amphotericine B liposoaml injection

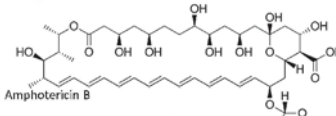
Amphotericine B – treatment of KALA – AZAR (visceral Leishmaniasis)



Pharmacovigil ance ensured the safety of patients

PV Drived the R&D to hunt new formulation

Higher blood conc. of Amph.B induce CKD/death noticed during PSUR



total dose of 21.0 - 30.0 mg/kg of body weight given over 10-21 days may be used in the treatment of visceral leishmaniasis.

The problem is conventional amphotericin injection dose cannot give more than 1.5mg/kg . Higher dose produce CKD and death

Hence medical professional facing very tough situation to treat Kala –Azar

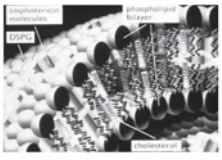
PV urged to develop safe/efficacious formulation

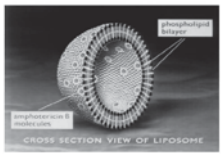
- Gilead, Germany developed Liposomal (single bilayer liposomal drug delivery system
- Phospholipids+ Cholesterol +Amphotericin

single bilayer liposome of unilaminar structure with amphotericin

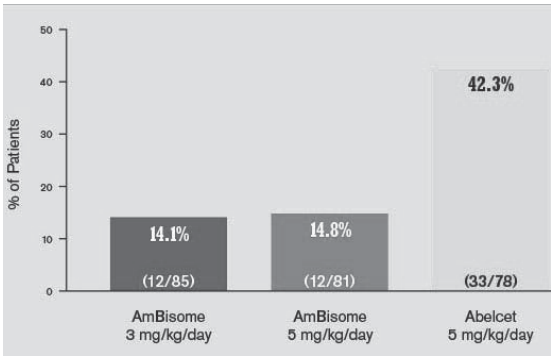
Hence physicians easily treated kaka-Azar with Liposomal -Amph-B

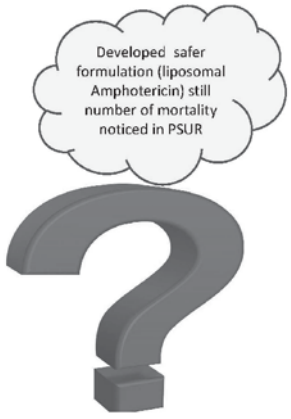
Clinical study proved that up to 5 mg/kg of Liposomal -Amph-B not producing CKD





Nephrotoxicity in patients



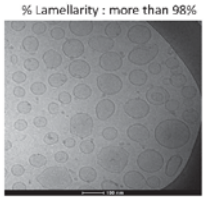


Liposomal Characteristics

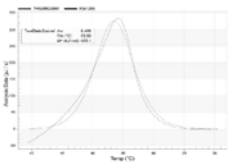
The reason is not all pharma companies ensures liposomal characteristics hence sudden drugs release in plasma causes mortality

List of characterization techniques as per USFDA guidar
Morphology by Cryo Transmission electron microscopy (Cryo-TEM)
Differential Scanning Calorimetry (DSC)
Particle size distribution and Zeta potential
In-vitro Drug Release study
Plasma Stability study
Additional characterization techniques
Bacterial Endotoxin Test (BET)
Free drug estimation
Internal volume measurement by ^1H NMR
Free Flow Electrophoresis study
Small Angle Neutron Scattering Study

% Lamellarity : more than 98%



Glass Transition Temperature (Tg)



The zeta potential measurement depicts that the surface charge around liposome bilayer Should be more than-50

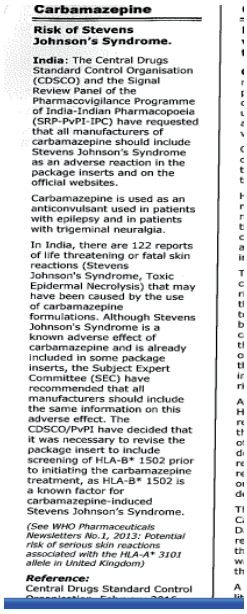
Free drug present in the liposomal preparation Should be less than 1%

The **identical bilayer thickness of** liposome characteristics by Small Angle Neutron Scattering (SANS) Study

Internal volume determination

Internal aqueous volume, which is also termed as 'Captured volume' or 'Entrapped volume' is an important parameter for liposomal formulations. The internal aqueous volume of liposomes was determined by NMR technique.

How PVPI drive drugs regulations



Carbamazepine

Risk of Stevens Johnson's Syndrome.

India: The Central Drugs Standard Control Organisation (CDSCO) and the Signal Review Panel of the Pharmacovigilance Programme of India-Indian Pharmacopoeia (SRP-PvPI-IPC) have requested that all manufacturers of carbamazepine should include Stevens Johnson's Syndrome as an adverse reaction in the package inserts and on the official websites.

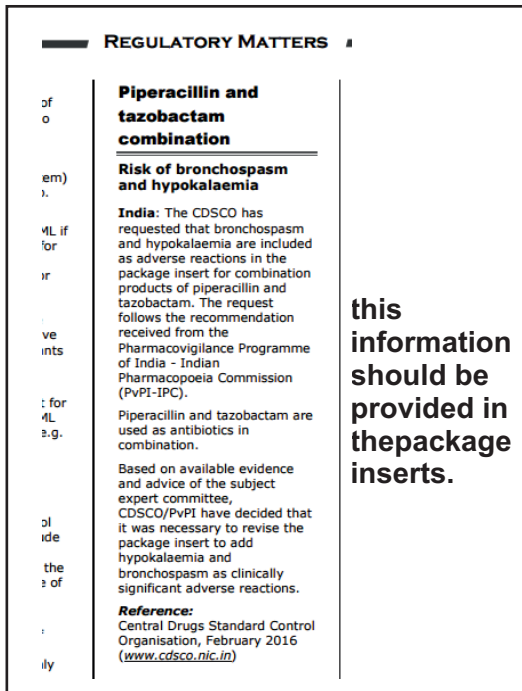
Carbamazepine is used as an anticonvulsant used in patients with epilepsy and in patients with trigeminal neuralgia.

In India, there are 122 reports of life threatening or fatal skin reactions (Stevens Johnson's Syndrome, Toxic Epidermal Necrolysis) that may have been caused by the use of carbamazepine formulations. Although Stevens Johnson's Syndrome is a known adverse effect of carbamazepine and is already included in some package inserts, the Subject Expert Committee (SEC) have recommended that all manufacturers should include the same information on this adverse effect. The CDSCO/PvPI have decided that it was necessary to revise the package insert to include screening of HLA-B* 1502 prior to initiating the carbamazepine treatment, as HLA-B* 1502 is a known factor for carbamazepine-induced Stevens Johnson's Syndrome.

(See WHO Pharmaceuticals Newsletters No.1, 2013: Potential risk of serious skin reactions associated with the HLA-A 3101 allele in United Kingdom)*

Reference:
Central Drugs Standard Control

this information should be provided in the package inserts.



REGULATORY MATTERS

Piperacillin and tazobactam combination

Risk of bronchospasm and hypokalaemia

India: The CDSCO has requested that bronchospasm and hypokalaemia are included as adverse reactions in the package insert for combination products of piperacillin and tazobactam. The request follows the recommendation received from the Pharmacovigilance Programme of India - Indian Pharmacopoeia Commission (PvPI-IPC).

Piperacillin and tazobactam are used as antibiotics in combination.

Based on available evidence and advice of the subject expert committee, CDSCO/PvPI have decided that it was necessary to revise the package insert to add hypokalaemia and bronchospasm as clinically significant adverse reactions.

Reference:
Central Drugs Standard Control Organisation, February 2016 (*www.cdsco.nic.in*)

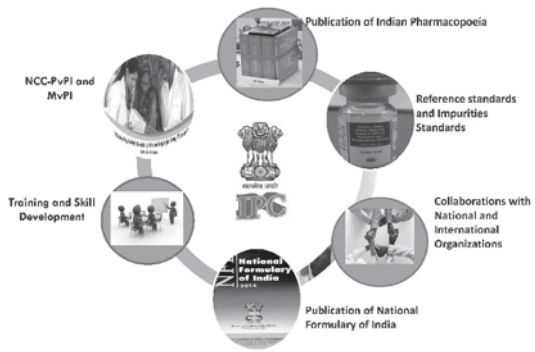
this information should be provided in thepackage inserts.

ICSRs AND PSURs FORMAT AND REPORTING

by

Dr. V. Kalaiselvan,
Principal Scientific Officer, Indian Pharmacopoeia Commission, Ghaziabad
(Lecture delivered during Pharmacovigilance Training Course conducted by Trust – 22nd & 23rd February 2019)

Major Functions of IPC

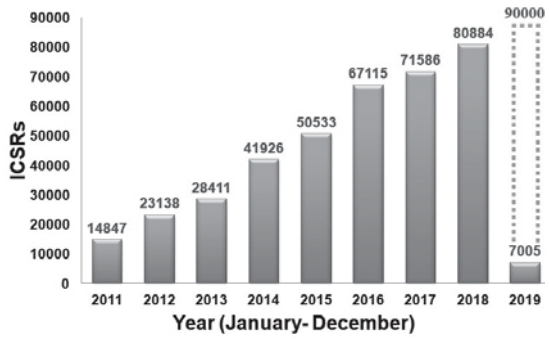


Functions

The Pharmacovigilance Programme of India (PvPI) is inhoused at Indian Pharmacopoeia Commission from 15th April 2011 and functioning as National Coordinating Centre for PvPI.

National Coordination Centre-PvPI	AIIMS	IPC
	2010-2011	2011- till date

Spontaneous ADR Reporting Status at NCC-PvPI



ICSRs

ADR reporting Forms	Types	Versions	Total Fields	Other Relevant Fields
PvPI	• Suspected ADR Reporting Form for HCPs	1.0 (2010) 1.1 (2012) 1.2 (2015) 1.3 (2018)	**4 Fields divided into 17 sub sections** A. Patient Information B. Suspected ADR C. Suspected Medication (s) D. Reporter Details	AMC Report Number Worldwide Unique Number Relevant Tests Data Complete Seriousness Criteria Reaction Outcome Reporter Information
	• Medicine Side-effects Reporting Form for Consumers	1.1 (2014)	Comprehensive form divided into 7 fields Patient Details Health Information Reporter Details Details of Medicines Side effect information Side effect seriousness Describe reaction	Available in 10 regional languages- Gujarati, Kannada, Bengali Malayalam, Oriya, Tamil Marathi, Telugu, Assamese
CIOMS	Form 1	1 (1986)	**4 Fields divided into 25 sub sections** I. Reaction Information II. Suspected Drug(s) Information III. Concomitant Drug(s) & History IV.Manufacturer Information	Country Name Specific Identification Number

Role

1. The Drugs and cosmetics Act, 1940 and Rules, 1945 there under clearly states for **Patient safety** and effectiveness of Drugs on Indian Population.

2. **Rules 122E** under the definition of **New drug,** "A new drug shall continue to be considered as a new drug for a period of four years from the date of its first approval".

Role

1. **'Schedule Y'** deals with the requirements and guidelines for permission to import and/or manufacture of new drugs for sale or to undertake clinical trials.

2. **Post marketing surveillance under Schedule Y** indicates that subsequent to the approval of the product, new drugs shall be closely monitored for its clinical safety once it is marketed.

Role

1. The applicants shall furnish Periodic Safety Update Reports (PSURs) in order to –

a) Report all relevant new information from appropriate sources

b) Relate the data to patient exposure

c) Summarize the market authorization status in different countries and any significant variations related to safety; and

d) Indicate whether changes shall be made to product information in order to optimize the use of the product.

Role

1. The PSURs shall be submitted every six months for the first two years after approval of the drug is granted to the applicant. For subsequent two years – the PSURS need to be submitted annually.

2. Licensing Authority may extend the total duration of submission of PSURs if it is considered necessary in the interest of Public health.

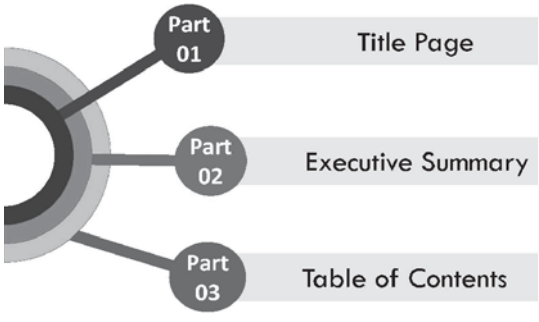
PSURs

- Periodic Safety Update Report provides…
- Detailed information on drug safety
- Systematic analysis and evaluation of the risk benefit profile
- Based on cumulative data from all sources, including national and international publications as well as a report on any necessary consequences.

PSUR Requirement as per Schedule Y

- For New Drugs
- Once marketed
- Periodicity: every six months for the first two years and annually next two years
- PSURs must be submitted within 30 calendar days of the last day of the reporting period

Content and Format



PSUR Requirement as per Schedule Y

PSUR should be structured as follows:

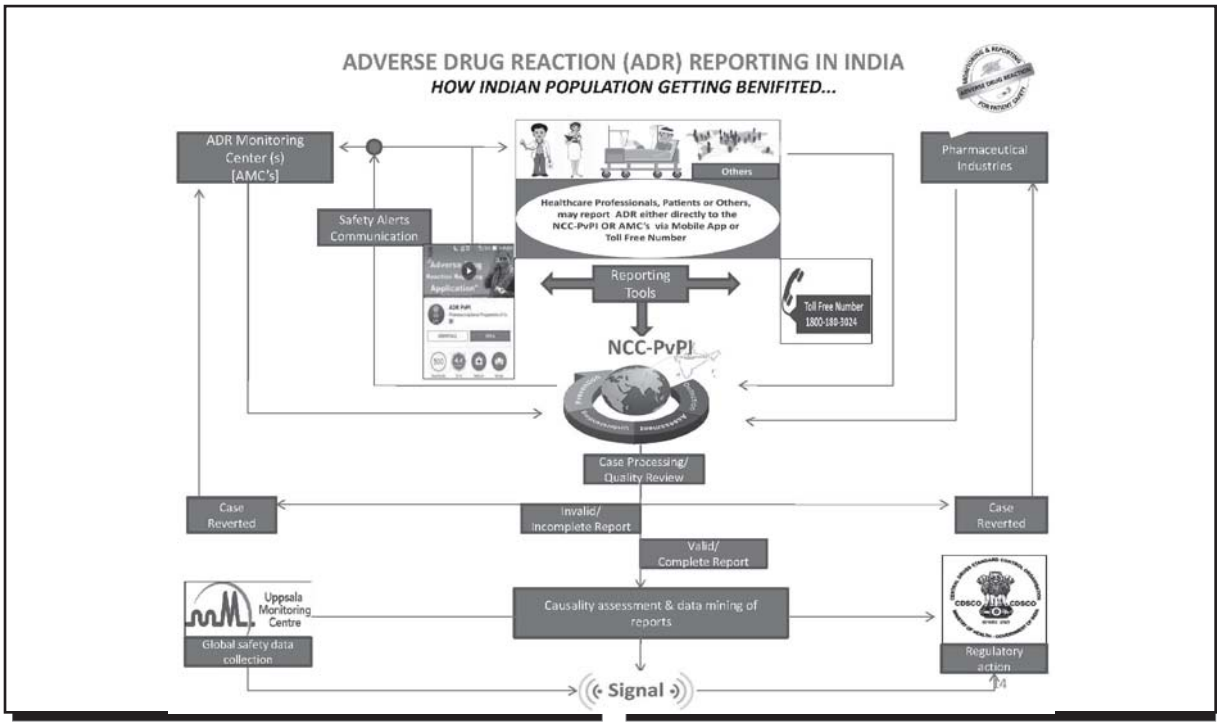
- A title page stating: Periodic safety update report for the product, applicant's name, period covered by the report, date of approval of new drug, date of marketing of new drug and date of reporting;
- Introduction,
- Current worldwide market authorization status,
- Update of actions taken for safety reasons,

PSUR Requirement as per Schedule Y

- Changes to reference safety information,
- Estimated patient exposure,
- Presentation of individual case histories,
- Studies,
- Other information,
- Overall safety evaluation,
- Conclusion,
- Appendix

PSURs Evaluation

- PMS/PSUR being conditions for Market Authorization and Licensing and therefore in order to ensure the regulatory conformance and proper design of post marketing studies, this cell shall work within the licensing division of CDSCO HQ.
- This division is responsible for collecting, compiling and collating the data received from the MAH as per the requirements of Schedule Y.
- The compiled PMS/ PSUR data will then be reviewed by the advisory committee constituted
- Based on the analysis of the advisory committee regulatory decision will be taken by CDSCO for further generation of safety and efficacy data not limiting to the initial pre licensure study.



Responsibilities

S. No.	CDSCO	IPC
1. Surveillance	Pharmacovigilance/Post marketing Surveillance as per provisions of Drugs and Cosmetics Rule 1945 under Schedule Y and Schedule M	Collection, Collation and analysis of Adverse events captured through spontaneous reporting on generic dugs
2. Monitoring and data collection	Monitoring the safety of New drugs through Periodic Safety Update report (PSURs) – Real-time data is obtained during the first four years period. Pharmacovigilance Audit and Inspection	↓ Data Mining ↓ Signal detection ↓
3.	Appropriate Regulatory decisions ←	Inputs to CDSCO

Utilisation of ICSRs and PSURs data

Drug Alerts	Updating Package insert	Signals
79	38	05

Self assessment

S. No	Activity	ICSRs	PSURs
1	Reporting form/format		
3	Reporting status		
3	Reporters		
4	Reported to		
5	SAE reporting time line		
6	Drugs category		

Basic understanding of Individual Case Safety Reports (ICSRs) and Periodic Safety Update Reports (PSURs)

S. No	ICSRs	PSURs
1	Reported in suspected ADRs reporting form/CIOMS etc	Reported as per the requirement of Schedule Y of Drugs & Cosmetic Act 1940 and rules 1945 therunder
2	Spontaneous reporting – voluntary	Mandatory – Legal requirements
3	For new drugs and generic and others	For new drugs only
4	Reported to IPC –PvPI/CDSCO	Reported to CDSCO
5	Single case report	Compiled data of India and global as well
6	No benefit and risk assessment	Benefit and risk assessment is included
7	Reporting of serious cases – within 15 calendar days to CDSCO and PvPI	First two years – six monthly Next subsequently two years – annually
8	Submitted by Hospitals, Healthcare professionals and patients	Submitted by pharmaceutical industries

THE LEADERSHIP CHALLENGES IN THE PHARMACEUTICAL SECTOR

by
Ms. Sharon Christina Pearline. V
C.L. Baid Metha College of Pharmacy, Chennai
Note: This article was awarded 2nd prize in the Essay Competition conducted by our Trust

Change, being the only constant, is inevitable.

With constant change comes tremendous Challenges.

'GLOBALIZATION' is influencing and directing the growth trajectory of the Pharmaceutical sector. As the key influencers of this phenomenon, Technology, and Science exhibit new discovery and innovation at an unprecedented rate. These modern theories and inventions have set the ball rolling for the production of new Pharmaceuticals. However, for every pro there is a con, for every change there is a challenge and globalization causes a falter in the economic status of our country, resulting in mammoth challenges that need rapid recognition and solution.

Drug Price Control Orders (DPCO) was issued to make medicines affordable for the betterment of the people. But it is inflicting pressure upon the Pharmaceutical professionals who are burdened to perceive alternate ways to manufacture good quality consumer products at less cost. To produce products that can be marketed at a low price in accordance with the policies framed by the government and concurrently being profitable is a challenge. It is important that the needs of the consumers be met with highly reproducible standards.

The low cost of **Generic drugs provide affordable treatment for people,** and India is emerging as a prominent supplier of generic drugs globally. But reports of compromised quality, violation of authenticity of data, and a shortage of qualified scientists for R&D of generic drugs emanated in the ban of such companies by the US FDA. Further, Statistical data reveal 30% of generic drug imports of US is from India. This **fosters competition with the US Pharmaceutical Leaders** who use legal provisions to delay the launch of generic drugs in their country. As India is a significant export platform for generic drugs, the above-stated issues foist a challenge on the Leaders of the Indian Pharmaceutical export sector, who have to be prepared to face such backfires.

Though India is able to export generic drugs at one-tenth the price of branded drugs, it is **not able to slash prices of the branded drugs** in the domestic market which has led the Government of India to promote sales of generic drugs through the Jan Aushadhi Scheme.

This move by the government will severely perturb the sale of branded drugs in the market - a more recent challenge, which requires an imminent working solution.

Allopathic drugs cannot be made with nil side effects. Drugs taken to cure a particular disease may afford relief to the patient in the short term, but the side effects developed in the long run may be from moderate to drastic. Hence a **sincere post marketing surveillance is required.** A lingering challenge indeed!

India has an enormous reservoir of medicinal plants. Around 20,000-50,000 medicinal plants have been studied, but only around 7000 plants are being used in natural systems of medicine like Ayurveda and Siddha. As we are about to move into a new phase of the social order, plant drugs will soon be the demand of society. Indian leaders must be prepared to mass-produce standardized Ayurveda and other herbal medicine to the people. The **need for standardization procedures for plant-based drugs** is a scathing challenge in the sector.

The higher **positions of the Pharmacists in the hospital pharmacy and clinical pharmacies** are being snatched and substituted by medical officers, and administrative officers. These designated posts legally belong to the pharmacists only. Besides, vacancy in pharmacist postings and complete ignorance in sanctioning of pharmacist postings have been reported. It is the obligation of the pharmaceutical leaders to fight for what rightfully belongs to pharmacists. Although measures are being taken to launch a nationwide campaign against this controversy, pharmaceutical leaders must draw efforts to designate more qualified people with B.Pharm or Pharm.D degree for those positions in the hospital pharmacy and clinical sector respectively.

Finally, the **Research and Development** of Pharmaceuticals will thrive till mankind has the capacity to think extensively and come up with feasible ideas contemporaneous with the current scenario. Comparing statistical data of the past three to four years with the current year show a rapid increase in growth of the pharmaceutical industry in the near past and a decline to a moderate level towards the latter period. The main reason for such decline is the **minimal inflow of funds toward R&D.**

Ken Frazier, CEO of Merck stated - *"the problem with R&D is, it is not like engineering where you can incrementally innovate and make another version of the iPhone",* while defending accusations of their appropriated budget for research being exorbitant.

Additionally, Constraints on funding and drug testing in clinical trials, threaten the pioneering ability of the pharmaceutical industry.

India's focus in producing generic drugs to the market has caused a cutback in the innovation of breakthrough drugs. Though India gains profits through generic drugs **the innovative potential is being repressed.** Leaders have to find a solution to the problem.

CONCLUSION:

Failure is unavoidable, a part and parcel of success, but success will eventually transcend failure and alter the course of globalization favouring revolution.

The Pharmaceutical sector is not a solitary structure, but comprises of various complex segments, all of them soldered to each other functioning like a well-oiled machine. Leadership in the pharmaceutical sector does not pertain to a single person, but it demands an executive team of competent leaders, with profound commitment, passion for their profession and a quick wit to provide solutions.

The Pharmaceutical industry is a massive contributor to the society, bringing together various other industries of the world. Naturally, an unresolved hitch in the pharmaceutical sector will cause a cascade of setbacks in the connecting industries. Complications should be identified, disentangled and rectified promptly. With persistence and highly competitive standings amidst their adversaries, the pharmaceutical leaders are expected to show unremitting commitment to stay the course with determination and good will, scaling the mountain of a challenge to reach the summit.

EVENTS

AII INDIA PHARMACY QUIZ 2019

The All India Pharmacy quiz is being conducted by College of Pharmacy, Madras Medical College for the last 9 years. This year-2019, a total of 405 teams comprising of 58 colleges spread across 10 states participated in the Preliminary round which was conducted on Jan 24, 2019 at 27 centers throughout India.

75 teams qualified for Semi finals which were conducted on February 5, 2019, in the MMC College premises.

The following are the winners of the quiz program

Rank	Name of the Awardees	College	Amount (Rs.)
1st Prize	Mr. M. Yoga Prakash & Mr. S. Dhamodharan	Madras Medical College, Tamil Nadu.	25,000/-
2nd Prize	Ms. Harsimran Kaur & Ms. Bhavika Sharma	Poona College of Pharmacy, Pune, Maharashtra	15,000/-
3rd Prize	Mr. J. Pravin Kumar & Ms. D. Swetha	SRM College of Pharmacy, Kattangulathur, Tami Nadu.	10,000/-
4th Prize	Mr. L. Karthy Keyan & Mr. B.Hari Baskar	KMCH College of Pharmacy, Coimbatore, Tamil Nadu.	2,000/- per team
	Ms. N. Priyanka & Ms. R.N.Haritha	Madras Medical College, Tamil Nadu	2,000/- per team
5th prize	Ms. Mariya Joseph & Ms. Elizabeth John	Nirmala College of Pharmacy, Cochin, Kerala.	2,000/- per team

The quiz program was organised by Dr. A. Jerad Suresh, Principal, College of Pharmacy, Madras Medical College, Chennai. Prizes were distributed by the Dean Dr. R. Jayanthi and the Deputy Medical Superintendent Dr. Raghunanthan. The Chief guests were Mr. K. Pandian, General Manager – Purchase, M/s. Delvin Formulations Pvt. Ltd., Mr. K. S. Raghu, Assoiciate Vice President, M/s. Fourrts India Pvt. Ltd. & Mr. M. Radha Krishnan, HR Manager, M/s. Apex Laboratories Pvt Ltd.

INFORMATION

M. PHARM & PHARM D SCHOLARSHIPS 2018-19 AWARDED BY TNPSWT

Profile of 1st Rank Projects

PHARMACEUTICS

Name: Ms. Divyabharathi. M

Project Title: Investigation of the Effect of Anticancer Drugs Gemcitabine and 5-Fluoro Uracil on Herpes Simplex Virus Infection – A Drug Repurposing Approach.

College: J S S College of Pharmacy, Ooty

Guide's Name: Dr. Ashish Wadhwani

PHARMACEUTICAL CHEMISTRY

Name: Ms. Naina Merin Joy

Project Title: Design and Synthesis of novel 4-thiazolidinone derivatives bearing 1,3,4-oxadiazole moiety as IRT-3 modulators targeting Parkinson's disease.

College: JSS College of Pharmacy, Ooty

Guide's Name: Dr. S. Gomathy

PHARMACEUTICAL ANALYSIS

Name: Mr. Ramshankar Nayak

Project Title: QbD approach on analytical method development and validation for the estimation of Riociguat in their formulations by LC-MS-MS

College: JSS College of Pharmacy, Ooty

Guide's Name: Dr. S.N. Meyyanathan

PHARMACOLOGY

Name: Mr. Tenzin Choephel

Project Title: Neuroprotective Evaluation of Combination of PPAR-γ Receptor Agonist and NMDA Receptor Antagonist in Animal Model of Alzheimer's Disease.

College: JSS College of Pharmacy, Ooty

Guide's Name: Dr. A. Justin

PHARMACOGNOSY

Name: Ms. Ann Maria Alex

Project Title: Evaluation of anti-breast cancer potential of Bauhinia racemosa Lam. & in-silico studies of its isolated compounds.

College: JSS College of Pharmacy, Ooty

Guide's Name: Prof. P. Dhamodaran

PHARMACY PRACTICE

Name: Ms. Kousalya. B

Project Title: Simulated Y-site Compatibility Study of Meropenem with Certain Selected Co-administered Intravenous Medications

College: College of Pharmacy, SRIPMS, Coimbatore

Guide's Name: Dr. Manjula Devi. A.S

PHARM D- PHARMACY PRACTICE

Name: Mr. Muhammed Sufiyan, Ms. Sai Laharika, Ms. Roshni. S, Ms. Sheena Varghese

Project Title: Identification of Drug Related Problems among Chronic Kidney Disease Patients in a Tertiary Care Hospital

College: K. K College of Pharmacy, Chennai

Guide's Name: Dr. S. Ramalakshmi

CONGRATULATIONS

We are pleased to inform all our readers that Mr. J. Jayaseelan, Managing Director, M/s. Delvin Formulations Pvt. Ltd., elected as President, Tamilnadu Pharmacy Council.

He is one of the very active Governing Body Members of our Trust. He is the Chairman of Indian Drug Manufacturers Association, Tamilnadu State Board. Chairman, IPA-Industry Pharmacy division, Mumbai, and Vice President – IPA TN

We congratulate him for his elevation as President – Tamilnadu Pharmacy Council

NOTIFICATION

MINISTRY OF HEALTH AND FAMILY WELFARE

(Department of Health and Family Welfare)

NOTIFICATION

New Delhi, the 10th January, 2019

G.S.R. 20(E).—Whereas a draft of certain rules further to amend the Drugs and Cosmetics Rules, 1945 was published as required under section 12 and section 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940) vide notification of the Government of India in the Ministry of Health and Family Welfare (Department of Health and Family Welfare) number G.S.R. 1051(E), dated the 22nd October, 2018, in the Gazette of India, Extraordinary, Part II, Section 3, Sub-section (i), inviting objections and suggestions from persons likely to be affected thereby, before the expiry of a period of thirty days from the date on which the copies of the Official Gazette containing the said notification were made available to the public;

And whereas, copies of the Official Gazette were made available to the public on the 23rd October, 2018;

And whereas, no objections or suggestions were received from the public on the said rules for consideration by the Central Government;

Now, therefore, in exercise of the powers conferred by section 12 and section 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940), the Central Government, after consultation with the Drugs Technical Advisory Board, hereby makes the following rules further to amend the Drugs and Cosmetics Rules, 1945, namely:—

1. (1) These rules may be called the Drugs and Cosmetics (Second Amendment) Rules, 2019.

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

2. In the Drugs and Cosmetics Rules, 1945, in rule 43A, for the word “Tuticorin” the words “Tuticorin and Kamrajar Port”; and for the word “Gandhinagar” the words “Gandhinagar and Mundra Port” respectively shall be substituted.

[F. No. X.11014/25/2018-DRS]
Dr. MANDEEP K. BHANDARI, Jt. Secy.

Note : The principal rules were published in the Gazette of India vide notification number F. 28-10/45-H (1), dated 21st December, 1945 and last amended vide notification number G.S.R. 19(E), dated 10th January, 2019.

MINISTRY OF HEALTH AND FAMILY WELFARE

(Department of Health and Family Welfare)

NOTIFICATION

New Delhi, the 15th January, 2019

G.S.R. 30(E).—Whereas a draft of certain rules further to amend the Medical Devices Rules, 2017, was published as required by sub-section (1) of section 12 and sub-section (1) of section 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940) vide notification of the Government of India in the Ministry of Health and Family Welfare (Department of Health and Family Welfare) number G.S.R. 848 (E), dated the 7th September, 2018, in the Gazette of India, Extraordinary, Part II, Section 3, Sub-section (i), inviting objections and suggestions from persons likely to be affected thereby, before the expiry of a period of thirty days from the date on which the copies of the Official Gazette containing the said notification were made available to the public;

And whereas copies of the Official Gazette were made available to the public on 14th September, 2018;

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

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

1. (1) These rules may be called the Medical Devices (Amendment) Rules, 2019.

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

2. In the Medical Devices Rules, 2017 (hereinafter to be referred as said rules), in rule 3, in clause (v), after the words “instructions for use”, the words “or electronic instructions for use” shall be inserted.

3. In the said rules, in rule 59, in sub-rule (3), in clause (iii), after the words “instructions for use”, the words “or electronic instructions for use” shall be inserted.

4. In the said rules, in Fourth Schedule,

(A) in Part II, under the heading “Document to be submitted with the application for grant of Import Licence or licence to manufacture for sale or for distribution of a Class A medical device” in paragraph (a), in the Table, against serial number 4, for the letters “IFU” occurring in both columns (2) and (3), the words “instructions for use or electronic instructions for use” shall be substituted;

(B) in Part III, in Appendix II,

(i) in para 2.1, in clause (a) for the words "instructions for use", the words "instructions for use or electronic Instructions for use" shall be substituted;

(ii) in para 3.0, for clause (b) the following clause shall be substituted, namely:

"(b) Instructions for use or electronic instructions for use (Prescriber's manual);";

(C) in Part IV,

(i) in paragraph (a), for serial number 8 and the entries relating thereto, the following serial number and entries shall be substituted, namely:

"8. Proposed instructions for use or electronic instructions for use and labels.";

(ii) in paragraph (b), for serial number 5 and the entries relating thereto, the following serial number and entries shall be substituted, namely:

"5. Proposed instructions for use or electronic instructions for use and labels.".

5. In the Seventh Schedule,

(a) in paragraph 1, in sub-paragraph (1), in clause (v),

(i) for the words "Instructions for use", the words "instructions for use or electronic instructions for use" shall be shall be substituted;

(ii) in the proviso, for the words "Instructions for Use", the words "instructions for use or electronic instructions for use" shall be shall be substituted;

(b) in Table 3, for serial number 11 and the entries relating thereto,, the following serial number and entries shall be substituted, namely:

"11. Proposed instructions for use or electronic instructions for use and labels.".

[F.No.X.11014/20/2018-DR]
Dr. MANDEEP K. BHANDARI, Jt. Secy.

Note : The principal rules were published in the Gazette of India, Extraordinary, Part II, Section 3, Sub-section (I) vide notification number G.S.R. 78(E), dated the 31st January, 2017 and last amended vide notification number G.S.R. 729(E), dated the 1st August, 2018.

MINISTRY OF HEALTH AND FAMILY WELFARE

(Department of Health and Family Welfare)

NOTIFICATION

New Delhi, the 2nd April, 2019

S.O. 1500(E).— In pursuance of sub-clause (iv) of clause (b) of section 3 of the Drugs and Cosmetics Act, 1940 (23 of 1940), the Central Government, after consultation with the Drugs Technical Advisory Board, hereby specifies the following device intended for external or internal use in human beings as drugs with immediate effect, namely:—

"Organ preservative solution"

[F. No. X. 11014/7/2019-DR]
1990 GI/2019 Dr. MANDEEP K. BHANDARI, Jt. Secy.

MINISTRY OF HEALTH AND FAMILY WELFARE

(Department of Health and Family Welfare)

NOTIFICATION

New Delhi, the 25th January, 2019

G.S.R. 47(E).—Whereas a draft of certain rules further to amend the Drugs and Cosmetics Rules, 1945 was published as required under sub-section (1) of section 12 and sub-section (1) of section 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940) vide notification of the Government of India in the Ministry of Health and Family Welfare (Department of Health and Family Welfare) number G.S.R. 719(E), dated the 30th July, 2018 in the Gazette of India, Extraordinary, Part II, section 3, sub-section (i), inviting objections and suggestions from persons likely to be affected thereby, before the expiry of a period of forty-five days from the date on which the copies of the Official Gazette containing the said notification were made available to the public;

And whereas copies of the Gazette were made available to the public on the 4th August, 2018;

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

Now, therefore, in exercise of the powers conferred under sections 12 and 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940), the Central Government, after consultation with the Drugs Technical Advisory Board, hereby makes the following rules further to amend the Drugs and Cosmetics Rules, 1945, namely:

1. (1) These rules may be called the Drugs and Cosmetics (Third Amendment) Rules, 2019.
   (2) They shall come into force on the date of their publication in the Official Gazette.

2. In the Drugs and Cosmetics Rules, 1945, in Schedule K, after serial number 37 and the entries relating thereto, the following serial number and entries shall be inserted, namely:

Class of Drugs	Extent and Conditions of Exemption
"38. Sterile solutions intended for parenteral administration with 100 ml in one container of the finished dosage form for single use manufactured for export only.	The provisions of Chapter IV of the Act and rules made thereunder which require them to obtain a licence in Form 28D or 28DA from the Central Licence Approving Authority subject to the condition that such drugs have been manufactured for export purpose only under a licence granted by the State Licensing Authority.".

[F.No. X.11014/10/2018-DR]
Dr. MANDEEP K BHANDARI, Jt. Secy.

Note: The principal rules were published in the Official Gazette vide notification number F.28-10/45-H (1), dated 21st December, 1945 and last amended vide notification number G.S.R. 20(E), dated 10th January, 2019.

MINISTRY OF HEALTH AND FAMILY WELFARE

(Department of Health and Family Welfare)

NOTIFICATION

New Delhi, the 6th March, 2019

G.S.R.186(E).—Whereas a draft of certain rules further to amend the Drugs and Cosmetics Rules, 1945 was published as required under sub-section (1) of section 12 and sub-section (1) of section 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940) vide notification of the Government of India in the Ministry of Health and Family Welfare (Department of Health and Family Welfare) number G.S.R. 922(E), dated the 25th September, 2018, in the Gazette of India, Extraordinary, Part II, section 3, sub-section (I) inviting objections and suggestions from persons likely to be affected thereby, before the expiry of a period of forty-five days from the date on which the copies of the Official Gazette containing the said notification were made available to the public;

And whereas, copies of the Gazette were made available to the public on the 26th September, 2018;

And whereas, no objections or suggestions were received from the public on the said rules for consideration by the Central Government;

Now, therefore, in exercise of the powers conferred under sections 12 and 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940), the Central Government, after consultation with the Drugs Technical Advisory Board, hereby makes the following rules further to amend the Drugs and Cosmetics Rules, 1945, namely:—

1. (1) These rules may be called the Drugs and Cosmetics (Fifth Amendment) Rules, 2019.

(2) They shall come into force on the 1st day of April, 2019.

2. In the Drugs and Cosmetics Rules, 1945, in Schedule H, in the Note appended thereto, in paragraph 4, for the word 'steroids', the words "steroids or Hydroquinone" shall be substituted.

[F. No. X.11014/23/2018-DR]
Dr. MANDEEP K. BHANDARI, Jt. Secy.

Note : The Drugs and Cosmetics Rules, 1945 were published in the Gazette of India vide notification number F. 28-10/45-H(1), dated the 21st December, 1945 and was last amended vide notification number G.S.R. 153(E), dated the 26th February, 2019.

MINISTRY OF HEALTH AND FAMILY WELFARE

(Department of Health and Family Welfare)

NOTIFICATION

New Delhi, the 26th February, 2019

G.S.R. 153(E).—Whereas a draft of certain rules further to amend the Drugs and Cosmetics Rules, 1945 was published as required under sub-section(1) of section 12 and sub-section (1) of section 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940) vide notification of the Government of India in the Ministry of Health and Family Welfare (Department of Health and Family Welfare) number G.S.R. 1190(E), dated the 10th December, 2018, in the Gazette of India, Extraordinary, Part II, Section 3, Sub-section (I), inviting objections and suggestions from persons likely to be affected thereby, before the expiry of a period of ten days from the date on which the copies of the Official Gazette containing the said notification were made available to the public;

And whereas copies of the said Official Gazette were made available to the public on the 10th December, 2018;

And whereas, no objections or suggestions were received from the public on the said rules for consideration by the Central Government;

Now, therefore, in exercise of the powers conferred under sections 12 and 33 of the Drugs and Cosmetics Act, 1940, the Central Government, after consultation with the Drugs Technical Advisory Board, hereby makes the following rules further to amend the Drugs and Cosmetics Rules, 1945, namely:—

1. (1) These rules may be called the Drugs and Cosmetics (Fourth Amendment) Rules, 2019.

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

2. In the drugs and Cosmetics Rules 1945, in the Schedule H, in the note appended thereto, after paragraph 4, the following paragraph shall be inserted, namely:—

"5. Notwithstanding anything contained in these rules, the provisions of rule 65 and rule 97 in respect of drugs specified from serial number 538 to serial number 551 inserted vide Notification number G.S.R. 277(E), dated 23rd March, 2018 published in the Gazette of India, Extraordinary, Part II, Section (3), Sub-section (i) shall be on voluntary basis for a period commencing on the day on which this notification shall come into force and ending on the 31st March, 2019 and thereafter shall be mandatory.".

[F. No. X. 11014/14/2017-DRS]
Dr. MANDEEP K BHANDARI, Jt. Secy.

Note : The principal rules were published in the official gazette vide notification number F.28-10/45-H (1), dated the 21st December, 1945 and last amended vide notification number G.S.R. 47(E), dated the 25th January, 2019.

MINISTRY OF HEALTH AND FAMILY WELFARE

(Department of Health and Family Welfare)

NOTIFICATION

New Delhi, the 8th March, 2019

G.S.R. 205(E).—Whereas a draft of certain rules further to amend the Drugs and Cosmetics Rules, 1945 was published as required under sub-section(1) of section 12 and sub-section (1) of section 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940) vide notification of the Government of India in the Ministry of Health and Family Welfare (Department of Health and Family Welfare) number G.S.R. 88(E), dated the 4th February, 2019, in the Gazette of India, Extraordinary, Part II, section 3, sub-section (i), inviting objections and suggestions from persons likely to be affected thereby before the expiry of a period of fifteen days from the date on which the copies of the Official Gazette containing the said notification were made available to the public;

And whereas copies of Official Gazette were made available to the public on the 5th February, 2019;

And whereas, no objections or suggestions were received from the public on the said rules for consideration by the Central Government;

Now, therefore, in exercise of the powers conferred under sections 12 and 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940), the Central Government, after consultation with the Drugs Technical Advisory Board, hereby makes the following rules further to amend the Drugs and Cosmetics Rules, 1945, namely:-

1. (1) These rules may be called the Drugs and Cosmetics (Sixth Amendment) Rules, 2019.

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

2. In the Drugs and Cosmetics Rules, 1945, in rule 96, in sub-rule (1), in clause (i), in sub-clause (A), the words “in brackets” shall be omitted.

[F. No.X.11014/3/2019-DR]
SUDHIR KUMAR, Jt. Secy

Note: The principal rules were published in the Gazette of India vide notification number F.28-10/45-H (1), dated the 21st December, 1945 and last amended vide notification number G.S.R. 186(E), dated the 6th March, 2019

MINISTRY OF HEALTH AND FAMILY WELFARE

(Department of Health and Family Welfare)

NOTIFICATION

New Delhi, the 11th March, 2019

G.S.R. 213(E).— Whereas a draft of certain rules further to amend the Drugs and Cosmetics Rules, 1945 was published as required by section 6, section 12 and section 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940) vide notification of the Government of India in the Ministry of Health and Family Welfare (Department of Health and Family Welfare) number G.S.R. 654(E), dated the 17th July, 2018 in the Gazette of India, Extraordinary, Part II, section 3, subsection (i), inviting objections and suggestions from persons likely to be affected thereby, before the expiry of a period of fifteen days from the date on which the copies of the Official Gazette containing the said notification were made available to the public;

And whereas, copies of the said Official Gazette were made available to the public on the 19th July, 2018;

And whereas, no objections or suggestions were received from the public on the said rules for consideration by the Central Government;

Now, therefore, in exercise of the powers conferred by section 6, section 12 and section 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940), the Central Government, after consultation with the Drugs Technical Advisory Board, hereby makes the following rules further to amend the Drugs and Cosmetics Rules, 1945, namely:

1. (1) These rules may be called the Drugs and Cosmetics (Seventh Amendment) Rules, 2019.

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

2. In the Drugs and Cosmetics Rules, 1945, in rule 3A, after sub-rule (8), the following sub-rule shall be inserted, namely:-

   "(9) The functions of the laboratory in respect of testing of the following veterinary vaccines shall be carried out at the Chaudhary Charan Singh National Institute of Animal Health, Baghpat, Uttar Pradesh and the functions of the Director in respect of the said veterinary vaccines shall be exercised by the Director of the said Institute, namely:-

   (i) Haemorrhagic Septicaemia vaccine;
   (ii) Ranikhet Disease vaccine.".

[F.No. X.11035/285/2018-DRS]
DR. MANDEEP K. BHANDARI, Jt. Secy.

Note: The principal rules were published in the Official Gazette vide notification number F.28-10/45-H (1), dated the 21st December, 1945 and last amended vide notification number G.S.R 205(E), dated the 8th March, 2019.

MINISTRY OF HEALTH AND FAMILY WELFARE

(Department of Health and Family Welfare)

NOTIFICATION

New Delhi, the 18th March, 2019

G.S.R. 223(E).—Whereas a draft of certain rules further to amend the Drugs and Cosmetics Rules, 1945 was published as required under sub-section(1) of section 12 and sub-section(1) of section 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940) vide notification of the Government of India in the Ministry of Health and Family Welfare (Department of Health and Family Welfare) number G.S.R. 720(E), dated the 30th July, 2018 in the Gazette of India, Extraordinary, Part II, section 3, sub-section (i), inviting objections and suggestions from persons likely to be affected thereby, before the expiry of a period of forty-five days from the date on which the copies of the Official Gazette containing the said notification were made available to the public;

And whereas copies of the Gazette were made available to the public on the 4th August, 2018;

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

Now, therefore, in exercise of the powers conferred under section 12 and section 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940), the Central Government, after consultation with the Drugs Technical Advisory Board, hereby makes the following rules further to amend the Drugs and Cosmetics Rules, 1945, namely:-

1. (1) These rules may be called the Drugs and Cosmetics (Eighth Amendment) Rules, 2019.

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

2. In the Drugs and Cosmetics Rules, 1945 (hereinafter to be referred as said rules), in PART XV(A), in the heading, after the words, "MANUFACTURE FOR SALE OF DRUGS / COSMETICS", the words, "OR AN INDIVIDUAL OR ORGANISATION OR PROCUREMENT AGENCY" shall be inserted.

3. In the said rules, in rule 150B, in sub-rule (1) for the words "for sale of drugs or cosmetics, shall be made in Form 36" the words "for sale of drugs and cosmetics or an individual or organisation or procurement agency shall be made in Form 36" shall be substituted.

4. In the said rules, in rule 150C,-
   (i) In heading, after the words, "for manufacture of drugs/cosmetics", the words "or for an individual or organisation or procurement agency" shall be inserted.

   (ii) In sub-rule (1), after the words, "for manufacture of drugs or cosmetics", the words "or an individual or organisation or procurement agency" shall be inserted.

5. In the said rules, in rule 150E, for clause (f) the following clause shall be substituted, namely:-

"(f) The approved institution shall furnish reports of the results of test or analysis on the samples received from manufacturer in Form 39 and from an individual or organisation or procurement agency in Form 39A."

6. In the said rules, in Schedule A,-

(i) In Form 36 and Form 37, in the heading, after the words, "MANUFACTURE FOR SALE OF DRUGS/ COSMETICS", the words, "OR FOR AN INDIVIDUAL OR ORGANISATION OR PROCUREMENT AGENCY" shall be inserted.

(ii) In Form 36, in paragraph (1), after the words, "manufacture for sale of drugs/ cosmetics", the words, "or for an individual or organisation or procurement agency" shall be inserted.

(iii) after the Form 39, the following Form shall be inserted, namely:-

"Form 39A
[See sub-rule (f) of rule 150E]

Report of test or analysis by approved institution for an Individual or Organisation or Procurement agency

(1) Name of individual or organisation or procurement agency from whom sample is received…….
(2) Serial number and date of sender's memorandum……..
(3) Number of samples……..
(4) Date of receipt of the sample……
(5) Name of drug or cosmetics or raw material purporting to be contained in the sample…..
(6) Details of raw material or final product in bulk or final product in finished pack* as obtained by sender:
   (a) Name and address of the Manufacturer and Licence number mentioned on the label …….
   (b) Name of original Manufacturer in the case of raw materials and re-packed drugs ……
   (c) Batch number ……
   (d) Date of manufacture, if any …….
   (e) Date of expiry, if any …….

(7) Results of test or analysis with protocols of test or analysis applied.

In the opinion of the undersigned, the sample referred to above is *of standard quality/is not of standard quality as defined in the Act and the rules made thereunder for the reasons given below.

Date..... Signature of Person-in-charge of testing

Note:- Final product includes repacked material.
*Delete whichever is not applicable."

[F. No. X.11014/14/2018-DR]
Dr. MANDEEP K. BHANDARI, Jt. Secy.

Note: The Drugs and Cosmetics Rules, 1945 was published in the Official Gazette vide notification number F.28-10/45-H (1), dated the 21st December, 1945 and last amended vide notification number G.S.R. 213(E), dated the 11th march, 2019.

MINISTRY OF HEALTH AND FAMILY WELFARE

(Department of Health and Family Welfare)

NOTIFICATION

New Delhi, the 18th March, 2019

G.S.R. 224(E).—Whereas a draft of certain rules further to amend the Medical Devices Rules, 2017 was published as required under sub-section (1) of section 12 and sub-section (1) of section 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940) vide notification of the Government of India in the Ministry of Health and Family Welfare (Department of Health and Family Welfare) number G.S.R 660(E) dated the 19th July, 2018, in the Gazette of India, Extraordinary, Part II, Section 3, Sub-section (i) by the Central Government, inviting objections and suggestions from all persons likely to be affected thereby, before the expiry of a period of thirty days from the date on which copies of the said Official Gazette containing the said notification were made available to the public;

And whereas, copies of the Official Gazette containing the said notification were made available to the public on the 21st July, 2018;

And whereas, no objections or suggestions were received from the public on the said rules for consideration by the Central Government;

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

1. (1) These rules may be called the Medical Devices (Second Amendment) Rules, 2019.

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

2. In the Medical Devices Rules, 2017, in the Fifth Schedule, in Annexure 'A', in the Table,-
(a) for the entries relating to the medical device "Condom" and entries relating thereto in column (1), (2) and (3) thereof, the following entries shall be substituted, namely:-

"Condoms	Compounding	Well ventilated area with neat and clean environment, free from dust and other particulate matter
	Moulding	Well ventilated area with neat and clean environment, free from dust and other particulate matter
	Vulcanising	Normal Air
	Primary Packing	Air Conditioned" ;

(b) for the entries relating to the medical device "Surgical dressings" and entries relating thereto in column (1), (2) and (3) thereof, the following entries shall be substituted, namely:-

"Sterile surgical dressings	Final Primary Packing	9".

[F.No. X.11014/17/2018-DR]
Dr. MANDEEP K. BHANDARI, Jt. Secy.

Note: The principal rules were published in the Official Gazette vide notification number 78(E), dated 31st January, 2017 and last amended vide notification number G.S.R. 30(E), dated the 15th January, 2019.

MINISTRY OF HEALTH AND FAMILY WELFARE

(Department of Health and Family Welfare)

NOTIFICATION

New Delhi, the 20th March, 2019

G.S.R.231(E).—Whereas a draft of certain rules further to amend the Drugs and Cosmetics Rules, 1945 was published as required under sub-section(1) of section 12 and sub-section(1) of section 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940) vide notification of the Government of India in the Ministry of Health and Family Welfare (Department of Health and Family Welfare) number G.S.R. 1185(E), dated the 7th December, 2018, in the Gazette of India, Extraordinary, Part II, section 3, sub-section (i), inviting objections and suggestions from persons likely to be affected thereby, before the expiry of a period of seven days from the date on which the copies of the Official Gazette containing the said notification were made available to the public;

And whereas, copies of the said Official Gazette were made available to the public on the 7th December, 2018;

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

Now, therefore, in exercise of the powers conferred by sections 12 and 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940), the Central Government, after consultation with the Drugs Technical Advisory Board, hereby makes the following rules further to amend the Drugs and Cosmetics Rules, 1945, namely:

1. (1) These rules may be called the Drugs and Cosmetics (Ninth Amendment) Rules, 2019.

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

2. In the Drugs and Cosmetics Rules, 1945, after rule 97 the following rule shall be inserted, namely:

"97A. Modified application of rules 96 and 97 for certain period.- Notwithstanding anything contained in these rules, the modified or additional requirements of labelling as may be specified in the notification of the Government of India in the Ministry of Health and Family Welfare number G.S.R. 408(E), dated the 26th April, 2018, shall be on voluntary basis for a period commencing on the date of coming into force on this rule and ending on the 31st day of March, 2019, and thereafter shall be mandatory.".

[F.No. X.11014/06/2016 - DFQC]
Dr. MANDEEP K. BHANDARI, Jt. Secy.

Note : The Drugs and Cosmetics Rules, 1945 was published in the Official Gazette vide notification number F. 28-10/45-H (1), dated the 21st December, 1945 and last amended vide notification number G.S.R. 223(E), dated the 18th March, 2019.

MINISTRY OF HEALTH AND FAMILY WELFARE

(Department of Health and Family Welfare)

NOTIFICATION

New Delhi, the 5th February, 2019

S.O. 697(E).— In exercise of the powers conferred by section 26A of the Drugs and Cosmetics Act, 1940 (23 of 1940), the Central Government hereby rescinds the notification of the Government of India in the Ministry of Health and Family Welfare (Department of Health and Family Welfare), published in the Gazette of India, Extraordinary, Part II, Section 3, Sub-section (ii), vide number S.O. 4616 (E), dated the 7th September, 2018 with immediate effect.

[F.No. X.11035/53/2014-DFQC (Pt. II)]
Dr. MANDEEP K. BHANDARI, Jt. Secy.

MINISTRY OF HEALTH AND FAMILY WELFARE

(Department of Health and Family Welfare)

NOTIFICATION

New Delhi, the 8th February, 2019

S.O. 775(E).—In pursuance of sub-clause (iv) of clause (b) of section 3 of the Drugs and Cosmetics Act, 1940 (23 of 1940), the Central Government, after consultation with the Drugs Technical Advisory Board, hereby specifies the following devices intended for use in human beings as drugs with effect from the 1st day of April, 2020, namely:—

(i) All implantable medical devices;

(ii) CT scan Equipment;

(iii) MRI Equipment;

(iv) Defibrillators;

(v) Dialysis Machine;

(vi) PET Equipment;

(vii) X-Ray Machine; and

(viii) Bone marrow cell separator.

[F. No. X. 11014/12/2018-DR]
Dr. MANDEEP K. BHANDARI, Jt. Secy.

NEWS

Indian-Made Diagnostic Test for TB Being Validated

WHO chief scientist calls for higher investment on TB control

The World Health Organisation (WHO) is working with the Indian Council of Medical Research (ICMR) on validating an Indian-made diagnostic test for tuberculosis.

If this is validated, India would have developed a TB diagnostic test for the world, Soumya Swaminathan, chief scientist, WHO, said on Friday.

"We have the Indian-made diagnostic test — TruNat — that is in the process of getting validated. It will be the first point of care molecular TB diagnostic test that can be taken into a primary health centre and used because it is battery-operated. It is much more user-friendly than GeneXpert," she said, while taking part in a felicitation programme at the National Institute for Research in Tuberculosis (NIRT) on World TB Day.

She said the first United Nations high-level meeting on TB was held in September last year. "Since then, the call from the UN meeting was to ask all countries, especially TB high-burden countries, to invest more in TB control. Currently, we have a gap of about two-thirds of what is needed annually for TB, including research and development. It is estimated that you need $2 billion per year to generate new tools, diagnostics, drugs, vaccines, and we are only spending less than a third of that," she said.

TB burden

Dr. Swaminathan said India and some BRICS countries accounted for at least 70% of the TB burden. "India, Russia and China together have 50% of the world Multi Drug-Resistant TB burden. India has 27% of the world's TB cases," she added.

Pointing to the Lancet Commission on TB, Dr. Swaminathan, who was one of the co-chairs, said, "India has set a target of 2025 for elimination of TB.

The modelling shows it will at least be 2045 by the time we can make any difference. We need to add on new things and studies to reduce TB incidence and burden at the community-level."

"We seem to be moving faster on MDR and XDR (Extensively Drug-Resistant) TB than on drug-sensitive TB. We need to look at other innovative approaches," she said.

NIRT remembered "heroes" who made ICMR-NIRT what it is today on the occasion. They offered tributes to D. A. Mitchison, founder of bacteriology laboratory. Former director general of ICMR S.P. Tripathy was felicitated. Srikanth Tripathy, director in-charge of NIRT and Lt. Gen. D. Raghunath, principal executive (retd.), were present.

Source: *The Hindu,* 23rd March 2019

Centre Notifies New Rules for Drugs, Clinical Trials

The Union Health Ministry has notified the Drugs and Clinical Trials Rules, 2019 with the government stating that the move is aimed at promoting clinical research in the country. The rules will apply to all new drugs, investigational new drugs for human use, clinical trials, bio-equivalence studies and ethics committees.

The highlights of the notification includes reduction in time for approving applications, which has now come down to 30 days for drugs manufactured in India and 90 days for those developed outside the country. "Also, in case of no communication from Drugs Controller General of India, the application will be deemed to have been approved," the notification said.

As per the new rule the requirement of a local clinical trial may be waived for approval of a new drug if it is approved and marketed in any of the countries (EU, UK, Australia, Japan and US) specified by the Drugs Controller General with the approval of the government.

"The new rules will ensure patient safety and an ethics committee will monitor the trials and decide on the amount of compensation in cases of adverse events," the ministry said.

Meanwhile, the Indian Society for Clinical Research (ISCR) said that the new Clinical Trial Rules are well balanced and will further the conduct of ethical and quality clinical trials in the country which, in turn, will benefit patients.

In a release issued on Tuesday, ISCR president Dr. Chirag Trivedi said: "The new rules protect the rights, safety and well-being of patients while ensuring a strong scientific base for the conduct of clinical trials."

"We hope this will lead to more stability and growth in clinical research being done in India, which will ultimately ensure that our patients have access to faster and more effective treatment. India has the second largest population in the world and the highest disease burden but does less than 1.2% of global clinical trials," he said.

Source: *The Hindu,* 26th March 2019

Prices of Essential Medicines, Stents to Go Up by Over 4%

Prices of essential medicines, including painkillers, antiinfectives, supplements and antibiotics, will go up by over 4%, after the government gave its nod to the increase, in line with the annual Wholesale Price Index (WPI). Hike in prices of cardiac stents have also been allowed on the basis of WPI at 4.26% for calendar year 2018. The revision in prices of both stents and medicines will come into effect from 1st April.

While prices of 871-odd medicines that are part of the National List of Essential Medicines are expected to go up by over 4%, ceiling prices of drug-eluting stents (DES)

have been revised upwards of Rs 30,080, and bare metal stent at Rs 8,261 (exclusive of GST).

Prices of essential medicines are revised according to change in annual WPI, according to the Drug Price Control Order (2013). Earlier, the price for DES (metallic and biodegradable) was Rs 28,849, and bare metal stood at Rs 7,923.

Those manufacturers who sell branded/generic, or both versions of scheduled formulations at a price higher than ceiling price (plus goods and services taxes as applicable), shall revise the prices downward, not exceeding the ceiling price specified (plus goods and services taxes as applicable), the notification says. On the other hand, those companies with scheduled formulations with MRP lower than the ceiling price, can revise it upwards in line with WPI.

Source: *The Times of India,* 2nd April 2019

Dr Reddy's subsidiary sells, assigns US rights for 3 brands to Encore Dermatology

Dr Reddy's Laboratories through its wholly owned subsidiary Promius PharmaTuesday announced sale and assignment of the US rights for its marketed dermatology brands to Encore Dermatology. Promius Pharma, LLC, announced the sale of its rights for SERNIVO spray, 0.05 per cent and assignment of its rights to market and distribute, PROMISES topical cream and TRIANEX 0.05 per cent (Triamcinolone Acetonide ointment, USP) in the United States, to Encore Dermatology.

"Under the terms of the agreement, Promius Pharma is eligible to receive an upfront payment and future milestone payments contingent upon achievement of certain commercial objectives," Dr Reddy's Laboratories said in a regulatory filing.

The company, however, did not disclose how much payment its subsidiary Promius Pharma will receive.

Dr Reddy's co-chairman and CEO G V Prasad said the announcement is in line with its renewed strategy to enable us achieve self-sustainability and profitable growth for each of its businesses.

"We are confident in Encore's ability to realise the full potential of the enlisted products. We look forward to working with Encore to ensure a smooth transition of these brands and to ensure they are able to quickly deliver these products to providers and patients." says Anil Namboodiripad, Ph.D., Senior Vice President, Proprietary Products, and President, Promius Pharma, said. Source:

Source: *ET Healthworld,* 2nd April 2019

Launch of Intas Cancer Drug Could Lower Prices

Ahmedabad-based Intas Pharmaceuticals is launching a life-saving breast cancer drug, trastuzumab biosimilar, at Rs 19,995 (per 440 mg vial) — priced 65% lower than the existing MRP of major brands. The development, say experts, could unleash a price war of sorts in the market. With the Intas launch, the cost of treatment may reduce substantially for a breast cancer patient to Rs 4 lakh from over Rs 10 lakh.

At present, the MRP of most trastuzumab brands in India is in the Rs 58,000-Rs 63,000 range, though industry experts say the price paid by patients could be lower due to discounts offered by companies. The price cap on the drug was revised by the government in March to Rs 58,000 (per 440 mg vial). It was first put under a ceiling price of Rs 56,000 in 2016, but health activists had pointed out the ceiling price was steep, and hence unaffordable for patients.

The MRP of Intas brand, Eleftha is Rs 19,995 for 440 mg, and Rs 6,295 mg for a 150 mg injection. In patients with HER2 (human epidermal growth factor receptor 2) positive early breast cancer, almost 18 cycles of trastuzumab-based therapy are required, a company official said, adding about 60% patients cannot afford the treatment.

Breast cancer affects about two lakh women in India, of which one-fourth are HER2-positive. Trastuzumab is a targeted therapy, which has revolutionised the management of HER2-positive breast cancer, he added. Over a dozen companies in India market the drug, led by Biocon, with others including Zydus Cadila, Reliance Life Sciences, and the innovator company, Roche.

Industry experts say Intas introduces products at a lower price to grab market share, often disrupting the space. “We had used a similar strategy a few years back for cancer drug Bevacizumab, a biosimilar of Avastin,” Intas senior VP marketing (oncology) Manoj Kumar told TOI.

The move led to many companies slashing prices of their brands, which could also happen in this case. “This could lead to other players also reducing prices to sustain and grow market shares, ” Reliance Life Sciences president & CEO K V Subramaniam told TOI. Others may introduce schemes where patients get two doses free with one vial.

However, Biocon chairperson & MD Kiran Mazumdar-Shaw says the company “has global impact, and will not be impacted by Intas pricing in India”. “Moreover, if biosimilars are developed just for Indian market, the cost of development is much lower than if it is for the US and Europe.”

Biocon and Mylan's co-developed biosimilar of Roche's blockbuster cancer drug Herceptin, trastuzumab, was approved in the US in 2017.

Though trastuzumab, the innovator drug, has been available in India since 2000, but before the entry of trastuzumab biosimilars, almost 80% of patients could not afford it.

Source: *ET Healthworld,* 10th April 2019

medopharm

With best compliments from:

medopharm

We Value... Life

Corporate Office : "MEDO HOUSE" No. 25, Puliyur 2nd Main Road, Trustpuram, Kodambakkam, Chennai - 600 024, India
Phone: +91 44 40149999 Visit: www.medopharm.com

Factory : 50, Kayarambedu Village, Guduvanchery - 603 202, INDIA.

SRI RAMACHANDRA
INSTITUTE OF HIGHER EDUCATION AND RESEARCH
(Deemed to be University)
Porur, Chennai – 600 116

SRI RAMACHANDRA COLLEGE OF PHARMACY

COURSES OFFERED

B. Pharmacy
4 years
(8 semesters)
Approved by
AICTE & PCI,
New Delhi

Intake:
100/year

Eligibility:
HSC/CBSE/ISE

For Diploma holders in Pharmacy (Lateral entry to B.Pharmacy II year)

M. Pharmacy
2 years (4 semesters)
Approved by AICTE & PCI, New Delhi

Eligibility:
B. Pharm

Specializations (Intake)

Pharmaceutics (15)

Pharmacy Practice (12)

Pharmaceutical Quality Assurance (15)

Pharmacognosy (15)

Pharmaceutical Analysis(15)

Pharmacology (15)

Pharm. D.
6 years
Approved by
PCI, New Delhi

Intake:
30/year

Eligibility:
HSC/CBSE/ISE

Pharm. D.
(Post Baccalaureate
3 years Approved
by PCI, New Delhi

Intake:
10/year

Eligibility
B.Pharmacy

HIGHLIGHTS

- ✓ International Students Exchange for Pharm. D. Internship
- ✓ GPAT Training – B. Pharmacy students
- ✓ Hands on Clinical Research Training
- ✓ Chancellor's Summer Research Fellowship for Undergraduates
- ✓ Campus placement assured
- ✓ Active alumni network
- ✓ Industry - Institute Participation Cell for Industry/ Academia Consultancy
- ✓ Skill development Programs
- ✓ Longitudinal Mentorship

ACCREDITATIONS

ISSSDC Life Sciences Sector Skill Development Council

NBA NATIONAL BOARD OF ACCREDITATION

NAAC

nirf NATIONAL INSTITUTIONAL RANKING FRAMEWORK

AICTE CII Confederation of Indian Industry AICTE-CII AWARD PLATINUM





FOR CONTACT:
Tel : 044 - 45928533
principal.pharmacy@sriramachandra.edu.in
Website : www.sriramachandra.edu.in