SRI RAMACHANDRA
INSTITUTE OF HIGHER EDUCATION AND RESEARCH
(Category - I Deemed to be University) Porur, Chennai

SRMC PHARMVIGIL

A Passion for Better Medicine

Pharmacovigilance News Letter

Department of Pharmacology

SRMC & RI
Volume: 1

Jan-2022
Issue: 1

News Letter Insights

Page No:

Message from Vice Chancellor

Prof. P.V. Vijayaraghavan

Dear Faculties and Students,

"Knowledge is power. Information is liberating.

Education is the premise of progress, in every society, in every family" ***Kofi Annan***

In this digital era, the information available is limitless. There is abundant information and it is easily accessible also. But too much information may distract us from the truth. It is also important to identify the correct information.

The field of drug discovery and development brings a lot of new information to our scientific literature, and it can have a huge impact on patient care as well as therapeutic decision-making.

I am really excited and enthralled to know that the Department of Pharmacology has taken initiatives to bring out a newsletter named **"SRMC PHARMVIGIL"**. This newsletter will provide hand-picked information on medication use and patient safety, to widen our knowledge.

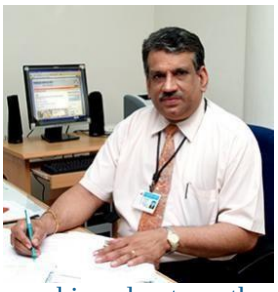
I wish the department all success in bringing regular updated information in this field which will hugely benefit the students and faculties of our esteemed institution.

All the very best…!

Message from Dean -Medical College

Prof. S. Anandan

Greetings to all



The rational use of medicines for therapeutic, diagnostic or preventive purposes in Healthcare is pivotal as their benefits are always accompanied by variable degree of risks.

The SRMC Pharmacovigilance centre had been recognized by pharmacovigilance programme of India and designated as Adverse Drug Reaction Monitoring Centre under PVPI in January 2014. The centre has made tremendous growth through its worthy contributions towards nationwide drug safety by reporting Adverse Drug Reactions directly to NCC-PVPI. Recently during October 2021, SRMC – AMC has achieved yet another prestigious milestone by gaining recognition as medical device adverse event monitoring centre under Materiovigilance Programe of India (MvPI).

I am happy to learn that in addition to the above the department of pharmacology has taken up yet another novel task of providing noteworthy information regarding drugs and their safety by means of a newsletter. I wish to congratulate the department of pharmacology for this initiative and I am certain that the Healthcare professionals of SRMC will be benefited immensely by this **SRMC Pharmvigil** newsletter.

Message from Professor & Head - Department of Pharmacology

Dr. K. Punnagai

I am happy and proud to publish the first newsletter ***"SRMC Pharmvigil"*** from the department of Pharmacology, SRMC & RI. It has been a dream come true for us as a team to create an e-newsletter and to create awareness about the importance of adverse drug reaction reporting by healthcare professionals and to disseminate the information about the various activities of the Pharmacovigilance and materiovigilance programmes of India and about the activities of Sri Ramachandra Adverse drug monitoring centre (SRMC-AMC).

The successful publishing of the first edition of ***"SRMC Pharmvigil"*** is possible in these pandemic times with the encouragement given by our beloved Vice Chancellor Dr. P.V. VIJAYARAGHAVAN, Dean – Medical College Dr. S. ANANDAN of Sri Ramachandra Institute of Higher Education and Research. I congratulate the Chief Editor of the first edition of the newsletter Dr.R. Kavitha, and Co-editors Dr. S. Ramya and Dr.K. Kranthi and the whole team of editorial board members of the ***"SRMC Pharmvigil"*** Newsletter for this wonderful package of information. I also wish to thank the SRIHER communication team for designing the e-newsletter.

The primary aim of ***"SRMC Pharmvigil"*** is to create awareness about the adverse drug reactions (ADRs) monitoring among the healthcare professionals and inculcate the culture of prompt reporting of ADRs. For this we need the constant and continuous support of health care professionals for capturing the dangerous adverse effects of the new drugs, vaccines and devices as well as the rare adverse effects of established old drugs from our hospital practice. This has also been the major goal of Pharmacovigilance programme of India and World Health Organization. In addition to this there are many other interesting plethora of new information related to drugs, diseases, COVID-19 vaccines and pharmacotherapy which are included in the various sections of the ***"SRMC Pharmvigil"*** e-newsletter. I request the readers to feel free to give your suggestions and thoughts on medication safety and to improve the content and design of the newsletter.

Message from Editor in chief

Dr. R. Kavitha

Dear Colleagues,

Greetings

It is my great pleasure to release First Edition of the **SRMC PHARMVIGIL**, Pharmacovigilance (PV) newsletter from the department of Pharmacology, SRMC & RI. It has been launched with an objective of providing updates regarding our institute's ADR reporting statistics, new drug regulations and emerging pharmacovigilance issues to healthcare professionals.

Medicines are relied upon to treat disease and improve health. While medicines provide enormous health benefits, no medicine is without risk. Adverse drug reactions (ADRs) are the very widespread problem of all drugs/medicinal products. Hence, to minimize ADR, PV came in a focus for appropriate and effective monitoring of ADR which can safeguard the public health.

Pharmacovigilance (PV) is concerned with the detection, identification and assessment of adverse reaction to drugs/medicinal products. The scope of pharmacovigilance is to improve the patient care and safety in relation to use of medicines and all medical and paramedical interventions. It is an important and integral part of clinical research and medical practice.

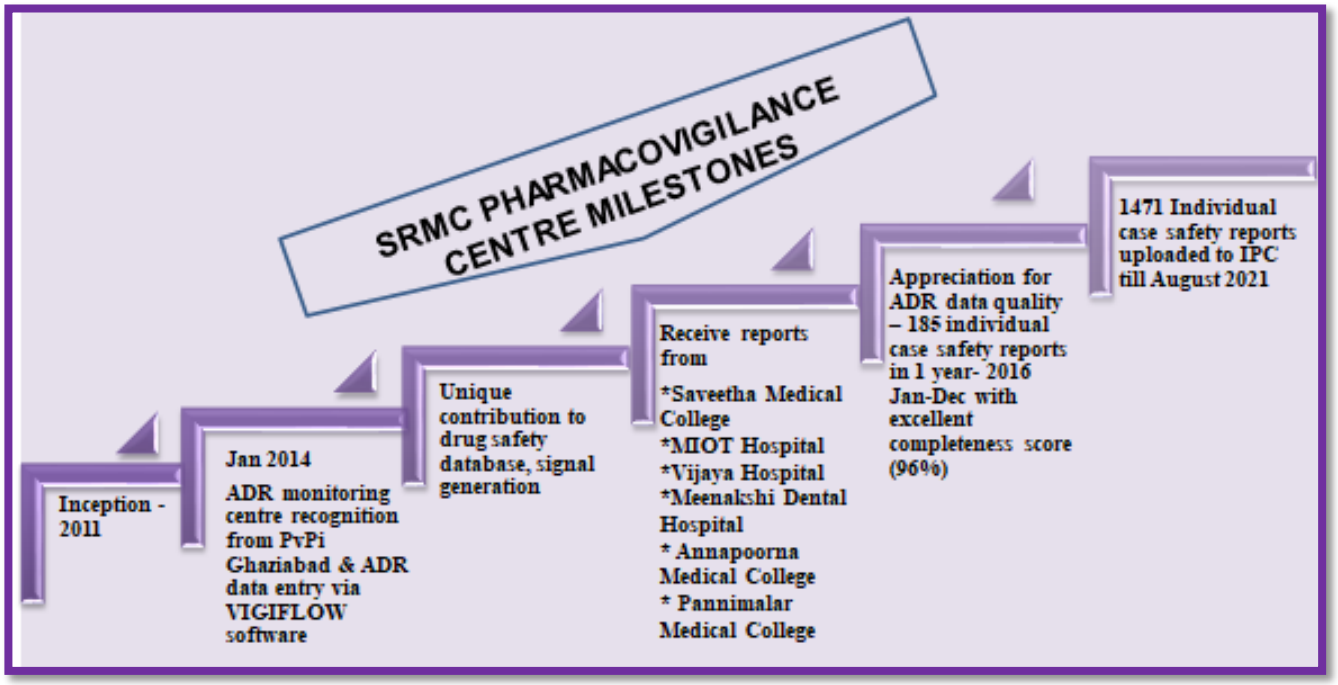
Pharmacovigilance is a dynamic clinical and scientific discipline. It provides reliable, balanced information for the effective assessment of the risk/benefit profile of medicines. However, under-reporting remains the corner stone that hinders pharmacovigilance activities.

Through the **SRMC PHARMVIGIL**, the healthcare professionals can access information on safety of medicinal products and gain responsibility of spontaneous ADR reporting. We ensure that our PV newsletter remains a relevant and trusted source of information on drug safety and one that meets the needs of healthcare professionals in patient care.

I thank Vice Chancellor, Dean of Medical College and our Head of the Department for giving me this opportunity.

Over view of SRMC-AMC and its activities

SRMC-AMC was established in 2014 by NCC-PVPI, Indian Pharmacopoeia Commission. ADRs are received from various hospitals at SRMC, i.e., is UDAYAR Block-1000 and G-Block 1500 bedded tertiary care teaching hospital providing both in-patient and out-patient services with Medicine, Surgery, OBG, Paediatrics, Oncology, Urology, Orthopaedics, Psychiatry, Skin and VDL, ENT, Ophthalmology, Rheumatology catering to provide healthcare treatment for over 75,000 inpatients and 3,50,000 outpatients every year. ADRs are also received from peripheral hospitals located in and around Chennai which includes Saveetha Medical College and Hospital, MIOT International Hospital, Panimalar Medical College and Hospital, Annapoorna Medical College and Hospital, Vijaya Hospital and Meenakshi Dental Hospital.



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, ipclab@vsnl.net, Web: www.ipc.gov.in

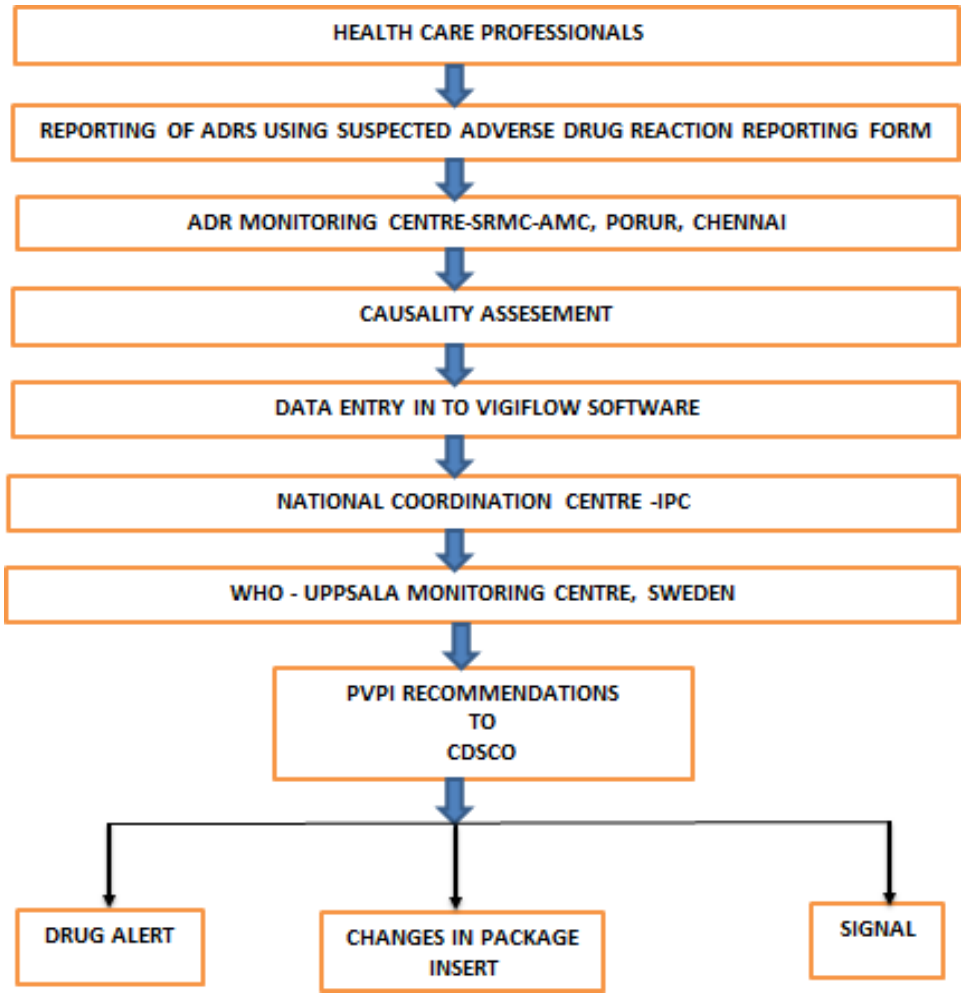
File No:- IPC/NCC-PvPI/QA-Appreciation Letter-10/636 Date: - 8th May 2017

To,
Dr. Darling Chellathai David
Sri Ramachandra Medical College and Research Institute, Porur,
Chennai-600116,
Tamil Nadu

Subject: - Appreciation Letter for submission of ICSRs to National Coordination Centre- Pharmacovigilance Programme of India

2017

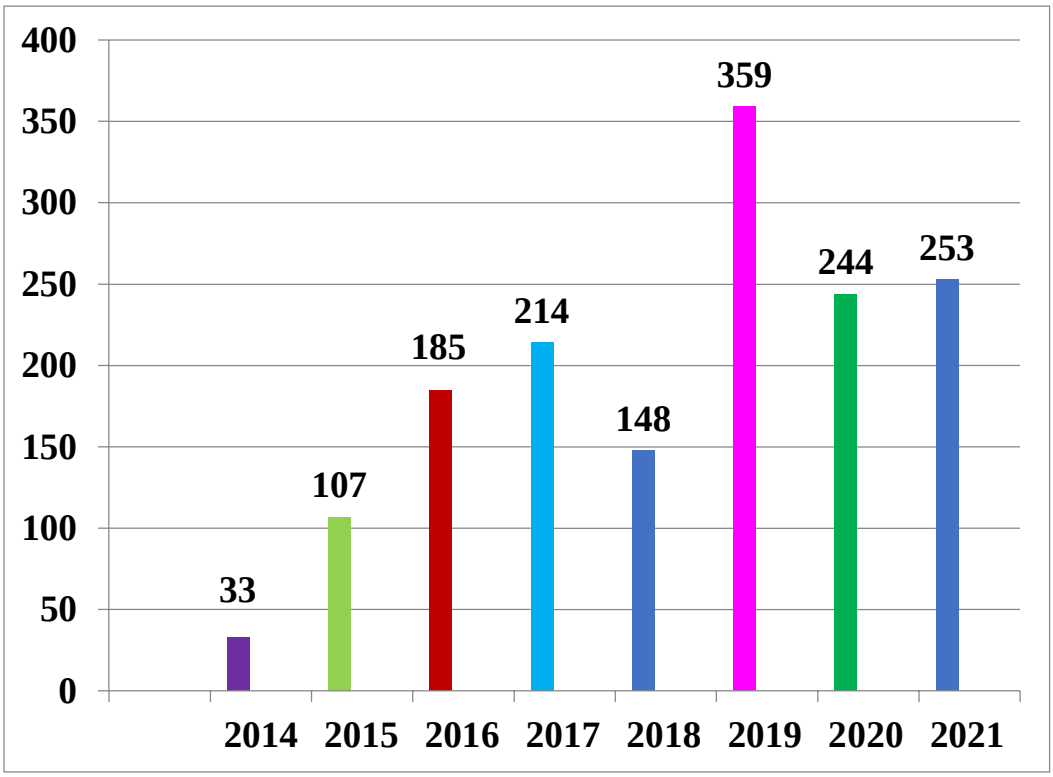
PROCESS OF ADVERSE DRUG REACTIONS (ADR) REPORTING – SRMC&RI



ADR reporting statistics at SRMC AMC

Adverse drug reaction monitoring is a process of continuous monitoring of undesirable effects suspected to be associated with the use of medicinal products.

From 2014 to 2021(August) the SRMC-AMC received altogether 1,471 ADR reports from hospitals like G-Block, Sri Ramachandra Medical Centre and from peripheral hospitals located in & around Chennai like Vijaya Hospital, Saveetha Hospital, MIOT Hospital, Panimalar Hospital, Annapoorna Hospital and Meenakshi Hospital.



Story of Covaxin – India's first indigenous vaccine against Covid-19

Dr.Kruthi
IInd yr MD PG

COVAXIN is an inactivated virus based COVID-19 vaccine developed by **BHARAT BIOTECH** in collaboration with the ICMR.

The team of scientists behind this herculean project included:

Dr. Krishna Ella, Chairman and Managing Director of Bharath Biotech, a research scientist in molecular biology, the vaccine and bio-therapeutics manufacturer that is behind India's first indigenously made Covid-19 vaccine along with an additional contribution from his wife Dr. Suchitra Ella, cofounder and director - BHARAT BIOTECH

Dr. Sumathy. K, head of Research and Development wing at Bharath Biotech, was also the mastermind behind developing vaccines for Chikungunya and Zika for the company.

Dr. Raches Ella, Project Lead for SARS-CoV-2 vaccine and head of Business Development at Bharat Biotech, has also earlier been the lead scientist in data analysis and manuscript preparation of Typhoid conjugate, Rotavirus vaccines.

Covaxin is an inactivated vaccine developed and manufactured in the company's BSL-3 (Bio-Safety Level 3) bio-containment facility. The common adverse events associated with covaxin are headache, fatigue, fever and nausea and vomiting.

This product was developed in collaboration with the Indian Council of Medical Research (ICMR) and National Institute of Virology (NIV). The vaccine was subjected to rigorous clinical trials at various medical centres across India and got a final approval by DCGI for emergency use in Jan 2021.

The approval of Covaxin for emergency use is a giant leap for innovation and novel product development in India. It is a proud moment for the nation and a great milestone in India's scientific capability, a kick-start to the innovation ecosystem in India.

Reference:

Kaur RJ, Dutta S, Bhardwaj P, et al. Adverse Events Reported From COVID-19 Vaccine Trials: A Systematic Review. Indian J Clin Biochem. 2021;36(4):1-13.

In a validation of the role Covaxin has played in battling the Covid-19 pandemic, Bharat Biotech's founding duo Dr Krishna Ella and his wife Suchitra Ella were conferred the Padma Bhushan on 25-Jan-2022

WHO APPROVED COVAXIN FOR EMERGENCY USE – NOV 2021

DCGI APPROVED COVAXIN FOR EMERGENCY USE IN CHILDREN – 12-18 YEARS DEC 2021

History of PVPI & its role in patient safety

Dr. K. Kranthi
Assistant Professor

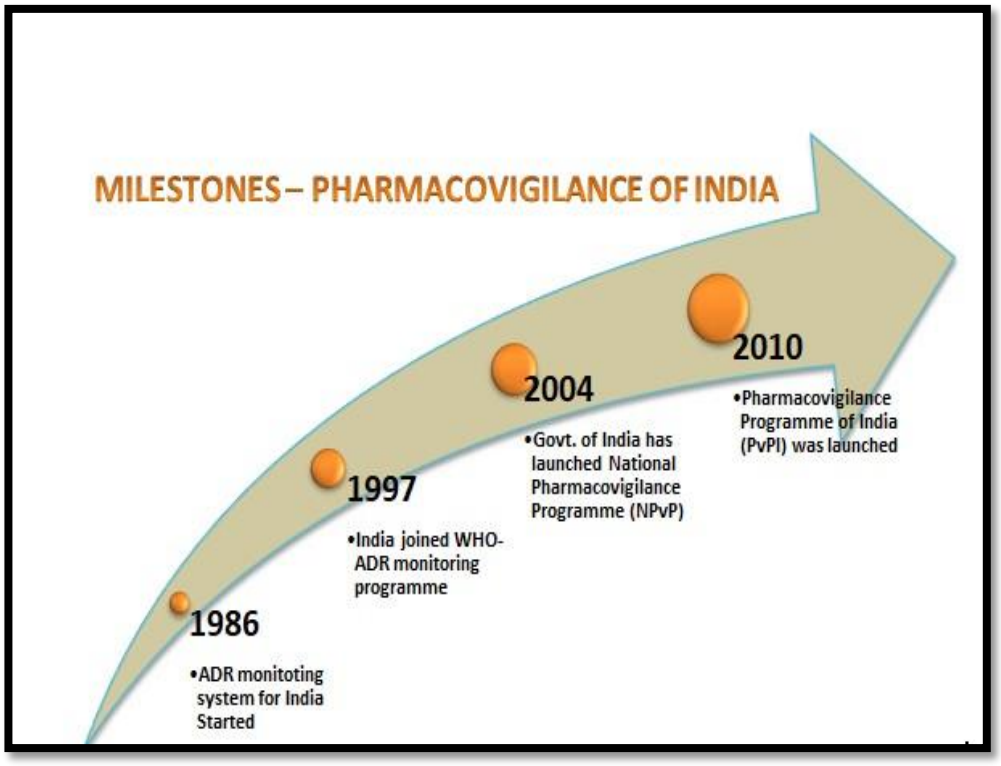
The etymological roots for the word "pharmacovigilance" are: pharmakon (Greek for drug) and vigilare (Latin for to keep watch). Pharmacovigilance (PV) has been defined by the WHO (2002) as the ' science and activities relating to the detection, assessment, understanding and prevention of adverse effect or any other drug related problems.'

History of Pharmacovigilance dates back to 1902. The Biologics Control Act of 1902 (Virus-Toxin Law), was the first law that implemented federal regulations of biological products such as vaccines in the United States in response to the deaths of 22 children who had contracted tetanus from contaminated vaccines. This law paved the way for further regulation of drug products under the Pure Food and Drug Act of 1906 and the Federal Food, Drug, and Cosmetic Act of 1938. Later the Council for International Organizations of Medical Sciences (CIOMS) an international, non-governmental, non-profit organization established jointly by WHO and UNESCO in 1949 came with a mission to advance public health through guidance on health research including ethics, medical product development and safety. A significant shift happened in 1961, following the tragedy of Thalidomide when 10,000 children in 46 countries were born with birth defects.

In India, a formal ADR monitoring system was started in 1986 with 12 regional centers. In 1997, India became the member of WHO Programme for International Drug Monitoring managed by the Uppsala Monitoring Centre (UMC), Sweden. In November 2004, Govt. of India launched National Pharmacovigilance Programme (NPvP)

Pharmacovigilance Programme of India (PvPI) was launched in India by the Union health ministry in July 2010 to capture adverse drug reactions of drugs already in the market in a systematic manner. Initially AIIMS, New Delhi was the National Coordination Centre (NCC) and on 15th April, 2011, it was shifted to Indian Pharmacopoeia Commission (IPC), Ghaziabad, UP. Dr. G. N. Singh, Scientific Director of IPC was designated as a National Coordinator of PvPI.

Under PvPI, ADRs are being identified and spontaneously reported by the healthcare professional of Adverse Drug Reaction Monitoring Centres (AMC). These AMCs are set up across the country in medical colleges approved by Medical Council of India (MCI). These AMCs are responsible for collecting adverse event as per Standard Operating Procedure (SOP), performing follow up if required for the completeness of ADR reports and uploading these reports in Vigiflow, a net-based software used for ADR reporting.



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2. Thatte, Urmila M.; Chaudhari, Nayan L.; Gogtay, Nithya J. (October 2018). "Pharmacovigilance Program of India: history, evolution and current status". Adverse Drug Reaction Bulletin. 312 (1): 1207–1210.

"Spontaneous adverse drug reporting - backbone of pharmacovigilance" Challenges and strategies

Dr. K. Punnagai
Professor & Head of Department

Adverse drug reactions (ADR) are unintended and noxious effects of drugs which are preventable in most of the situations. Monitoring and detecting the adverse effects of drugs will enable the drug regulatory authorities to assess and prevent the risks due to these drugs by various measures like withdrawal from the market and labeling changes. This is the main aim and objective of Pharmacovigilance programme throughout the world.

The cornerstone of pharmacovigilance programme is the spontaneous adverse drug reaction reporting by healthcare professionals. Clinicians play a vital role in detecting and reporting whether an adverse reaction in a patient is related medicines or disease. Unfortunately, the percentage of reporting of ADR by healthcare professionals is very less in many developing countries including India. This under reporting of ADR leads to delays in the prevention of unwanted harmful drug effects as was the case seen during thalidomide disaster. It took approximately 5 years for the regulatory authorities to ban thalidomide leading to the origin of concept of Pharmacovigilance.

Many studies have reported that under reporting of adverse effects by healthcare professionals can be due to various reasons viz., busy outpatient and inpatients consultations, ward rounds, lack of awareness, fear of legal problems, lack of awareness about ADR reporting, misconceptions about what should be reported, unfamiliarity and unavailability of ADR reporting forms. Many doctors opine that only unusual and rare adverse drug effects that must be reported and more so for the newly approved drugs.

According to a survey, In India, 90% of the hospital physicians were aware of ADR reporting and monitoring system, but only 41% had reported suspected ADR to PV system. Factors that facilitated ADR reporting were awareness, acknowledging the receipt of ADRs report, provision of feedback to the reported ADRs and continuous encouragement to reporting ADRs. Barriers against reporting suspected ADRs were time constraints, well known reactions, mild ADRs and immediate management of ADRs. In a study, 81.4% academic medical centre physicians suspected an ADR without reporting it, and 40% of them were not aware of various functions and purposes of ADR reporting system. A major determinant of under-reporting of ADRs was 'ADR was considered to be too trivial or too well known' and other factor was uncertainty of types of ADRs. Not reporting well-known ADRs reflects a misconception among physicians about the types of reactions to be reported to PV system.

A robust ADR reporting system is the need of the hour to overcome under reporting and thereby to motivate the healthcare providers to report ADR especially doctors. More innovative methods of reporting which can be included in the Pharmacovigilance system are targeted and focussed ADR monitoring of specific diseases like HIV Covid-19 etc, prioritizing the reporting of the ADRs based on the type, severity and unexpected reactions, Easy and convenient reporting tools like mobile Apps, SMS systems, social networking sites for the doctors and nurses, in-depth of analysis of computerized medical case records, ADR related Case reports, case series, and articles in Newsletters and journals, rewards for the prompt reporting by the professionals, making the knowledge and practice of pharmacovigilance and drug safety as a part of undergraduate and postgraduate curriculum and regular teaching sessions on ADR reporting and Causality assessment.

Changing of the mindset of the doctors and nurses by developing a culture of spontaneous voluntary ADR reporting in routine day-to-day practice will be the supreme goal of pharmacovigilance programmes in India an throughout the world.

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Materiovigilance- A beginning in the journey of medical device safety

Dr. Ramya. S & Dr. K. Kranthi
Assistant Professor

Materiovigilance Programme of India (MvPI) was launched on 06th July 2015 at IPC, Ghaziabad by DCGI under Ministry of Health & Family Welfare, Govt. of India to oversee the safety of medical devices in the country. Its commencement was by the.

Mission of MvPI

To protect the health of individuals by ensuring that the advantages of use of medical devices outweigh the harmful effects associated with its use

Vision of MvPI

To track adverse events associated with use of medical devices and reduce their utilization related risks in order to enhance safety and welfare of patients.

Scope and Objectives

To capture the adverse events associated with the use of medical devices, to generate safety data, create awareness among the different stakeholders, and recommend the best practices and interventions to improve the patient's safety with regard to use of medical devices.

Until date there are 17 Materiovigilance monitoring centres in India. Our institution Sri Ramachandra Medical College and Research Institute is privileged to have recently received recognition as a Medical Device Monitoring Center under MvPI on October 07th, 2021 to contribute towards medical device safety.

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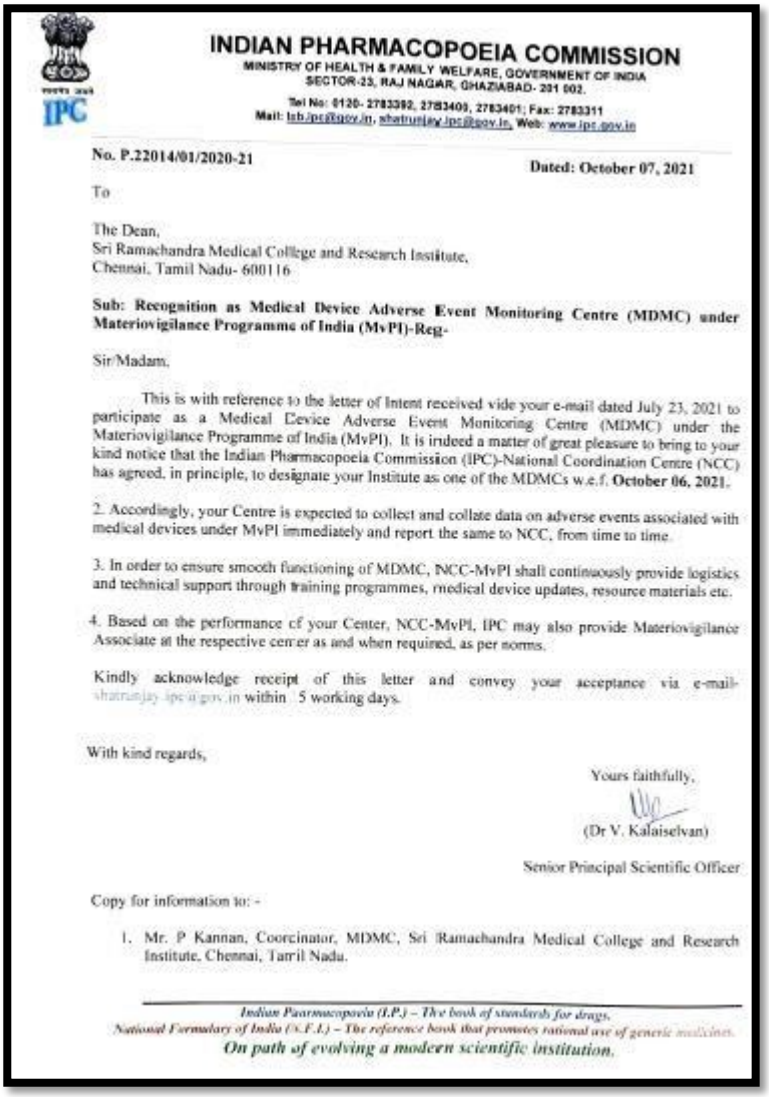

INDIAN PHARMACOPOEIA COMMISSION

MINISTRY OF HEALTH & FAMILY WELFARE, GOVERNMENT OF INDIA
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No. P.22014/01/2020-21 **Dated: October 07, 2021**

To

The Dean,
Sri Ramachandra Medical College and Research Institute,
Chennai, Tamil Nadu- 600116

Sub: Recognition as Medical Device Adverse Event Monitoring Centre (MDMC) under Materiovigilance Programme of India (MvPI)-Reg-

Sir/Madam,

This is with reference to the letter of Intent received vide your e-mail dated July 23, 2021 to participate as a Medical Device Adverse Event Monitoring Centre (MDMC) under the Materiovigilance Programme of India (MvPI). It is indeed a matter of great pleasure to bring to your kind notice that the Indian Pharmacopoeia Commission (IPC)-National Coordination Centre (NCC) has agreed, in principle, to designate your Institute as one of the MDMCs w.e.f. **October 06, 2021.**

2. Accordingly, your Centre is expected to collect and collate data on adverse events associated with medical devices under MvPI immediately and report the same to NCC, from time to time.

3. In order to ensure smooth functioning of MDMC, NCC-MvPI shall continuously provide logistics and technical support through training programmes, medical device updates, resource materials etc.

4. Based on the performance of your Center, NCC-MvPI, IPC may also provide Materiovigilance Associate at the respective center as and when required, as per norms.

Kindly acknowledge receipt of this letter and convey your acceptance via e-mail-shatrunjay.ipc@gov.in within 5 working days.

With kind regards,

Yours faithfully,

(Dr V. Kalaiselvan)

Senior Principal Scientific Officer

Copy for information to: -

1. Mr. P Kannan, Coordinator, MDMC, Sri Ramachandra Medical College and Research Institute, Chennai, Tamil Nadu.

Biosimilars – Paving the way for more affordable biologics

Dr. Alphienes Stanley . X
Associate Professor

Biologicals or biotherapeutics or biopharmaceuticals are the drug therapy products which are produced / extracted through a biological process or from a biological source. Significant proportion of newly approved drugs by regulatory authorities are biological products. These products include recombinant proteins, hormones, monoclonal antibodies (mAbs), cytokines, growth factors, gene therapy products, vaccines, cell-based products, gene-silencing/editing therapies, tissue-engineered products, and stem cell therapies. Many of the biotherapeutic molecules, under development and recently approved are mAbs, and these are considered the most rapidly growing drug class in cancer chemotherapy, auto-immune disorders, and chronic inflammatory diseases.

Biosimilars or follow-on biologics or generic biologics are the terms used to denote a generic version of the innovator biologic product. Once the patent of the innovator drug expires, pharmaceutical companies are allowed to manufacture and market the generic version, after submitting the bioequivalence proof of generics with innovator drugs. Similarly generic biologics also should be proven to have analytical, pre-clinical, and clinical similarities with that of innovator biologics, and then only they are allowed to be marketed.

Development of generic biologics is more complex than that of the process of developing small molecule generic drugs. It is very extensive and time consuming, which is mainly because of the difficulty in reproducing the manufacturing process which involved high biological variability. The biosimilars should possess similarity in primary order structure (similar amino acid sequence in case of protein biologics), post-translational modifications, product as well as process related impurities. The manufacturer should also prove that the biosimilars are similar to innovator biologics in pharmacokinetic (PK), pharmacodynamic (PD), and immunogenicity profiles.

Availability of biosimilars in the market has considerably improved the patient affordability with access to these medicines. This also helps to bring down the monopoly of the innovator product in the market. There are differences in the approval criteria followed by regulatory agencies across the world, some are more stringent and some are not. Many of the patents of innovator biological are expiring shortly; there will be a surge in availability of biosimilars in market. Cost reduction has helped clinicians to use these biologics widely among the needy people and it has been important to notify any adverse effects experienced by the patients through PvPI

(Pharmacovigilance Programme of India) which could help our country to have an extensive safety data on biosimilars for their effective usage.

Example: Drug Bevacizumab

Innovator product	Biosimilars
AVASTIN (Manufacturer – Roche) 400 mg Injection – Rs 1,16,000/- 100 mg injection – Rs 32, 250/-	**BRYXTA (Manufacturer – Zydus Cadila)** 400 mg Injection – Rs 43, 369/- 100 mg injection – Rs 16, 059/- **KRABEVA (Manufacturer – Biocon)** 400 mg Injection – Rs 35,777/- 100 mg injection – Rs 12, 214/- **Other biosimilar brands available:** **BEVAREST, ADVAMAB, BEVAZZA, BEVATAS.**

Drug Repurposing: A short journey for drug discovery

Dr. R. Kavitha
Professor

"The most fruitful basis for the discovery of a new drug is to start with an old drug".

Sir James Black

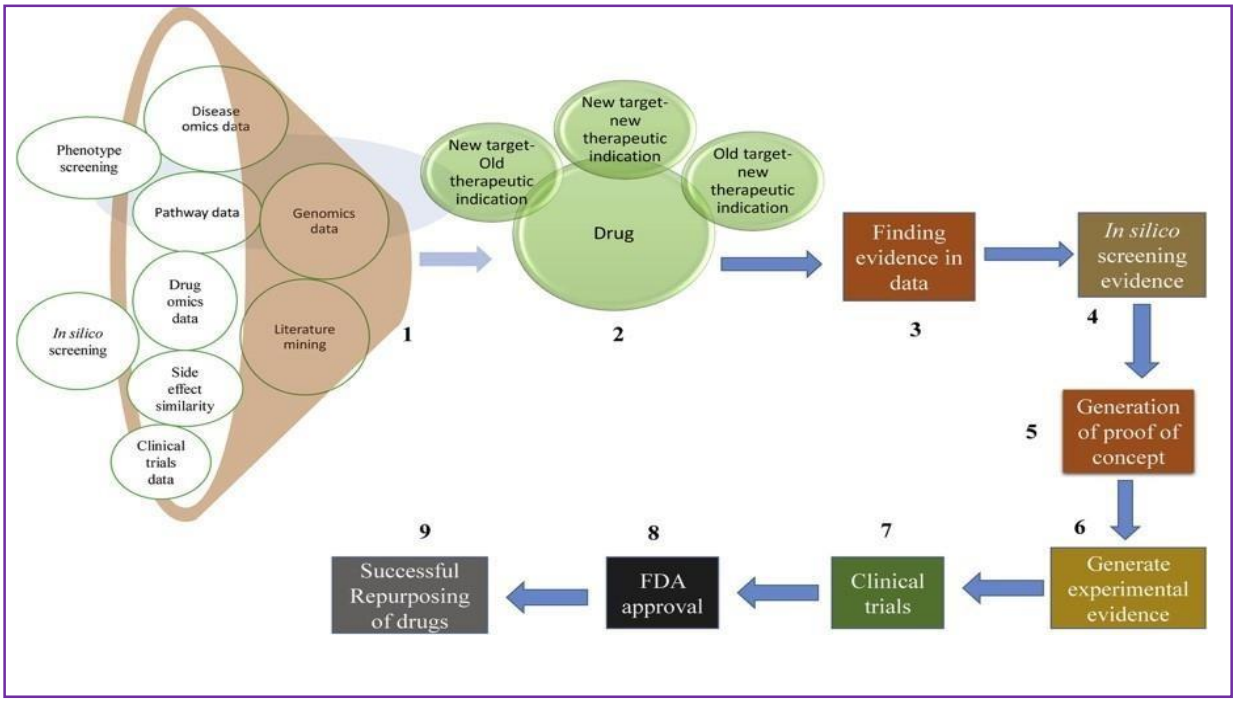
Drug repurposing, also termed drug repositioning, re-profiling or re-tasking, is a strategy for identifying new indications for approved or investigational (including clinically failed) drugs that have not been approved. The discovery and licensed use of a drug come with a long-gestation period. The cost of the new drug development process amounts to more than a billion dollars extending for a period of 10–15 years with the success rate of only 2.01%. This creates a lag in the productivity of pharmaceutical research to develop a new drug which results in a persistent gap between therapeutic needs and available treatments.

In recent times, repurposing of available drugs for the management of several disease conditions is increasingly becoming a popular strategy as it uses de-risked compounds with known preclinical, pharmacokinetic, pharmacodynamic profiles which can directly enter phase III or IV clinical trial making the drug development process potentially a low-cost and relatively rapid. Given the high attrition rates, substantial costs, and low pace of de-novo drug discovery, exploiting known drugs can help improve their efficacy while minimising side-effects in clinical trials

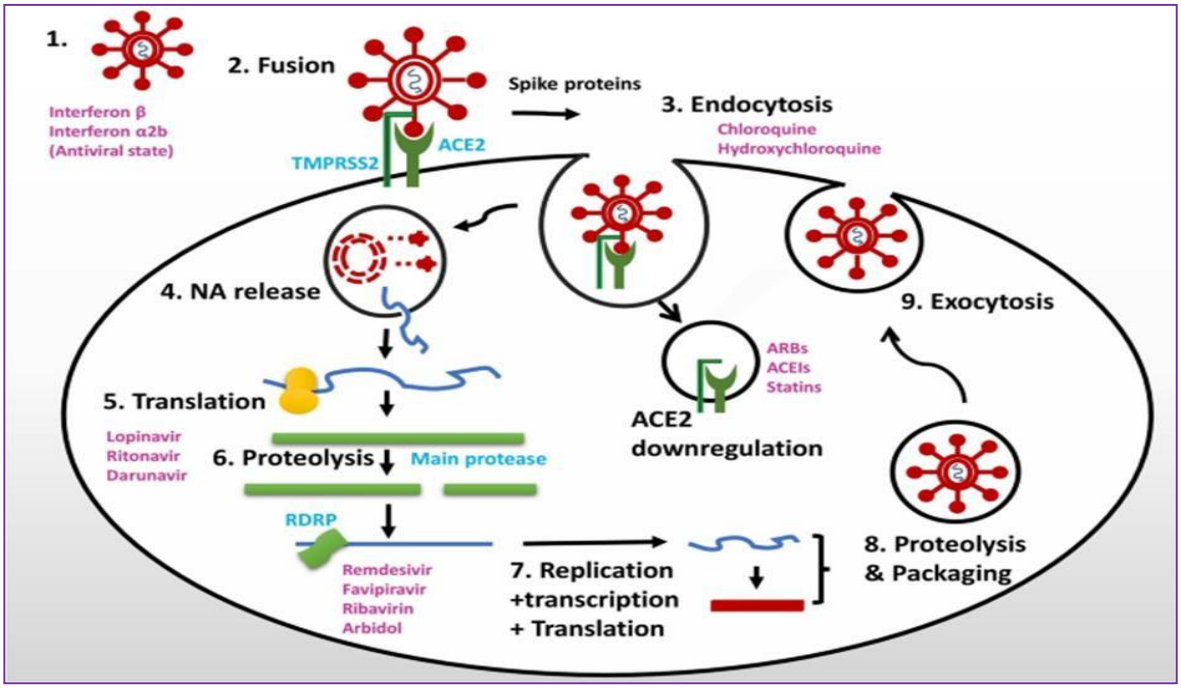
One-third of the new drug approvals correspond to repurposed drugs which currently generate around 25% of the annual revenue for the pharmaceutical industry. It has been accounted that approximately 30% of the US Food and Drug Administration (FDA) approved drugs and biologics (vaccines) are repositioned drugs. Well known examples include Sildenafil citrate for erectile dysfunction, Thalidomide for multiple myeloma and Minoxidil for hair loss. Using the basic knowledge of viral pathogenesis and pharmacodynamics of drugs as well as using computational tools, many drugs are currently in pipeline to be repurposed.

In this scenario, drug repurposing played a crucial role in accelerating advanced clinical testing and shortening the time to access the regulatory review. Drug repurposing proved highly successful in response to the current pandemic, with Remdesivir becoming the first specific antiviral drug approved for the treatment of COVID-19. In parallel, a number of drugs such as corticosteroids and low molecular weight heparin (LMWH) are used to treat hospitalized COVID-19 patients, while clinical testing of additional therapeutic options is ongoing. It is reasonably expected that these research efforts will deliver optimized and specific therapeutic tools that will increase the preparedness of health systems to possible future epidemics

Success of Repurposing drugs



Drug repurposing approach to fight COVID-19-Therapeutic targets of the currently considered drugs for repurposing against COVID-19



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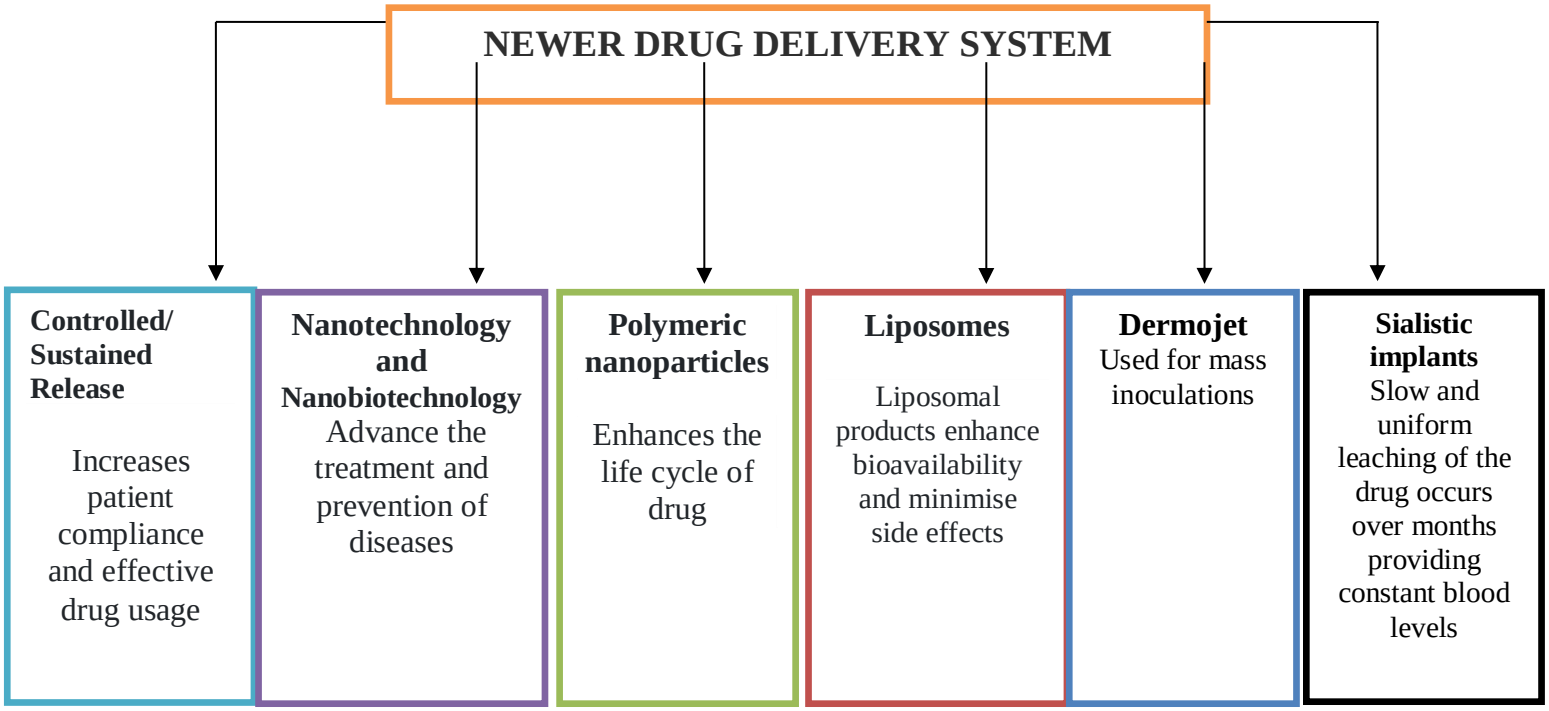
Newer Drug Delivery System - A promise for future

Dr. D. Anusha
Professor

Recent advances in biopharmaceutical technology have produced sophisticated delivery systems that permit precise control of drug input into the body. They offer better efficacy, cost-effectiveness, and reduce side effects which ultimately leads to better therapy.

They release the drug at a controlled rate. Pulsatile release is often the preferred method of drug delivery, as it closely mimics the way by which the body naturally produces hormones such as insulin.



References:

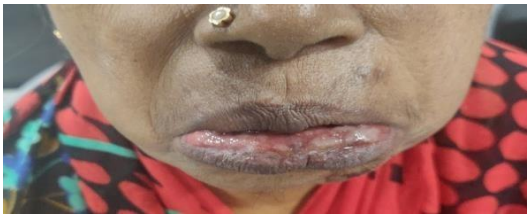
1. Yudi Deng , Haibin Shen etal. Application of the Nano-Drug Delivery System in Treatment of Cardiovascular Diseases Front. Bioeng. Biotechnol., 31 January 2020 | https://doi.org/10.3389/fbioe.2019.00489

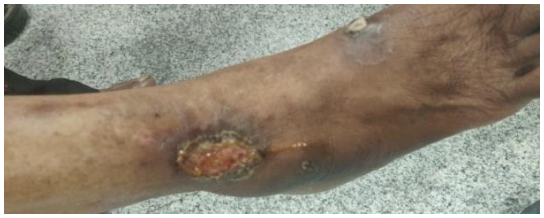
2. ChongL,†JianchengWan etal Recent progress in drug delivery, Acta Pharmaceutica Sinica B Volume 9, Issue 6, November 2019, Pages 1145-1162

Methotrexate misadventures – A case series from a tertiary care hospital

Dr. Sowmya Parvathareddy
Assistant Professor

Methotrexate (MTX) is a commonly prescribed safe immunosuppressant in Rheumatology. We report 6 consecutive cases of MTX toxicity. Five cases received MTX for Rheumatoid arthritis and one case received MTX for granulomatosis with polyangitis. These cases have been divided into 2 groups- acute and chronic. Four cases in acute group developed toxicity due to erroneously taking MTX daily (cumulative mean dose 50 mg) during initiation of treatment. Two cases in chronic group developed toxicity on stable doses of weekly MTX (weekly mean dose 20mg). Clinical manifestations of toxicity were oral mucositis (n=6), gastrointestinal intolerance (n=5), skin ulcer (n=1). Cytopenia observed in chronic group were more severe than the acute group. Mean folinic acid dose administered was 230 mg and 470 mg in acute and chronic groups respectively. Oral mucositis was treated with topical squish of syrup prednisolone and antacid. Both patients in chronic group had persistent cytopenia and prolonged illness which responded to recombinant Human Granulocyte-Colony Stimulating Factor (G-CSF) and platelet transfusion.





Discussion

MTX a drug widely used by Rheumatologists due to proven efficacy and affordability has the potential to cause toxicity. Both acute and chronic toxicity present with similar manifestations though chronic toxicity is more severe and needs prolonged treatment. Educating patients regarding importance of drug correct administration, potential toxicity including warning symptoms, along with regular monitoring of renal function can prevent incidence of toxicity.

Conclusion

We observed that Chronic MTX toxicity is associated with more severe mucositis and myelosuppression which needs prolonged and aggressive treatment including higher doses of folinic acid and G-CSF when compared with cases of acute MTX toxicity

Zinc – a friend or a foe in SARS-CoV-2 Pandemic?

Dr Jaba Chauhan[1], Dr Swathy Moorthy[2]

1-Senior Resident, 2- Associate Professor, Department of General Medicine

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is currently the leading healthcare problem globally with high morbidity and mortality, increasing with comorbidities. The clinical presentation of the diseases ranges from being asymptomatic to severe disease with multi-organ failure, being attributed to cytokine storm. Presently we only have supportive therapeutic options to combat this global pandemic.

Zinc (Zn) is a trace element with known potent immunoregulatory and antiviral properties. Zn supplementation has a potential to improve both innate and humoral antiviral immunity, and to restore and improve immune cell function, especially in the immunocompromised and elderly population. Synergistic effect of Zn administration along with standard antiviral therapy has been demonstrated in patients with Hepatitis C, HIV and SAR-CoV-1.

Role of zinc in antiviral immune response

Zn ions are closely involved in development and normal function of immune cells, thereby having a significant role in the immune response led by interferons and cytotoxic T lymphocytes, which is required to clear viral infection[1]. Zinc plays a significant role in antibody production, natural killer cell activity, cytokine production, chemotaxis as well as proper functioning of the thymus.[2]

In vitro studies have been used to demonstrate that Zn can induce the production of IFN α and IFN γ. Zn has also shown to enhance cell's resistance to apoptosis, induce capillary epithelial alteration which inhibits transcapillary shifting of plasma proteins, reduces local edema, exudation and mucus secretion.[2] Zn ions are also believed to stabilize the cell membrane, thereby inhibiting the virus entry into the cell.[3]

Role of Zinc in SARS-CoV-2

Higher concentrations of Zinc inhibit RNA virus replication by interfering with viral polyprotein processing as seen in influenza, RSV, picorna and coronaviruses[4]. Zinc has been found to inhibit the RNA synthesizing activity in the nidovirus group, which includes the SARS-CoV in vitro[5].

Potential side effects of zinc supplementation

Zinc supplementation of more than 100 mg daily for more than 5 years can cause copper deficiency[6], leading to sideroblastic anaemia. Excessive zinc ingestion has also been linked with reversible bone marrow depression[7]. Over supplementation of zinc with intranasal gel formulations can cause hyposmia and anosmia. With the current pandemic seeing a surge in zinc supplementation, anosmia due to COVID 19 can be confused with that due to over use of zinc[8].

The other common side effects of zinc supplementation are nausea, diarrhoea, GI bleeding, flu like symptoms and decrease in HDL cholesterol levels.

Hence a judicious use of Zinc in these times is very crucial in order to avoid futuristic problems.

References

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2. Ibs KH, Rink L. Zinc altered immune function. J. Nutr 2003;133(5suppl1): 1452S-6S

3. Pasternak CA. A novel form of host defence: membrane protection by Ca^{2+} and Zn^{2+}. Biosci Rep 1987; 81-91.

4. Denison MR, Zoltick PW, Hughes SA. Intracellular processing of the N-terminal ORF1a proteins of the coronavirus MHV-A59 requires multiple proteolytic events. Virology. 1992;189:274-284.

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6. Patterson WP, Winkelmann M, Perry MC. Zinc-induced copper deficiency: megamineral sideroblastic anemia. Ann Intern Med. 1985 Sep;103(3):385-6. Doi: 10.7326/0003-4819-103-3-385.

7. Broun ER, Greist A, Tricot G, Hoffman R. Excessive zinc ingestion. A reversible cause of sideroblastic anemia andbone marrow depression. JAMA. 1990 Sep 19;264(11):1441-3. Doi: 10.1001/jama.264.11.1441.

8. Alexander, Thomas & Davidson, Terence. (2006). Intranasal Zinc and Anosmia: The Zinc-Induced Anosmia Syndrome. The Laryngoscope. 116. 217 20.10.1097/01.mlg.0000191549.17796.13.

Recent Drug safety alerts by PVPI (2021)

Sl. No.	SUSPECTED DRUG	INDICATION	ADVERSE DRUG REACTION
1.	Fexofenadine	Seasonal allergic rhinitis, chronic idiopathic urticarial	Blurred Vision
2.	Ambroxol	Anti-tussive in acute and chronic disease of the respiratory tract	Fixed Drug Eruption
3.	Cefpodoxime	Acute bronchitis, exacerbations of chronic bronchitis	Drug Reaction with Eosinophilia systemic symptoms (DRESS) Syndrome
4.	Clarithromycin	Mild to moderate infections	Burning Sensation
5.	Hydroxyzine	Pruritus	Photosensitivity reaction
6.	Salicylic Acid	Acne vulgaris	Photosensitivity reaction
7.	Baclofen	Neuronal spasticity	Encephalopathy
8.	Clobazam	Acute and chronic anxiety	DRESS Syndrome
9.	Etoricoxib	Pain, swelling & inflammatory conditions	Acute generalized exanthematous pustulosis
10.	Torsemide	Oedema associated with CHF & HTN	DRESS Syndrome
11.	Sofosbuvir	Chronic hepatitis C .	Stevens-Johnson Syndrome
12.	SGLT-2 Inhibitors	Type-II Diabetes	Toe amputation, Diabetic ketoacidosis, Fournier's gangrene

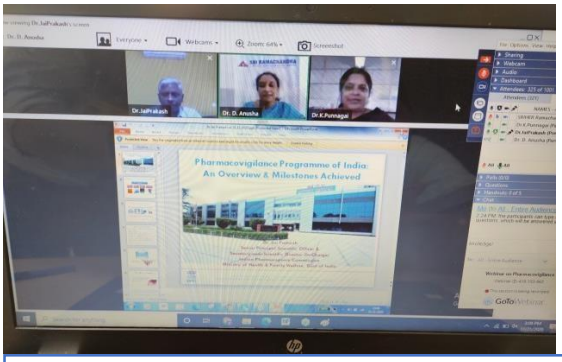
Reference link : https://publicsafetyandvigilance.com/2020/07/drug-safety-alerts-from-pvpipharmacovigilance-system-for-india/

AEFIs reported with COVID-19 vaccination (SRMC- 2021)

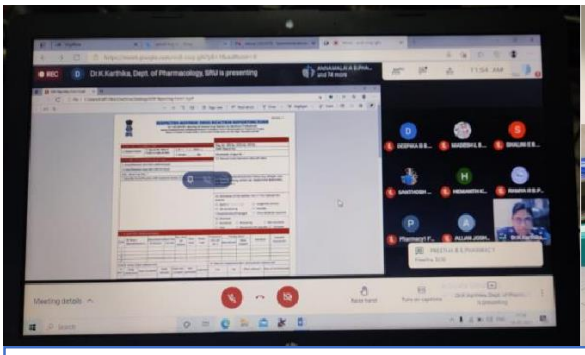
Sl No.	Type of AEFI	Number of ICSRS
1.	Itching	09
2.	Rash	10
3.	Itching & Rash	09
4.	Injection Site Pain	05
5.	Injection Site Swelling	07
6.	Injection Site Discoloration	05
7.	Fever	06
8.	Fever With Headache	11
9.	Fever, Headache, Body Pains	19
10.	Loss Of Consciousness	09
11.	Giddiness	07

Departmental Happenings

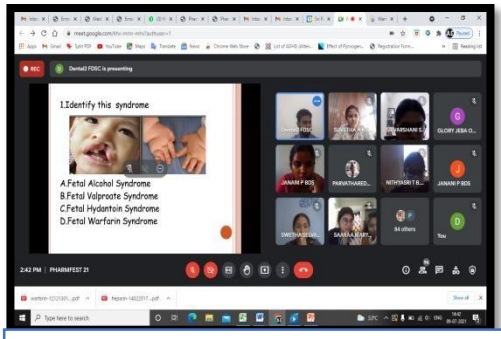
Notable events conducted to create awareness regarding ADR reporting- 2020-2021



Overview of Pharmacovigilance –Pivotal Role of Health Care professionals in ADR Reporting –Webinar-21.11.2021



Adverse Event Following Immunization – Sensitisation Programme (Pharmacy Students & Staff Nurses) 19.05.2021 & 20.05.2021

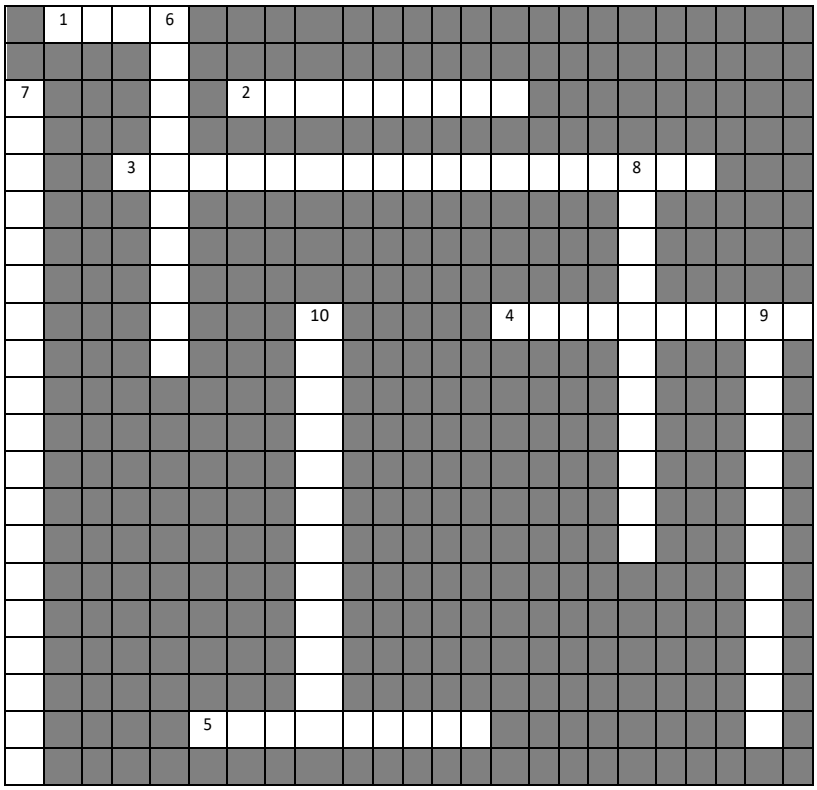


PHARM FEST – IInd year BDS-02.07.2021

Department of Pharmacology, in collaboration with the Indian Pharmacopeia Commission, had organized the National Pharmacovigilance week celebrations from 17th to 23rd September, 2021

(Many innovative competitions like Slogan writing, Video making, E Poster making and Leaflet designing were conducted. Students from all over the university participated with enthusiasm and bagged many prizes)

Cross Word Puzzle



ACROSS:	DOWN:
1. Pharmacovigilance document intended to provide an update of the experience of a medicinal product to regulatory authorities at defined authorization 2. Headquarters of Indian Pharmacopeia Commission is located at 3. My doctor told me I had attention deficit hyperactivity disorder. He said, it's a complex disorder blah blah blah. I didn't pay attention to the rest. He also said, there is a new drug approved in 2021 which reuptakes 2 neurotransmitters, I again didn't pay attention, I just remember it starts with D 4. This drug belongs to a novel group of drugs called potassium competitive acid blockers used to treat Gastric ulcer. 5. Purple glove syndrome is caused by	1. This drug was developed first to treat Hepatitis C, now repurposed to treat COVID 19 2. What causes Chinese restaurant syndrome? 3. Aprototypic neuromodulator in the treatment of alcohol dependence 4. I was considered to be a miraculous drug for people experiencing hallucinations. FDA punished me by giving me a Black box warning because I create suicidal thoughts. People often confuse me with proton pump inhibitors as my name sounds similar to that. 5. First Antibiotic introduced as an anti-neoplastic agent

MD Pharmacology PGs: Dr.V.Ariarasudhan**,** Dr.U.Kirthana**,** Dr.S.Kaphila**,** Dr.N.Kruthi**,** Dr.K. Priya Gayathri**,** Dr. D. Malathi

Pharmble

Task 1: Untangle- Pharmacovigilance Watch words

1. GASINL
2. BOBPERAL
3. TEARIG
4. DGCONI
5. CPCLOIMAEN

Dr. K. Karthika
Assistant Professor

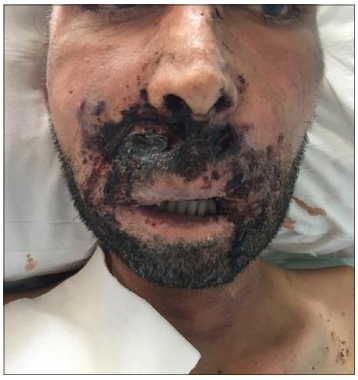
Task 2: Untangle- Explore Drug Names

1. SNDEMEHTOEAAX
2. SNTEAUETAR
3. VCRNUMIOUE
4. CLRRMZNEIAOPOH
5. AIVARBENDI
6. SFSUIVRBOO
7. YXUEARHDORY
8. XBNAARVRIAO
9. DBGAIARANT
10. NITCEMREVI

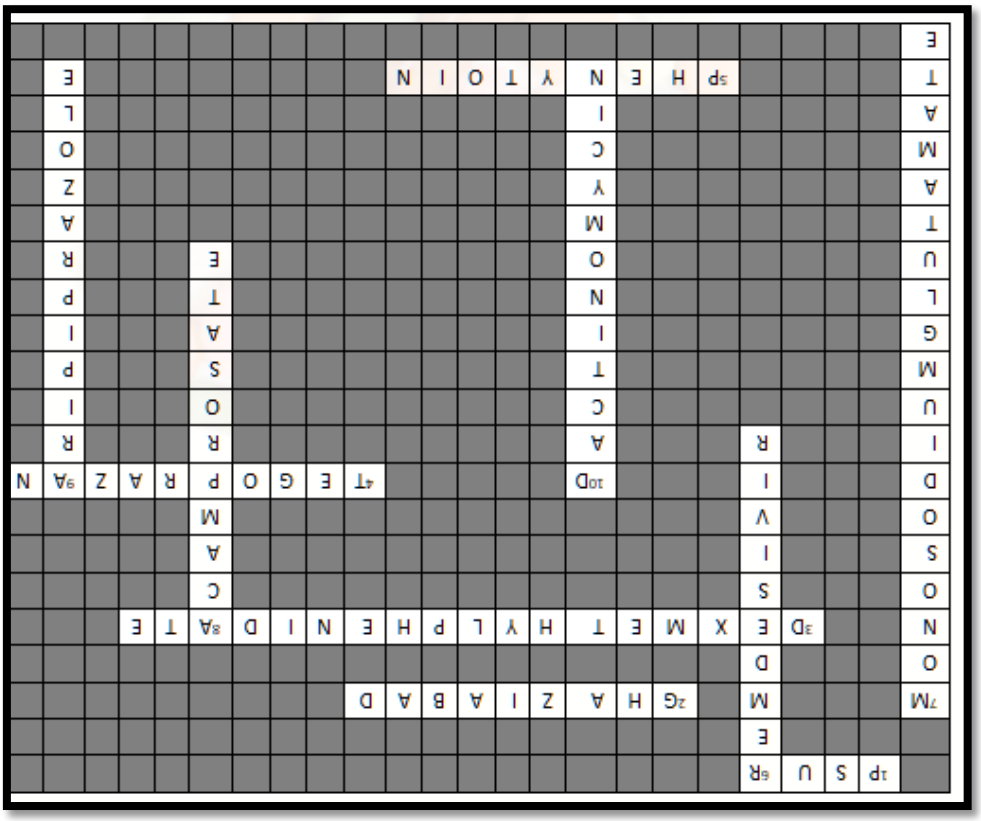
By: Dr Basith Ahmed[1], Dr Swathy Moorthy[2]
1- Senior Resident, 2- Associate Professor,
Department of General Medicine, SRMC, SRIHER

GEEK SQUAD TO SOLVE PHARMACOLOGY MYSTERIES:

1. Name the international medical terminology dictionary used by regulatory authorities and the biopharmaceutical industry.
2. Name the medicinal products available to the public without a prescription.
3. Which is the science of study relating to the detection, assessment, understanding and prevention of adverse effects?
4. The concomitant use of more than one drug, sometimes prescribed by different practitioners is called _____
5. Name the main regulatory body that is responsible for overseeing pharmaceuticals and medical devices within India.
6. Identify this adverse effect.



Answer: Cross Word Puzzles



Answer Pharmble

Task 1	Task 2
1. Signal 2. Probable 3. Triage 4. Coding 5. Compliance	1. DEXAMETHASONE 2. ARTESUNATE 3. VECURONIUM 4. CHLORPROMAZINE 5. IVABRADINE 6. SOFOSBUVIR 7. HYDROXYUREA 8. RIVAROXABAN 9. DABIGATRAN 10. IVERMECTIN

Answer Key: GEEK SQUAD TO SOLVE PHARMACOLOGY MYSTERIES

1. MedDRA - Medical Dictionary for Regulatory Activities
2. Over the counter medicines
3. Pharmacovigilance
4. Polypharmacy
5. Central Drugs Standard Control Organization (CDSCO)
6. Mucormycosis

For any suggestions/comments kindly email to hod.pharmacology@sriramachandra.edu.in

Annexure

Version 1.4

SUSPECTED ADVERSE DRUG REACTION REPORTING FORM

For **VOLUNTARY** reporting of ADRs 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

PvPI Helpline (Toll Free) :1800-180-3024 (9:00 AM to 5:30 PM, Monday-Friday)

Initial Case ☐ | Follow-up Case ☐

FOR AMC / NCC USE ONLY

Reg. No. / IPD No. / OPD No. / CR No. :

AMC Report No. :

Worldwide Unique No. :

A. PATIENT INFORMATION *

1. Patient Initials:

2. Age or date of birth:

3. Gender: M ☐ F ☐ Other ☐

4. Weight (in Kg.)

B. SUSPECTED ADVERSE REACTION *

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

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

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

12. Relevant investigations with dates :

13. Relevant medical / medication history (e.g. allergies, pregnancy, addiction, hepatic, renal dysfunction etc.)

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

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

15. Outcome:

☐ 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.	Expiry Date (if known)	Dose	Route	Frequency	Therapy Dates		Indication	Causality Assessment
								Date Started	Date Stopped		
i											
ii											
iii											
iv#											

9. Action taken after reaction (*please tick*)

10. Reaction reappeared after reintroduction of suspected medication (*please tick*)

S. No. as per C	Drug withdrawn	Dose increased	Dose reduced	Dose not changed	Not applicable	Unknown	Yes	No	Effect unknown	Dose (if re-introduced)
i										
ii										
iii										
iv										

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

S. No.	Name (Brand / Generic)	Dose	Route	Frequency (OD, BD, etc.)	Therapy Dates		Indication
					Date Started	Date Stopped	
i							
ii							
iii#							

Additional Information :

D. REPORTER DETAILS *

16. Name & Address : _____

_____

Pin : _____ Email : _____

Contact No- : _____

Occupation : _____ Signature : _____

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

Signature and Name of Receiving Personnel :

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

* Mandatory Fields for suspected ADR Reporting Form

Annexure

ADVICE ABOUT REPORTING

A. What to report?

All adverse events should be reported

Report non-serious, known or unknown, frequent or rare adverse drug reactions due to Medicines, Vaccines & Herbal Products.

Report every 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
- Report intervention to prevent permanent impairment or damage

NOTE : Serious/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 Nurse etc.) can report adverse drug reactions

C. Where to report?

Duly filled in Suspected 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.ipc@gov.in

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-PvPI 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 reviews the data and suggests 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) & reporter information.

For Adverse Drug Reaction Reporting Tools

- **E-mail : pvpi.ipc@gov.in**
- **PvPI Helpline (Toll Free) : 1800 180 3024** (9:00 AM to 5:30 PM, Monday-Friday)
- **ADR Mobile App : "ADRPvPI"**

NOTIFICATION SLIP FOR SUSPECTED ADVERSE DRUG REACTION FROM SRI RAMACHANDRA MEDICAL COLLEGE HOSPITAL

SRI RAMACHANDRA HOSPITAL

ADVERSE DRUG REACTION MONITORING CENTRE

DEPARTMENT OF PHARMACOLOGY, SRI RAMACHANDRA MEDICAL COLLEGE & RESEARCH INSTITUTE
SRI RAMACHANDRA UNIVERSITY, PORUR, CHENNAI - 600 116. Email : adrsrmc@gmail.com

NOTIFICATION OF SUSPECTED ADVERSE DRUG REACTION FORM **CONFIDENTIAL**
(As per CDSCO, Ministry of Health & Family Welfare, Govt. of India)

Patient Name : Age: Sex: I.P/O.P No: Unit/Dept:
Suspected drugs/vaccines Generic name: Trade name: Batch No:
Concomitant drugs:
Diagnosis for use:
Outcomes: Fatal ☐ Recovering ☐ Recovered ☐ Continuing ☐ Unknown ☐ Others(specify) ☐
Drug started on: Drug stopped on: Date of reaction:
Brief description of reaction:

Name of the Doctor/Reporter: Signature: Date:

Please drop it in ADR drop box at DMS office (OP building) or DNS office (IP building)

SRI RAMACHANDRA PHARMACOVIGILANCE CENTRE

ADVERSE DRUG REACTIONS MONITORING CENTRE OF PvPI

PLEASE REPORT

Adverse Drug reactions

(Known or unknown, Serious or Non-Serious, Frequent or Rare)

Associated with Medicines, Medical Device, Blood Products, Vaccine and Herbal

To

Adverse Drug Reaction Monitoring Centre,
Sri Ramachandra Medical College, Porur, Chennai.

Dr.K.Punnagai M.D.,
HOD & Coordinator SRMC-AMC Chennai,
PH No: 9840574080,
Email:hod.pharmacology@sriramachandra.edu.in

Dr.D.Anusha M.D.,
Deputy Coordinator SRMC-AMC Chennai,
PH No: 9884313112,
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