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ROLE OF PHARMACOVIGILANCE, HAEMOVIGILANCE, AND MATERIOVIGILANCE PROGRAMME OF INDIA TO ENSURE SAFETY PROFILE AMONG HUMAN POPULATION

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ABSTRACT

In India, various programme run to ensure the health among population living in diverse economic condition, one of them is Pharmacovigilance Programme of India (PvPI) which is begin by Government of India (GoI) with the objective to improve patient's safety during the administration of drugs in 2010. Under the umbrella of PvPI, evaluation of the benefits, drawbacks, efficacy, side effects, monitor adverse drug reactions and risk associated with the administration of pharmaceuticals by establishing an Adverse Drug Reaction Monitoring Centre (AMCs) which are set up to collect and report ADRs to the Indian Pharmacopoeia Commission (IPC), Ghaziabad's through online software called VigiFlow. IPC working as a National Coordination Centre (NCC). After two years later, the Haemovigilance Programme of India (HvPI) launched in India in 2012 with the aim to monitor the adverse reactions associated with the blood and blood product transfusions. While, Materiovigilance Programme of India (MvPI), was initiated in 2015 at the IPC, Ghaziabad for post-marketing surveillance or tracking of potential outcomes arising from the practice of medical devices among the population of India. Due to dramatic increase in number and use of medical instruments, adverse events occur more frequently. Together all programme shows an essential component of the drug/ medical devices development process and clinical research. The collected, documented and analyzed safety profile will helpful for healthcare professionals, patients, manufacturing industries, and regulatory

institutions like Central Drug Standard Control Organization (CDSCO) for taking regulatory decisions on the safe use of drugs/ medical devices among the Indian Population.

Keywords: Pharmacovigilance, Haemovigilance, Materiovigilance, IPC, CDSCO

1. INTRODUCTION

We all are aware that our food habits and today's polluted environment are one of the main reasons that medicines have reached every home today and at the same time we cannot deny that it has serious side effects. In the process of development of new drugs/ vaccines involve numerous bioinformatics, clinical pharmaco-informatics, preclinical and clinical studies. These studies primarily help to detect the severe as well as common side effects. Sometimes, clinical trials may not detect some significant reactions, especially those that take a long duration to develop or occur rarely. Therefore, researchers and authorities are always interested to acknowledge the efficacy data as well as the safety profile data gathered at various stages of clinical trials. In 1961, “The Thalidomide Tragedy" in which popular sedative class drug thalidomide was consumed by a pregnant lady which leads to absence of limbs in baby. Since then, it is discussed all over the world that how to overcome the adverse effects. Then, the idea of pharmacovigilance begins to take shape among the health care professionals to study the adverse drug reactions and drug interactions through patient monitoring **[1]**. In today’s scenario, post marketing surveillance plays an essential role in drug design and development by monitoring for any known or unknown adverse reactions. World Health Organization (WHO) taking an initiative globally to increase awareness among population regarding ADR **[2]**. The word ‘Pharmacovigilance’ itself a unique terminology by its origin because ‘pharmakon’ is a Greek word which means “drug”, and ‘vigilare’ is a Latin word which means “to keep a watch”. The WHO defines pharmacovigilance as "the pharmacological knowledge and activities relating to the detection, assessment, understanding, and prevention of adverse effects or any other drug-related problems, particularly long-term and short-term adverse effects of medicines" **[3-5]**. The International Drug Monitoring Programme began in 1968 by WHO after the worldwide need for drug surveillance. In 1968, 10 nations became the member of WHO initiative, namely USA, UK, Canada, Federal Republic of Germany, Australia, Ireland, Netherlands, New Zealand, Sweden, and Czechoslovakia. Today, about 170 nations and territories are the member of the WHO programme **[1]**. In order to improving the system of ADR monitoring, WHO established Uppsala Monitoring Centre

(UMC) in Sweden. It was the collaborating centre for the International Drug Monitoring Programme **[2]**. UMC collect and analyze the global data on ADRs. India is a participant in the UMC, Sweden programme. About 23 million ADRs reports to the WHO global database i.e. VigiBase **[3]**. After the identification of lead molecule it will undergoes into the pre-clinical phases and once the result will be optimum. The Researcher and the manufacturing company will fill the Investigational New Drug (IND) Application to the regulatory authorities to get the approval for the clinical trials. In India, Drugs Controller General of India (DCGI) approved for the clinical trials and he/ she is an official of the CDSCO. Once approval is done then researcher undergoes to the clinical trials. In clinical trials, a candidate drug is administered to the human volunteer and determines the safety profile and efficiency. All the three phases of clinical trial is closely monitored by the researcher and the manufacturing company which are performed under the strict regulations. During the clinical trial phases, it is a legal requirement to account all ADRs within a specified time period. By the initiation of the Pharmacovigilance programme, the approach in the context of clinical trials is shifted from a reactive to a proactive and for this change whole credit goes to "good clinical practice" **[4]**.

2. Pharmacovigilance Programme of India (PvPI)

As we already see how the concept of pharmacovigilance begin. Now, we understand that why the need of pharmacovigilance whereas pre-clinical and clinical trials was already done during the drug development process. In pre-clinical trials, animal toxicology and efficiency of the candidate drug is detected but it is frequently not a good predictor for human beings. These studies performed in the controlled environments, so that drugs do not always respond similar to the real world. Evidence related to safety profile obtained from clinical trials is not enough due to the limitations in size of the population, narrow population (age and gender), narrow indications (only for specific disease) and short duration. PvPI promote the patient compliance by the safe use of medicines, promoting rational use of medicines, and close monitoring of the ADRs. When GoI promote the PvPI, at the same time many roles and responsibilities also came like collection of data at the right time, maintain record, documentation and notification regarding the safety of drug or not, it helps to create appropriate structures for communication, prevent ADRs, **[5][6]**. In India, more than 1.25 billion potential drug consumers and is the most populated nation in the world. But, when question about the contribution of ADRs data to

the VigiBase database is not that much. The reason behind this is the lack of an authentic method for tracking ADRs and the ignorance among Indian medical professionals for ADR reporting. So, it is essential to emphasize the awareness programme and training among the medical community, to maximize the efficiency and minimize the toxicity of the active pharmaceutical ingredients (API). One another terminology used frequently is an "Adverse Event" (AE) which is different from ADRs in terms of causal relationship with the treatment. ADRs have a causal relationship with the treatment while AE do not have **[7][4]**. With the course of time, ADRs have a significant social and economic impact. By increasing awareness among population, well-structured programme is created for monitoring ADRs in the country. Sometimes, an AE may be severe, in which it may be life-threatening, may cause death or requires inpatient care or prolongs an existing stay in the hospital **[8][9]**.

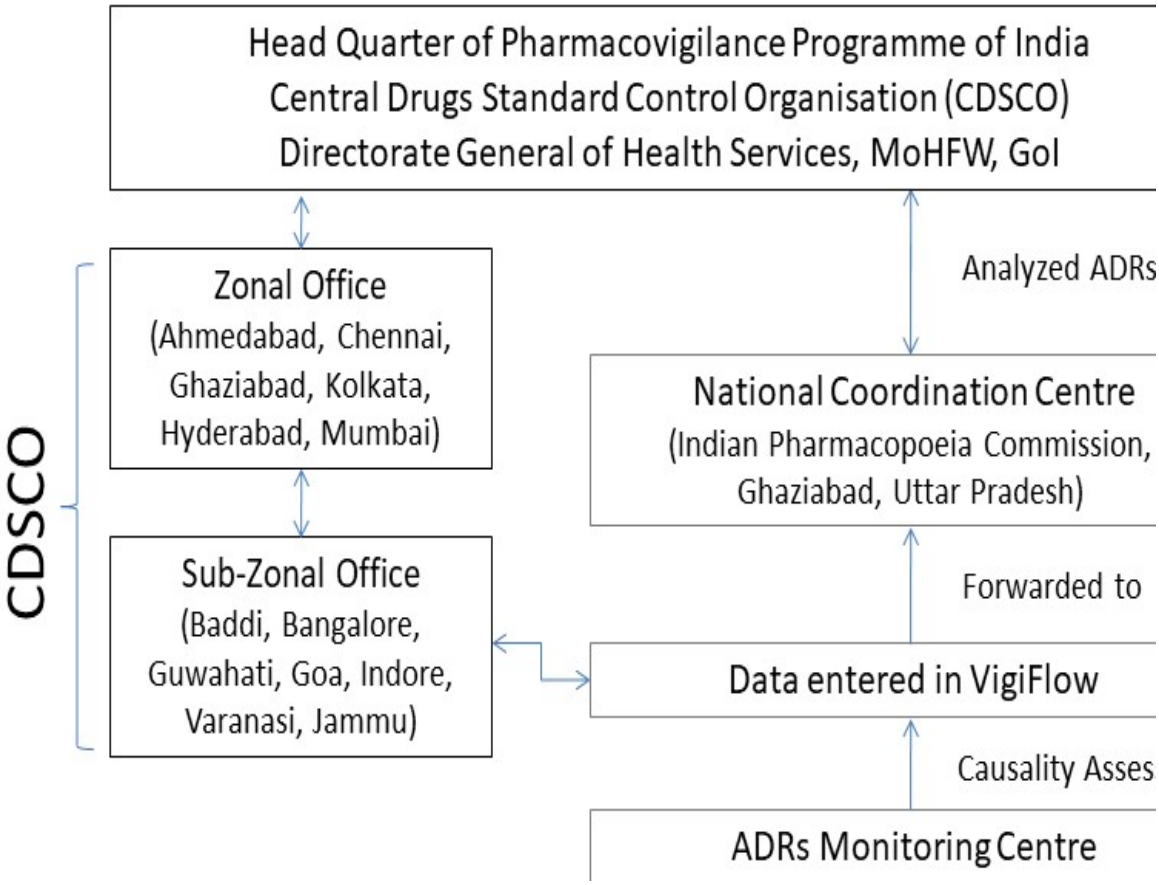

Figure 1: Structure of Pharmacovigilance Programme of India (PvPI) Functional Units

2.1 History of PvPI

After taking various step by the WHO in the field of reporting ADRs in 1960s. Finally in 1986, India designed a formal and official ADR monitoring system. After almost one decade in 1998, India became a member of the WHO's Programme for International Drug Monitoring **[10]**. The UMC in Sweden is responsible for the success of WHO Program by the collection of ADRs data on right time from the right source. The nation's ADR monitoring began in 1997 with six regional centers in New Delhi, Kolkata, Lucknow, Mumbai, Pondicherry, and Chandigarh **[11]**. After receiving unsatisfactory reporting from the majority of these centers, India has also realized that it needs a more robust ADR reporting mechanism **[12]**. As a team with the IPC, Ghaziabad, the CDSCO, Directorate General of Health Services is launched a public pharmacovigilance program to ensure the safety of patients' medications and safeguard their wellbeing **[13]**. Later, the 'National Programme of Pharmacovigilance' was launched in 2005, and it was renamed on July 14, 2010, as the 'Pharmacovigilance programme in India' established by the Indian government. 22 ADR monitoring centers were established as a result of this program in 2010, including AIIMS in New Delhi. The All India Institute of Medical Sciences (AIIMS) in New Delhi was designated as the NCC for the program. To ensure effective implementation of the programme, on April 15, 2011, the NCC was moved from AIIMS, New Delhi, to the IPC, Ghaziabad, Uttar Pradesh **[13]**. The PvPI will then be managed by the IPC, Ghaziabad, which will serve as an NCC. The IPC's primary responsibility is to maintain ADR database, which contains all observed suspected serious adverse drug reactions. The NCC is run by the steering committee, which also makes suggestions for regulatory interventions. The National Coordination Centre's primary responsibility is to develop and maintain its pharmacovigilance database and to keep track of all drug-related adverse reactions in the Indian population **[13]**. Apart from these responsibilities NCC also play a role in informing the general public and healthcare professionals about risks through PvPI-Newsletters as well as gathering, combining, and analyzing data on ADRs in order to make recommendations for regulatory actions to the CDSCO **[14]**. Under NCC, ADR monitoring centers (AMCs) are established to collect ADRs from patients. The establishment of AMCs was intended to facilitate the identification of rare ADRs that could not be discovered through clinical trial programs. In order for AMCs to function effectively and report ADRs, NCC provides them with manpower and logistical support. Under this program, different AMCs

were established across nation in all the medical colleges approved by NMC **[14]**. There are currently 250 AMCs operating all over the country and reporting ADRs to the NCC, PvPI, at the IPC, Ghaziabad. Numerous additional AMCs are being established annually. These AMCs' primary functions include uploading reports into the VigiFlow software, ensuring that AE reports are complete, and collecting AE in accordance with standard procedure **[15]**.

2.2 Objectives of PvPI

- To promote awareness and clinical training about effectiveness or toxicity of medications and implement the guidelines of the programme **[4]**.
- To promote the risk-benefit analysis associated to the administration of medicines, encouraging their safe and effective use to improve patient care **[16]**.
- To generate data-based information on medicine safety, it ultimately helps to take decision by the regulatory bodies **[15]**.
- To develop robust electronic reporting system (e-reporting) for patient in India **[7]**.
- To enrolled and expand the PvPI to all National Medical Commission (NMC) approved medical colleges and all hospitals (govt. and private) located across India.
- To improve medication's management and identify safety profile of pharmacological agents by monitoring the drug ADRs among patient and communicate it to various regulatory authorities to minimize the risk.
- To motivate and develop reporting culture of ADR so that maximum data can be tracked by the healthcare professionals **[7][4]**.

2.3. Implementation methods of PvPI

As AMCs registration under the PvPI programme, institution has to provide a 'Letter of Intent' to IPC, Ghaziabad. Once inspection is done, the concerned institute may be authorized as AMC under the aegis of national programme. Once institute is approved as AMCs, NCC sends all details to WHO-UMC, Sweden to get the login credentials of VigiFlow to upload ADRs. Each AMC under PvPI is assigned with a 'Coordinator' and a 'Technical Associate' responsible for its functioning. Coordinator is responsible for all daily activities associated with AMC so that it works properly. He/ She is also responsible to maintain ADRs reports obtained from the different sources as per SOPs and send the monthly reports of their AMC to NCC. The Technical associates is responsible for the collection and follow up of ADR reports,

which have to be reported to the AMC coordinator **[17]**. At present 250 AMCs are working under different offices of CDSCO. CDSCO provides all kind of support to the AMCs in their respective zone for reporting ADRs to NCC. These AMCs are responsible to monitor and report ADR to NCC via VigiFlow, a web-based Individual Case Safety **[17]**. IPC established the hospital based centers across the nation for the better patient safety. It was significant to monitor both the known and previously unknown side effects of medicines in order to get any new information available in relation to their safety profile **[13]**.

2.4. Methods of Pharmacovigilance

Various methods are used for the purpose of gathering and reporting of ADRs to the AMCs. Some are as follows:

a. Individual Case Safety Reports (ICSR).

b. Clinical Review of Case Reports (CRCR).

c. Cohort Event Monitoring (CEM).

d. Longitudinal Electronic Patient Records (LEPR).

e. Spontaneous Reporting (SR).

f. Periodic Safety Update Reports (PSUR).

g. Expedited Report (ER).

h. Record Linkage (RL).

2.5. Pharmacovigilance Inspection

There are mainly two main methods involved in Pharmacovigilance Inspection:

2.5.1. Routine Inspection

It is done to ensure that pharmaceutical companies have the ability to perform and work in compliance with pharmacovigilance activities.

2.5.2. Targeted Inspection

Targeted inspection is further bifurcate into two methods:

a. Inspections Irrelevant to Drug Safety.

b. Inspections Relevant to Drug Safety**.**

a. Inspections Irrelevant to Drug Safety

In this type of inspections, it mainly deals with those pharmaceutical industries that have not yet been inspected or launch their first product or companies which are newly merged.

b. Inspections Relevant to Drug Safety

It deals with companies that delay or fail to take their obligations on safety monitoring, companies that delay to submit or submit incomplete periodic safety update reports, companies that failed to report drug safety related issues (like drug withdrawal without reporting).

2.6. List of Drugs Banned due to Adverse Effects

Some of the below listed drugs **(Table 1)** are commonly used to treat various ailments but finally banned due to adverse drug reactions seen among recipient.

Table 1: List of Banned Drugs

S.N.	Drug Name	Withdrawn	Country	Used For	Remarks
01.	Ingenolmebutate gel (Picato)	2020	Suspended in Europe	To treat the skin condition actinic keratosis [47].	Higher incidence of skin malignancy [47].
02.	Ranitidine (Zantac)	2020	USA	To treat or prevent heartburn and acid reflux [48].	Found to spontaneously break down into the carcinogen i.e. N-nitrosodimethylamine (NDMA) [49].
03.	Flupirtine	2018	European Union	To treat acute (short-term) pain [50].	Risk of serious liver injury [50].
04.	Tetrazepam	2013	European Union	Used for muscle-relaxant, sedative-hypnotic effects [51].	Serious cutaneous alterations [51].
05.	Propoxyphene (Darvon)	2010	Worldwide	Prescribed for mild to moderate pain [52].	Increased risk of anaphylactic shock [52].
06.	Gatifloxacin	2011 2006	India USA	An antibiotic of the fourth-generation that inhibits the bacterial enzymes DNA gyrase and topoisomerase IV [53].	Increased risk of dysglycemia[54].
07.	Phenformin and Buformin	2003 1977	India USA	Most widely used for hypoglycaemic agent [55].	Increased lactic production in patients (lactic acidosis) [55].
08.	Nialamide	1974	USA, UK	An MAO inhibitor used as an antidepressive agent [56].	Hepatotoxicity, Interactions with food products [57].
09.	Iproniazid	1964	Canada	To treat tuberculosis, but was later most prominently used as an antidepressant drug [58].	Interactions with food products containing tyrosine [59].
10.	Thalidomide	1962 1961	Worldwide European Union	To treat morning sickness in pregnant women [60].	Withdrawn because of risk of teratogenicity (Phocomelia) in infants [60].

3. Haemovigilance Programme of India (HvPI)

Blood and its related product are essential life-saving products and it is required to be administered aseptically. It is most widely used therapy to treat severe problem in patients that may cannot be avoided or controlled by other methods of treatment. Transfusion of blood and its products have beneficial effects as well as hazards to the recipient depending on the administration of drug. Sometimes, patient experience adverse response during or after the blood transfusion and its elements and for this, no other explanation can be understood. AEs may be common to severe, or life-threatening depending on the therapeutic intervention **[18]**. History of blood transfusion begins in 1665 in dogs from other dogs by England physician

Richard Lower. In 1818 James Blundell, a British obstetrician, performed the first successful transfusion of human blood. And, in the 19th century, Henri Leacock and James Blundell pioneered human-human transfusion as a lifesaving therapy for severe blood loss **[19]**. When increase in the incident of transmission of infections after the transfusion process, then health care professionals and regulatory authorities felt that the need for a greater awareness on the safety of transfusion and the robust system to report AEs. 'Haemovigilance' term was coined in France in 1990 and it is derived from the Greek word 'haema' which means 'blood' and the Latin word 'vigilare' which means 'watchful' **[20][21][22]**. The European Haemovigilance Network (EHN) was established in 1998 to safeguard the public health, further it is evolved progressively on a global scale. And in today's scenario, International Haemovigilance Network (IHN) is working globally **[23][24]**. The International Haemovigilance Network (IHN) defines Haemovigilance (Hv) as "a set of surveillance procedures covering the entire transfusion chain (from the sampling of blood and blood products to the follow-up of its recipients i.e. from the vein of the donor to the vein of the recipient), intended to collect and assess information on unexpected or undesirable effects resulting from the therapeutic use of labile blood products, and to prevent their occurrence or recurrence of such incidents" **[25][26]**. IHN was established in the year 2009. It establishes for the purpose of education and support in haemovigilance and aspire to build and maintain a global collaborative organization by inviting individuals and organization from all over the world **[21]**. On 10th December, 2012, GoI launch a programme to ensure patient safety and promote public health in the country named as "Haemovigilance Programme of India (HvPI) **[27]**. The National Institute of Biologicals (NIB), Noida, U.P. is an autonomous Institute under the administrative control of Ministry of Health and Family Welfare, Government of India as the National Coordinating Centre engaged in Quality Control Evaluation of various biological products like vaccines, blood products, blood reagents, sera, immuno-diagnostic kits produced and imported into India. This programme is considered to be a part of vigilance which tracks the adverse reactions associated with blood transfusion and blood donation. This system include several analytical procedures that help determine the quality of blood transfusion including monitoring, reporting investigation, identification and analysis of adverse reactions related to transfusion and Donation **[28][29]**. After the initiation of programme, India became a member of IHN in December 2014. And

presently, 33 countries are members of IHN. Through this programme, it is easy to monitor adverse reactions associated with blood and blood product transfusions. To enhance the safety profile of blood transfusion an international database is introduced by the IHN for sharing AEs data across the globe with the help of International Surveillance of Transfusion Associated Reactions and Events **[30]**. Hv is considered to be a developing field in medical science that helps in safe operation of transfusion therapy and prevent the associated risk during blood transfusion. Hence, it is considered to be an integral part of blood safety across the world **[31]**.

3.1. History of HvPI

Haemovigilance is a structured scheme for monitoring, identifying, reporting, investigating and analyzing the AEs and reactions associated to the transfusion of blood and its products. After the establishment of IHN, haemovigilance setup was promoted throughout the world for the purpose to reduce the incident of AEs related to the blood donations and transfusions. IPC initiated HvPI under the umbrella of PvPI. Many events take place in 2012 and 2013 to initiate HvPI and develop Haemo-vigil software. Descriptions of some important event are given as follows **(Table 2)**.

Table 2: Classification of Medical Devices[61]

S. No.	Classes	Example
1.	Consumables & Disposables	Needles and syringes
2.	Diagnostic Imaging	MRI, X-Ray, Ultrasounds
3.	Dental Products	Dentures, braces
4.	Orthopaedics and Prosthetics	Knee implants, artificial joints
5.	Patient Aids	Hearing aids and pacemakers

3.2. Objectives of HvPI

- Main objective of HvPI is to collect, report, and evaluate the data related to the blood transfusion and its components to track adverse reactions/ events.
- Organize awareness program among healthcare personals regarding the importance of ADR monitoring and reporting.
- Give evidence-based recommendations to the CDSCO related with adverse reactions for safety related regulatory decisions.
- To transmit/communicate essential information and findings to all key stakeholders
- Establishing national and international relationships **[32]**.

3.3. Haemo-Vigil Software

The National Executive Committee (NEC) and the National Advisory Committee (NAC) have given their approval for the Transfusion

Reaction Reporting Form (TRRF), along with a guiding document and standardized definitions related to transfusion reactions. Additionally, the Haemo-Vigil software, designed to facilitate online reporting of transfusion reactions, has also received their endorsement. Correspondingly, the Haemo-Vigil Software and the Donor-Vigil Software, both created by the IT division of the National Institute of Biologicals (NIB), have been introduced to enable the online reporting of Adverse Transfusion Reactions (ATR) and Adverse Blood Donor Reactions (ABDR) respectively. These software tools can be accessed via the NIB's official website: www.nib.gov.in. Presently, a total of 226 centers, situated within Blood Banks, Medical Colleges/Institutions, Government, and Private Hospitals, have actively enrolled in this initiative.

The Transfusion Reaction Reporting Form (TRRF) was a simple one page form divided into six sections as follows:

a. Patient information,

b. Transfusion product(s) details,

c. Nature of adverse reaction(s),

d. Outcome of adverse reaction(s),

e. Reporter,

f. Casualty assessment **[33]**.

Adverse events/ reactions are reported in TRRF from the centers which are enrolled under HvPI through software. Reporting is voluntary. Overall adverse transfusion reaction reported is about 1.8% of total blood transfusion and its related components.

4. Materiovigilance Programme of India (MvPI)

Before 2015, India lacked a reliable mechanism for registering and monitoring adverse events connected to medical devices, as well as for monitoring the safety aspects of these devices. In the absence of a domestic system, data sourced from more developed countries were employed to evaluate the safety and adverse profiles of medical devices within India. Eventually, on February 10th, 2015, the Materiovigilance Programme of India (MvPI) received approval from the Ministry of Health and Family Welfare (MoHFW), Government of India. Subsequently, on July 6th, 2015, the program was inaugurated under the supervision of the Indian Pharmacopoeia Commission (IPC) in Ghaziabad, with the Drugs Controller General of India (DCGI) leading the effort. This initiative was established for the post-market surveillance of medical devices, aiming to ensure the mitigation of medical device-associated adverse events (MDAEs) among the Indian population **[34][35][36]**. The IPC situated in Ghaziabad operates as an autonomous institution under the MoHFW and serves as the NCC for the MvPI. Additionally, the Sree Chitra Tirunal Institute for Medical Sciences and

Technology (SCTIMST) in Thiruvananthapuram, Kerala, plays the role of the National Collaborating Centre for MvPI. Offering technical support and acting as the resource center for the program is the Division of Healthcare Technology. This division is earmarked as a proposed WHO collaborating center, focusing on priority medical devices and health technology policy, within the National Health Systems Resource Centre (NHSRC) located in New Delhi, India **[35]**. Currently, 293 MvPI Centres in India working to report Medical Devices Associated Adverse Events (MDAEs) **[37]**. The primary objective of this initiative is to oversee and document potential untoward incidents linked with the utilization of medical apparatus. The term "materiovigilance" is a fusion of two words: "material," signifying a tangible substance from which things can be fashioned, and "vigilance," representing a heightened attentiveness, particularly aimed at detecting potential hazards. The term “medical device” has been defined by the World Health Organization (WHO) as any instrument, apparatus, reagent for *invitro* use, implant, device for tissue cutting or wound covering, highly sophisticated computerized medical equipment, software or other related or similar materials which are intended to be used for diagnosis, prevention, monitoring, treatment of disease **[35][34][38][39][40]**. The core focus of MvPI is centered on identifying, gathering, reporting, and assessing any unfavourable occurrences linked to the usage of medical devices. Operating within the broader framework of PvPI, this initiative consistently improves the calibre of these devices, ensuring enhanced safety for patients and consumers. By meticulously monitoring the adverse events related to these devices, the program works to eliminate potentially harmful devices from the market and address any imperfections in medical equipment **[40]**. Medical devices is designed by the researcher or manufacturer to be used on human population for the following objective **[35][41]**:

- For diagnosis, prevention, control, treating or diminishing an illness.
- For compensating an injury or handicap due to accident or it may be congenital disorder.
- For studying, replacing or modifying part of the anatomy or a physiological process.
- For mastering conception **[35][41]**.

And, Medical devices are classified into five major segments discussed in **(Table 3)**.

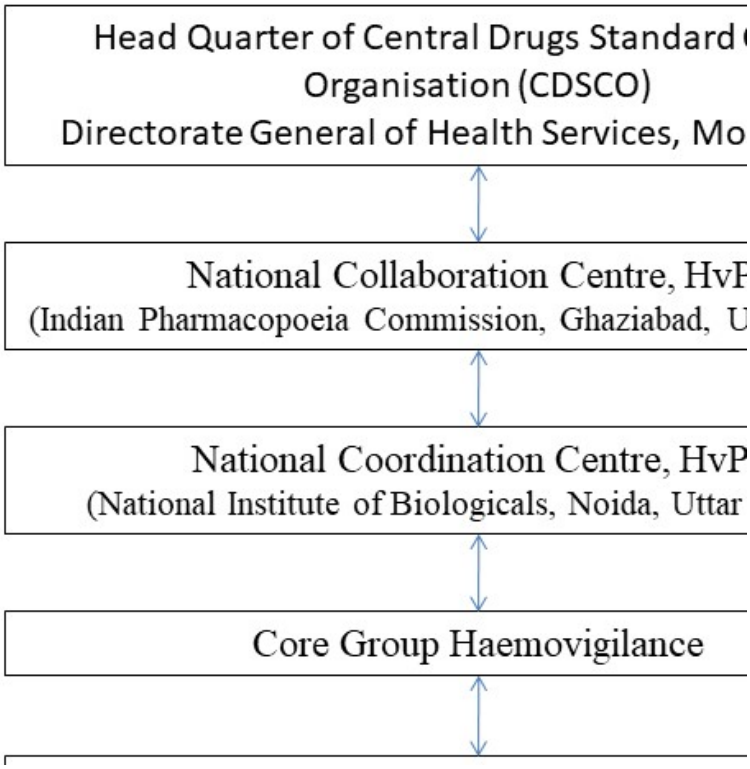

Figure 2: Organizational structure of Materiovigilance Programme of India [35][40]

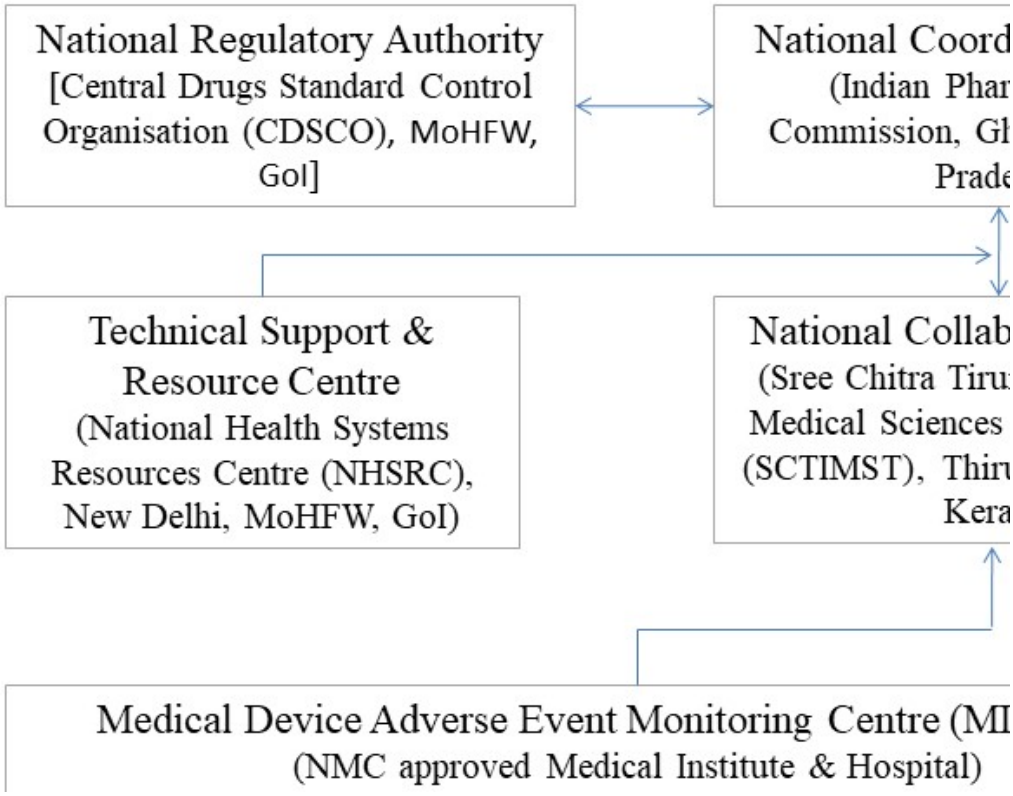

Figure 3:

4.1. Objectives of MvPI

The fundamental objectives of Materiovigilance encompass are:

- Establishing a nationwide mechanism for patient safety by generating data grounded in evidence concerning the safety of medical devices.
- To analyze the risk benefit ratio of medical devices among the patients, by reducing the frequency of an adverse event **[42][43]**.
- To implement the proposed framework, by the Indian medical device vigilance system to global harmonization, i.e., Global Harmonization Task Force (GHTF) **[39]**.
- To initiate the new innovative idea for the advancement of the use and productivity of the equipment **[44]**.
- To support CDSCO in the decision-making process on the use of medical devices.
- To communicate safety information on the use of medical devices to various stakeholders to minimize the risk **[38][40][43]**.

4.2. Classification of Medical Devices

In India, medical devices are classified as drugs under the drugs and cosmetic act and rules 1945 and it is regulated by same act and rules **[39][40]**. But in 2017, MoHFW, GoI has notified that Medical Devices Rules (MDR), primarily objective is to bring the highest degree of professionalism in regulating medical devices. As per the MDR, the devices are categorized into Class A (low risk), Class B (low moderate risk), Class C (moderate high risk) and Class D (high risk) **[45]**. List of some medical devices discussed in **Table 3**.

Table 3: List of some Medical Devices under the provisions of medical devices rules 2017[62]

S. No.	Risk Class	Device Name	Uses
1.	Class A (low risk)	Y-Connector as an accessory (Disposable perfusion sets)	It is used to connect to a catheter or perfusion set for the purpose of infusion of contrast media.
		Nasopharyngeal Catheter	It is used to remove air choke or obstruction by passing from the nares. A Resuscitator.
		Surgical Dressings	It is used as a non-adherent dressing, dressing aerosol, dressing pad.
		Umbilical occlusion device	In these devices it may be a clip, tie, tape or other article which is used to close the blood vessels in the umbilical cord of a new born infant.
2.	Class B (low moderate risk)	Blood Administration Kits	These kits are used to administer blood from a container to a patient's vascular system through a needle or catheter inserted into a vein.
		Insulin Syringes	It is used for the treatment of diabetes mellitus.
		Endo-lymphatic Shunt Tube	This tube is placed in the membranous labyrinth of the inner ear to drain excess fluid during a surgical procedure.
		Stomach Evacuator (Gastric Lavage) Tube	A tube is passed from the mouth, then down it into the stomach followed by sequential administration and remove out the small volume of liquid.
3.	Class C (moderate high risk)	Haemo-dialysis Catheter	Used to exchange blood to and from the patient. Venous and Arterial are the two lumens in dialysis catheter.

		Carotid Filter System	**It is used during angioplasty and stenting procedures in carotid arteries.**
		Anaesthetic Conduction Kit	**It is used to administer local anaesthesia to a patient.**
		Bone Cement	**It is used for the arthroplastic procedures of the knee, hip, and other joints for the fixation of polymer or metallic prosthetic implants to living bone.**
4.	**Class D (high risk)**	**Coronary Stents**	**It is a tube-shaped device which is placed in coronary arteries that will help to supply blood to the heart; it helps to keep open the arteries during the treatment of coronary heart disease.**
		Angiographic Guide Wire	**It helps to deliver radio opaque media and pharmacological agents to the selected sites in the cardiovascular system.**
		Heart valve	**It is used to perform the function of natural valves in the heart.**

4.3. Applications of Materiovigilance

Some of the applications of Materiovigilance are:

- Facilitating diagnosis, prevention, treatment of diseases, or providing compensation for injuries.
- Enhancing the design and effectiveness of medical devices.
- Reporting and probing adverse events linked to medical devices.
- Executing corrective measures to avert future adverse events.
- Investigating, modifying, replacing, or supporting anatomical or physiological functions.
- Supporting and sustaining life.
- Contraceptive control.
- Ensuring proper disinfection of medical devices.

Providing information for medical purposes by means of *in vitro* examination (such as reagents, calibrators, sample collection kits, control materials and related instruments) of specimens derived from the human body **[34][39][46][39]**.

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6. CONFLICT OF INTEREST STATEMENTS

There are no conflicts of interest to declare.

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