Available online on 15 Dec, 2020 at https://ijdra.com/index.php/journal

International Journal of Drug Regulatory Affairs

Published by Diva Enterprises Pvt. Ltd., New Delhi
Associated with Delhi Pharmaceutical Sciences & Research University

Review Article

An updated review on Materiovigilance for safe use of medical devices

Mansi Deshwal*[,a], Manju Nagpal[b], Gitika Arora Dhingra[c], Geeta Aggarwal[a]

[a]*Delhi Pharmaceutical Sciences and Research University, New Delhi-110017, India*
[b]*Chitkara College of Pharmacy, Chitkara University, Punjab, India*
[c]*NCRD's Sterling Institute of Pharmacy, Nerul, Navi Mumbai*

Abstract

In the last two decades, there has been an upsurge in the volume of medical devices and thereby increasing medical device-related adverse events. So, materiovigilance is an essential system for identifying, collecting, reporting and analysing adverse events related to medical devices. The Vigilance programme for the medical device was initiated in many countries many years ago but, is a quite new concept for India. The Materiovigilance programme in India was launched on July 6 2015, at the Indian Pharmacopoeial Commission (IPC) with the objective of monitoring adverse events, thereby reducing risks related to use of medical devices and also creating awareness among different stakeholders for improving patients' safety. The intent of this review article is to provide holistic understanding of medical device related adverse events; classification, reporting criteria, what, where, how, who and why, timeframe and tools used for reporting. Data collected using various search engines and compiled to give complete information regarding the subject matter. The thorough understanding of current status of materiovigilance programme in India including challenges involved in the programme and future directions for improving has been stated. Case studies have been reviewed for Johnson & Johnson's faulty hip implant and Medtronic premature battery depletion. Implementation of Materiovigilance programme of India (MvPI) version 1.1 lead to safeguard the health of device user by preventing recurrence and risk associated with medical device.

Keywords: Materiovigilance, post-marketing surveillance, Medical Device Monitoring Centres (MDMCs), medical device vigilance, adverse events, Medical Device Rule (MDR), CDSCO, FDA, Materiovigilance programme of India (MvPI), Indian Pharmacopoeial Commission (IPC)

Article Info: Received 19 Oct. 2020; Review Completed 07 Dec. 2020; Accepted 08 Dec. 2020

Cite this article as:
Deshwal M, Nagpal M, Dhingra GA, Aggarwal G. An updated review on Materiovigilance for safe use of medical devices. Int J Drug Reg Affairs [Internet]. 2020 Dec.15 [cited 2020 Dec.15];8(4):5-13. Available from: http://ijdra.com/index.php/journal/article/view/428

DOI: 10.22270/ijdra.v8i4.428
*Corresponding author Tel.: +91-8588953050;
E-mail address: mansi.deshwal14@gmail.com (Mansi Deshwal).

1. Introduction

Medical device has an important task in diagnosis, treatment and prevention of several diseases. They range from a simple thermometer or tongue depressor to complex lifesaving implants like coronary stents or heart valves. (1) According to Medical Device Rule (MDR) 2017, Medical device has been defined as "device intended for internal or external use in the diagnosis, treatment, mitigation or prevention of disease or disorder in human beings or animals which are notified from time to time under Drug and Cosmetics Act (DCA); including mechanical contraceptives (intrauterine devices, condoms, tubal rings), disinfectants and insecticides notified by government under DCA; surgical dressings, surgical staples, surgical bandages, surgical suture, ligature, blood and blood component collection bag with or without anticoagulant and substances used for *in vitro* diagnosis".(2) Medical devices are classified into three classes- Class I, II and III on the basis of risk Figure 1.(2,3)

All medical devices are associated with certain level of risk that could lead to miss diagnosis, injury or death in certain cases. Therefore, Post-marketing Surveillance of these medical devices i.e. Materiovigilance (Medical device vigilance) is conducted to ensure wellbeing of patients, health-care experts, and others by diminishing the probable re-occurrence of unfavourable events linked with the use of medical device. Materiovigilance comprising two words- 'materio' means 'the material from which a medical device is made of' and 'vigilance' means 'the great care that is taken to notice any signs of danger or trouble'. Hence, the term Materiovigilance is defined as the co-ordinated system of identification, collection, reporting and analysis of unacceptable performance or characteristics fluctuation of a device

and replying them with the 'field safety corrective actions' (FSCA) or the 'device recall'. (4)

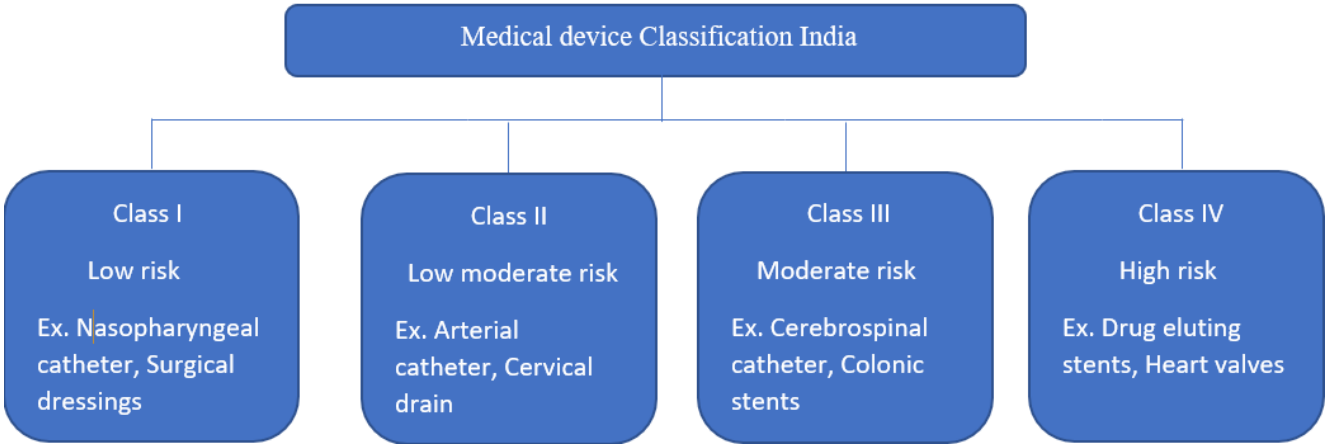

Figure 1. Medical Device Classification India (2,3)

2. Materiovigilance programme of India

In India, medical devices are regulated as per the DCA 1940 and Rules 1945. In 2017, the Government of India in consultation with Drug Technical Advisory Board (DTAB) enforced Medical Devices Rule, to import, manufacture, sale, and, distribute medical devices. This rule was notified on January 31, 2017 and came into effect from January 1, 2018. (2,5) 'Materiovigilance programme' of India (MvPI) was launched on July 6, 2015 in Indian Pharmacopoeial Commission (IPC), in Ghaziabad by Drug Controller General of India DCG(I). The fundamental principle of this program is to create awareness about relevance of 'medical device adverse events' (MDAE) among health-care professionals. It also emphasises on benefit-risk profile of a device, keep track of MDAE and communicate these findings to all relevant stakeholders. IPC is the National Coordination Centre (NCC) for MvPI and, its responsibility is to supervise adverse events of medical devices detected among Indian population. 'Sree Chitra Institute for Medical Sciences and Technology' (SCTIMST) operates as 'National Collaborating Centre'. 'Central Drug Standard Control Organisation' (CDSCO) is a regulator of MvPI and Technical support is rendered by National Health System Resource Centre (NHSRC). Twenty-six Medical Device Monitoring Centres (MDMCs)/ Adverse Drug Reaction Monitoring Centres (AMCs) has been setup for checking completeness of a case, scrutinizing the MDAE reports and sending reports to NCC. (4) The communication channel of this program is shown as a flow diagram in Figure 1.

Materiovigilance programme objectives *(4)*

- Establish and implement nation wise system for the vigilance in India on 'medical device' associated adverse events.
- Analyse causality assessment/ benefit-risk ratio of medical device.
- Aid decision-making process of regulatory agencies.
- Generate safety information and medical device alarm to regulator/healthcare experts.
- Convey safety information on medical device use to different stakeholders to limit hazard.
- Work together with other 'national healthcare organizations' for trade of data management and other information.
- Develop as national centre for Materiovigilance activities.

Adverse Event Reporting

MDAE are recorded through adverse event reporting system. It is an important tool to improve well-being of patients and medical device users by reducing occurrence of adverse events. Recorded incidents are evaluated and information is disseminated to avoid or mitigate the outcome of such repetitions.

1.3.1 Classification of adverse event on basis of severity

Adverse events are classified into three categories on the basis of severity- Death of patient or device user; Serious injury including life-threatening disease; congenital abnormality/ irreversible impairment; permanent destruction of a body function; and Near Miss Event. (4,5)

1.3.2 Reporting criteria for adverse event noticed

- **When manufacturer becomes aware of an adverse event related with their device** – Manufacturers initiate root cause of failure and intimate IPC-NCC, once they become aware of event. 'IPC-NCC' would send this information to the research associate located at nearest 'MDMC'.
- **When healthcare service- provider notice an event or incident–** The information's will be passed to the research associate at 'MDMC' and further root cause analysis of event is carried out by committee. Experts like biomedical/clinical engineers, research associate at MDMC, healthcare professional and technician handling device are part of the committee. (4)

Non-reportable Incidents

- If side effect associated with medical devices are predictable by the manufacturer's labelling,

documented with proper risk assessment in the device master record and are clinically well known.
- When the shelf-life of medical device exceeds as specified by manufacture at time of use by patient/end-user.
- When deficiency is observed by the end user before the use of medical device.
- When the root cause of incident is patient's pre-existing condition.
- When protection mechanism inbuilt in medical device functioned correctly. (4,6)

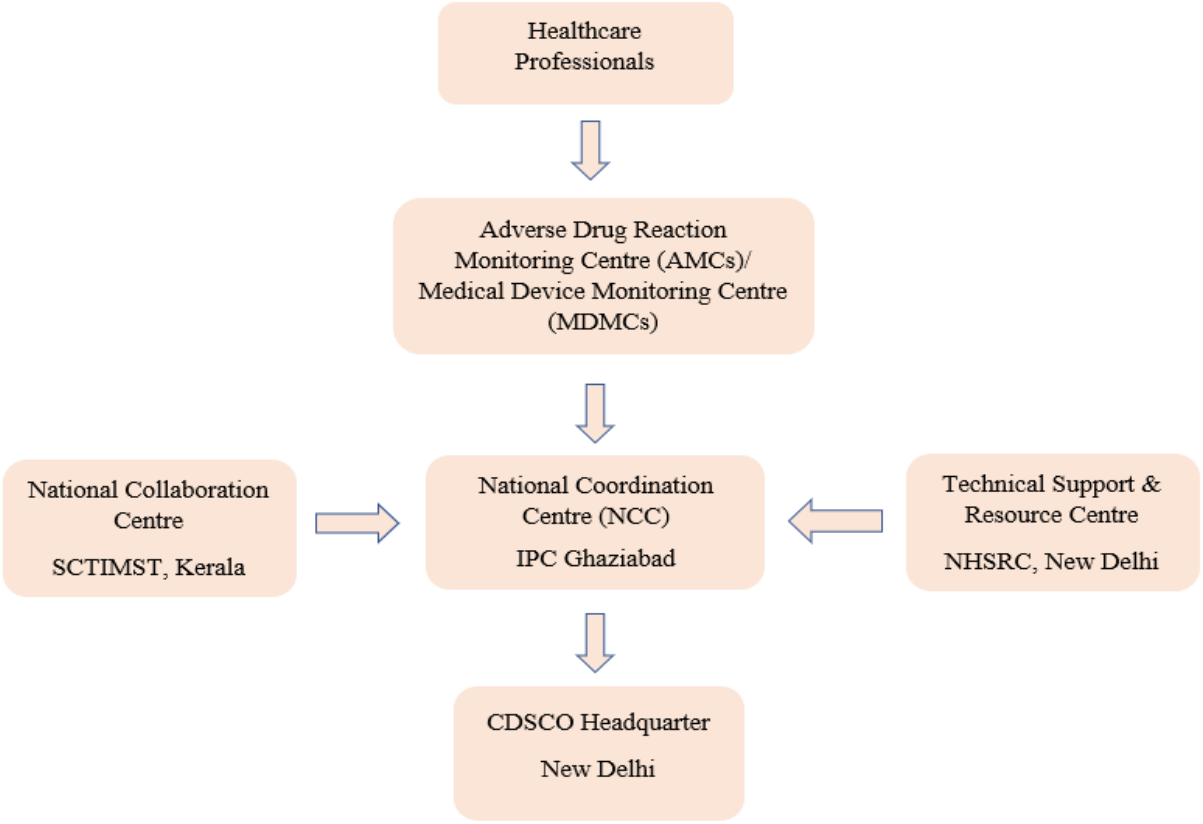

Figure 2. Communication Channel of MvPI (4)

What to report?

- All type of expected medical device adverse events whether they are serious, non-serious, known, unknown, frequent or rare are reported through Materiovigilance. Adverse event could be malfunctioning of medical device, unanticipated side-effect, destruction of device, higher rate of adverse events than expected and non-declaration of sufficient labelling/warning.

Who and why to report?

- Healthcare clinicians, hospital technology managers, medical device manufacturer, nurses, pharmacists, technicians, clinical engineers, and biomedical engineers can account medical device adverse events '(MDAEs)' and hence, safeguard public health.

Where and how to report?

- For reporting any adverse event a five-page MDAE reporting form is accessible on the official weblink of IPC- (www.ipc.gov.in) and CDSCO- (https://cdsco.gov.in/opencms/ resources/Upload CDSCOWeb /2018/UploadNewsFiles/MDAEform .pdf). Form is devised to be used voluntarily by manufacturer/ importer/ distributor of medical device, healthcare professional and anyone with the direct/indirect knowledge of medical device adverse event. Events need to be reported within a time frame as shown in Table 1.

Details to be filled in the form

Dully filled form can be sent to Indian Pharmacopoeial Commission or can be reported by sending e-mail to mvpi.ipcindia@gmail.com. Adverse event can also be reported by calling on Helpline no. 1800-180-3024.

The following is the information in the form to be filled:

General Information

- Reporting Date, Type of Report
- Reporter Reference for MDMC- Location, Month-Year, Centre, and case no.

Reporter Details

- Type of reporters- 'Manufacturer/Distributor/Importer /Healthcare professional/Patient/Others
- Name, Address, Contact Number and Email id of reporter

Device Category

- Medical device- Invasive, non-invasive, implantable, non-implantable, sterile, non-sterile, personal use or single use device
- In Vitro Diagnostics (IVD)- Kits, reagents, calibrator, control material, IVD electronic reader or other
- Medical equipment/ machines- therapeutic, diagnostic, assistive, imaging, invasive or non-invasive

Device Information

- Name of Device / brand name
- Manufacturer/ importer/ distributor address and name
- manufacturer/ importer license number
- Model no., Batch no. and Serial no.
- Version of software
- UDI no. if applicable
- Installation date
- Year of manufacturing
- Expiration date
- Is device regulated in India or not
- Nomenclature code if applicable; Global Medical Device Nomenclature (GMDN)/ Unique medical device nomenclature (UMDN)

Event Description

- Date of event
- Implant/ Explant date
- Event location-Manufacture/Distribution premise/ Home/ Hospital
- Serious event- Death(date)/ Life threatening/ Disability/ Hospitalisation/ congenital defect or Non-serious event
- Detailed description of event

Information, outcome and history of patient

- hospital id
- Name, Age, Weight and gender
- Patient outcomes- 'recovery date'/ 'not yet recovered'/ death report

'Causality assessment'

- Origin of problem and Investigational action taken

Table 1. Reporting timeframe of an event or incident (4)

'Reporter'	'What to report'	'To whom Report'	Timeline
Manufacturer	Initial report of an event on 'MDAE' reporting form with remedial action to prevent public from irrational risk. Initial report on Death or serious public threat due to adverse event or incident.	'MvPI'	Within 5 working days of becoming aware of an event
Manufacturer	'MDAE' reporting form with causality assessment report and future corrective or preventive actions taken in a define timeframe.	'MvPI'	'Within 30 calendar days' of becoming aware of an event
Healthcare service provider /clinical establishment	'MDAE' reporting form with 'causality assessment report'	'MvPI'	'MDAE' reporting should be submitted within 5 working days of becoming aware and root cause analysis in next '30 calendar days'

3. Medical Device Adverse Event Reporting tools

On February 8, 2019 MvPI developed tools to promote safety of Medical Devices. It includes-

a) 'Medical Device Adverse Event' (MDAE) Reporting form version 1.1 for reporting medical device related adverse events by manufacturer or healthcare professional.

b) 'Field Safety Corrective Action' (FSCA) Form for notifying the type of FSCA i.e. Product recall or other corrective actions taken for a medical device by a company. Five-page form is available on IPC website https://www.ipc.gov.in/images/'FIELD_SAFETY_CORRECTIVE_ACTION_NOTIFICATION_FSCA_FORM.pdf'. A scanned copy of PDF version can be mailed to 'CDSCO' at dci.nic.in. Additional information can be provided as attachment.

Information to be provided in the form as follows:

- Type of FSCA- product recall or other remedial actions
- Type of report and Date of report
- Particulars of reporters- Name, occupation, contact number, email address, office address, and local contact details
- Device information- Name, intended use, is device regulated in India (registered and marketed), Manufacturer contact details, product license holder/ local authorised representative name and address, Importer(s)/Distributor(s) contact details
- Impacted device information- model number, catalogue number, serial number, batch number/affected lot and UDI number
- Device related to FSCA information

c) Registered Medical Device Information Sharing Portal for gathering information on registered Medical

Device and its respective Manufacturer/Supplier/Others for strengthening MvPI. Online form is filled which is accessible on website of 'IPC' http://www.mvpi.co.in/.

Information to be filled in the form as follows:

- Type of Establishment
- Parent company name
- Registered office name
- Registered office address
- Company registration number
- Medical device detail- name, UMDN/GMDN, Model number, notified/ non-notified and Regulatory status

Recall

While marketing a device, the user, manufacturer or distributor may report quality defects of device. If a complaint about defect is not justified, then it is considered breakdown of the quality system and quick remedial action is undertaken by a product recall. (7)

Severity linked with the device intended for recall on the basis of health hazard:

Type I: If there is a reasonable possibility that exposure to or use of a 'recalled medical device' will lead to serious unfavourable health effects or may cause to death**.**

Type II: If the exposure to, or use of, a recalled medical device may lead to temporary adverse health consequences or the probability of serious adverse health consequences is remote.

Type III: If the exposure to, or use of, a recalled medical device is not likely to cause any adverse health effects.

Timeframe for recall: For recalling a medical device, first step is not the corrective action whereas a detailed recall strategy is required. It is based on factors such as risk associated with the device, complexity of the fix, geographical location and number of costumers, validation requirement and continuous availability of essential products. (4,8)

Challenges

Though a tentative start was made to report medical device related adverse events in 2014, there are several challenges involved in setting up Materiovigilance.

1. Reporting rate of MDAE is low
2. No mechanism to report malfunctioning of non-notified medical devices- There are about 5,000 categories of medical devices and only 23 are regulated in India, being one of the world's fastest growing medical device market. (9)
3. Poor tracking system- In the J&J's faulty hip replacement case, government did not have information on more than 3600 patients who received implant. (10)

4. Future directions

Reporting culture in India is catching up slowly. Data shows that total '1931 adverse events' have been reported since 'July 2015 to October 2019' of which 1277 were serious. There is an increase in adverse event reports from 40 cases in 2014 to 556 in 2018 and 252 reports during the period of January 1 to March 15, 2019. (11-13) Medical device monitoring centres have been established by government; number increases from 10 in 2015 to 26 in 2018 and further identifying new monitoring centres across the country**.** For encouraging culture of reporting, Indian pharmacopoeial commission is raising awareness about the programme among stakeholders, developing 'user-friendly' tools and guidelines, and conducting training for hospital personnel. Currently MDAER form is in English language only and to enhance participation of patients and users from different regions, commission is working for providing form in commonly used languages in India '(Hindi, Punjabi, Bengali, Tamil, Telugu**,** Malayalam, Gujarati, and Marathi)'. Mobile application for reporting of device related adverse event is also under development that will ease the access to MvPI. National database for medical device adverse events is developing for 'analysing and management' of adverse events reports to encourage coding of terminologies related to 'medical device adverse events'. (13)

5. 'Case studies'

'Case study 1'- Johnson& Johnson faulty hip implant case study

In 2006, J&J subsidiary DePuy Orthopaedics registered 'ASR XL' Acetabular and ASR hip resurfacing systems for the import and marketing in India. Device made of chromium, cobalt and molybdenum, were used in hip replacement surgeries for people suffering joint damage from injuries or arthritis. By 2007, Australian National Joint Replacement Registry (NJRR) reported Therapeutic Goods and Administration (TGA) that DePuy ASR resurfacing hip implant was associated with unacceptably higher number of repeat surgeries. It was found that leaching of chromium and cobalt from devices cause adverse effects. ASR hip implant was withdrawn from market in December 2009. While DePuy started voluntary global recall in 2010 after a UK study showed increasing number of repeat/ revision surgeries. On the other hand, CDSCO gave fresh import license on basis of renewed registration. In 2014, first revision surgery happened in India. Total 15,289 units of ASR XL Acetabular system & DePuy ASR hip resurfacing system has been imported in India and of which only 1295 was recalled by J&J. Total of (4,700 implants) were done only and a number of 1,032 patients had been traced till March 2017 as company claimed they had trouble tracking patients. Though global recall happened in 2010, Indian drug regulators did not issue the alert until November 2013. Key Learning is the Importance of Materiovigilance programme for tracking medical device related adverse events. If 'MvPI' had existence in 2007, maybe the Indian patients would have not been suffered. (14-16)

Case study 2- Premature battery depletion in certain Medtronic pacemakers

The 'US Food and Drug Administration' (FDA) raised a caution about premature battery depletion in certain 'Medtronic implantable pacemakers' or 'cardiac

resynchronization therapy pacemakers' (CRT-Ps). Major model affected are Azure, Astra, Percepta, Serena and Solar which are used for pacing bradycardia and heart failure. Made of lithium-ion batteries and have capacitor as a key component which stores electrical energy. Patients suffered adverse events such as dizziness, short-breathes and death because device stopped functioning. All three events happened within a year of implant, on an average of seven months whereas devices are intended to last between 7.5-10 years. On May 7 2019, FDA issued an alert warning patient. Though in India, no such case has been reported for available models Astra pacemaker, Solara CRT-P and Serena CRT-P devices. The Indian regulators has also alerted patients for their safety on 20 May, 2019 in the sequence of global occurrence. (16-19)

6. U.S. Medical device Reporting

In U.S., medical devices are defined as an 'instrument', 'apparatus', 'machine', contrivance, 'implant', in vitro reagent, or other similar or related article, including a 'component part' or an 'accessory' which is recognized in the 'Official National Formulary', or the 'United States Pharmacopoeia', or any supplement to them, which is projected for use in the diagnosis of disease or other conditions, or in the 'cure', 'mitigation', 'treatment', or 'prevention' of disease, in man or other animals, or anticipated to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its primary proposed purposes". The FDA need importers, manufacturers and device user-facilities to mandatorily report the device associated adverse events to the FDA under Form FDA 3500A and voluntarily by healthcare professionals, patients, caregivers and consumers under Form FDA 3500. (20-24) The US Food and Drug Administration (FDA) classify 'medical devices' into three classes: Class I, Class II, and Class III based on the level of control necessary to assure the safety and effectiveness of device and marketing requirements Figure 3. (6,21) Medical Device Reporting (MDR) is used as tool by FDA for post marketing surveillance of medical devices to monitor device performance, analyse benefit-risk assessment and detect potential device associated safety issues. There are differences in the Reporting of 'medical device' related adverse events in U.S. and India which are compiled in the Table 2. (4,20-24)

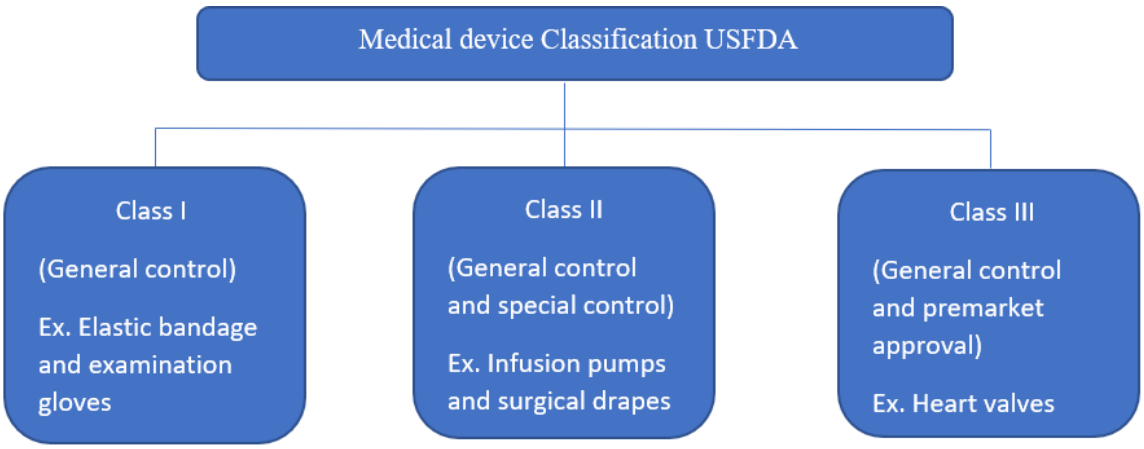

Figure 3. Medical Device Classification US (6,21)

Table 2. Differences in medical device vigilance of India and US (4,20-24)

Parameters of countries	CDSCO (India)	FDA (US)
Definition of medical devices	Include device proposed for 'internal' or 'external' use in the 'diagnosis', 'treatment', 'mitigation' or 'prevention' of disease or disorder in human beings or animals, mechanical contraceptives, disinfectants, insecticides, materials used for in vitro diagnosis, 'surgical dressings' and 'surgical bandages'	Include all instrument, implement, apparatus, machine, in vitro reagent, implant and some software that considered as medical devices.
'Medical device' Classification	4 Classes: Class I, Class II, Class III and Class IV	Three Classes: I, II and III
Basis of Classification	Risk based	Level of control and marketing requirements

Post marketing surveillance of medical device	Started in 2015 under Materiovigilance Programme of India	Started in 1990 under Safe Medical Device Act
Who can report adverse events	Manufacturers, Healthcare professionals, pharmacists, nurses, hospital technology managers, biomedical engineers	Manufacturer, importer, device user facility, patient, healthcare professionals, consumers
Criteria for reporting	Device malfunction, serious injury, death	Death, serious injury, device malfunction,
Non- reportable events	Side effects related to medical device are expected by manufacturer's labelling, exceeded shelf- life of device, root cause of event is patient's pre-existing condition, protection mechanism inbuilt in medical device functioned correctly, and deficiency found in medical device before using it.	Manufacturer can request remedial action exemption (RAE) if information received is erroneous When device is manufactured by other manufacturer
Reporting timeline	Death or serious public threat reported by manufacturer within 5 working days, 'MDAE' reporting form, 'causality assessment report', corrective, preventive action within 30 calendar days by manufacturer and health care professional.	30 calendar days- Death, severe injury and malfunction 5 working days- events requiring remedial action are reported by manufacturers. 30 calendar days- Importers need to report death, serious injuries and malfunctions. 10 working days- User facility report, 'device related death' and 'device related serious injury' and 'annual summary of death & serious injuries' by January 1 of preceding year.
Types of Reports	Initial Reporting; Trend Reporting; Final Reporting	30-day report 5-days report Individual adverse event reports Baseline report Supplemental report Semi-annual reports Annual report
Applicable forms	'Medical Device Adverse Event Reporting' (MDAER) Form 'Field Safety Corrective Action' (FSCA) Form	FDA 3500 FDA 3500A FDA 3419 FDA 3381 FDA 3417

7. Conclusion

This article thoroughly analyzed the Materiovigilance programme of India, challenges involved in reporting, future directions and case studies. From this article, some important facts stood out such as Medical devices are being widely used in recent years in India and carry the risk which might lead to adverse events. Despite that, there was no vigilance programme to protect the patients from adverse events related to medical devices. So, 'MvPI' is an enormous proposal by Government of India to document, analyse, scrutinize and prevent the reoccurrence of adverse effects due to medical devices. Guidelines have been laid down in Guidance document- 'Materiovigilance programme of India' '(MvPI)' version 1.1 which prevent errors from reoccurring and effective implementation of this program will safeguard the health of device user by preventing recurrence and risk associated with medical device. (25-30)

Acknowledgements

We would like to express our gratitude to Delhi Pharmaceutical Sciences and Research University for inspiring us to publish this article.

Financial Disclosure statement: The author received no specific funding for this work.

Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this article.

References

1. Gupta SK. Medical Device Regulations: A Current Perspective. J Young Pharm. 2016; 8(1):6–11
2. CDSCO. Medical Device Rule [Internet]. Ministry of Health & Family Welfare Government of India; 2017 [cited 2019 Sept 2]. Available from:

https://cdsco.gov.in/opencms/opencms/system/modules/CDSCO.WEB/elements/download_file_division.jsp?num_id=MzMzNg==

3. CDSCO. Classification of Newly Notified Medical Devices to be updated with Classification list of Medical Devices and IVDs, Drug Controller General (India) [Internet] India: CDSCO; 2019 [cited 2019 Jul 12]. Available from: https://cdsco.gov.in/opencms/opencms/system/modules/CDSCO.WEB/elements/download_file_division.jsp?num_id=NDM5Ng==
4. Guidance Document: Materiovigilance Programme of India (version 1.1) [Internet]. IPC;2009 [cited 2019 Sept 9]. Available from: http://www.ipc.gov.in/news-highlights/574-guidance-document-materiovigilance-programme-of-india-version-1-1.html
5. Rani SD, Singh KD. Materiovigilance: An Emerging Discipline. Int J Sci Res. 2018 June;7(6):15–6.
6. Chauhan P, Zarreen A, Iqubal Mk. Current Status of Materiovigilance Globally-an Utter Overview with Clinical Case Perusal. Int J Pharm Pharm Sci. 2019;11(10):1–8.
7. Kumar P, Kalaiselvan V, Kaur I, Thota P, Singh GN. Materiovigilance Programme of India (MvPI): A Step Towards Patient Safety for Medical Devices. Eur J Biomed Pharm Sci. 2016;3(12):497–501.
8. Gupta P, Janodia MD, Jagadish PC, Udupa N. Medical device vigilance systems: India, US, UK, and Australia. Med Devices Evid Res. 2010;3(1):67-79.
9. Medical devices Imports: Single regulatory framework likely for all medical devices. The Economics Times [Internet]. 2019 Oct 14 [cited 2019 Dec 23]. Available from: https://economictimes.indiatimes.com/industry/healthcare/biotech/healthcare/single-regulatory-framework-likely-for-all-medical-devices/articleshow/71450245.cms?from=mdr.
10. India strengthens medical device regulation. ICIJ [Internet]. 2019 Oct 21 [cited 2019 Dec 20]. Available from: https://www.icij.org/investigations/implant-files/india-strengthens-medical-device-regulation.
11. Nautiyal S. MvPI reports 1,213 medical devices adverse event reports from across country since 2014 [Internet]. Mumbai: Pharmabiz;2019 [cited 2019 December 15]. Available from: http://www.pharmabiz.com/NewsDetails.aspx?aid=117476&sid=1.
12. Implant Files – First official red flags: over 500 adverse events. The Indian Express [Internet]. 2018 Nov 26 [cited 2019 Dec 23]. Available from: https://indianexpress.com/article/india/implant-files-first-official-red-flags-over-500-adverse-events-5463990/
13. Shukla S, Gupta M, Pandit S, Thomson M, Shivhare A, Nath G. Implementation of adverse event reporting for medical devices, India. Bull World Health Organ. 2020 Mar 1; 98(3):206.
14. Shocking negligence: on need for materio-vigilance. The Hindu [Internet]. 2018 Aug 30 [cited 2019 Jan 8]. Available from: https://www.thehindu.com/opinion/editorial/shocking-negligence/article24823109.ece
15. J&J's subsidiary hip replacement row: A detailed timeline of events that hit this global giant. The Economic Times [Internet]. 2018 Sep 4 [cited 2019 Jan 14]. Available from: https://economictimes.indiatimes.com/…
16. Therapeutic Goods Administration. Recall of DePuy Orthopaedics ASR hip replacement device [Internet]. 2011 May 16 [cited 2019 Dec 23]. Available from: https://www.tga.gov.au/behind-news/recall-depuy-orthopaedics-asr-hip-replacement device
17. After US FDA, CDSCO issues device alert on 3 Medtronic pacemakers. The Indian Express [Internet]. Indianexpress; 2019 May 19 [cited 2019 Jun 20]. Available from: https://indianexpress.com/article/business/companies/after-us-fda-cdsco-issues-device-alert-on-3-medtronic-pacemakers-5735462/
18. Product Information Notice [Internet]. Medtronic; 2019 [cited 2019 Jul 22]. Available from: https://www.medtronic.com/in-en/patients/product-information-notice.html
19. USA. Food and Drug Administration. FDA issues alert on potential premature battery depletion of certain Medtronic implantable pacemakers, approves related enhancements to device [Internet]. 2019 May 7 [cited 2019 Jul 4]. Available from: https://www.fda.gov/news-events/fda-brief/fda-brief-fda-issues-alert-potential-premature-battery-depletion-certain-medtronic-implantable
20. Medical Device Overview [Internet]. US FDA; 2018 [cited 2019 Nov 11].Available from: https://www.fda.gov/industry/regulated-products/medical-device-overview
21. Classify Your Medical Device [Internet]. US FDA; 2020 [cited 2019 Nov 16]. Available from: https://www.fda.gov/medical-devices/overview-device-regulation/classify-your-medical-device
22. Medical Device Reporting (MDR): How to Report Medical Device Problems [Internet]. US FDA; 2020 [cited 2019 Aug 07]. Available from: https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems#voluntary
23. Medical Device Reporting for Manufacturers Guidance for Industry and Food and Drug Administration Staff Preface Public Comment [Internet]. US FDA; 2016. [cited 2020 Mar 23]. Available from: https://www.fda.gov/media/86420/download
24. Mandatory Reporting Requirements: Manufacturers, Importers and Device User Facilities [Internet]. US FDA; 2020 [cited 2020 Mar 23]. Available from: https://www.fda.gov/medical-devices/postmarket-requirements-devices/mandatory-reporting-requirements-manufacturers-importers-and-device-user-facilities
25. Markan S, Nath R, Sharma J, Chekuri DK. Indian Medical Device Sector - Blue Print & Regulatory Policy Roadmap. Int J Drug Reg Affairs [Internet]. 2020Jun.22 [cited 2020 Sept.18];8(2):25-. Available from: http://ijdra.com/index.php/journal/article/view/392
26. Tikoo S, Shukla VK. Global scenario of Medical Device vigilance system. Int J Drug Reg Affairs [Internet]. 2020Mar.16 [cited 2020 Sept.18];8(1):36-3. Available from: http://ijdra.com/index.php/journal/article/view/381
27. Jayanti VR, Madisi P, Murthy KVR. Requirements for introducing Medical devices in India and US market - A comparative study of regulations. Int J Drug Reg Affairs [Internet]. 2018Dec.15 [cited 2020 Sept.18];6(4):9-20. Available from: http://ijdra.com/index.php/journal/article/view/279
28. Budhwaar V, Rohilla Y, Choudhary M, kumar P. Regulations of registration and import of Medical device in India. Int J Drug Reg Affairs [Internet]. 2018Mar.15 [cited 2020 Sept.18];6(1):8-12. Available from: http://ijdra.com/index.php/journal/article/view/222

29. M AA. Regulatory environment for Medical devices in New Zealand. Int J Drug Reg Affairs [Internet]. 2018Mar.19 [cited 2020 Sept.21];5(1):1-12. Available from: http://ijdra.com/index.php/journal/article/view/191
30. Kulshreshtha C, Venkatesh MP, Shrisha K, Kumar PT, Kumar PT. CLINICAL TRIAL IN INDIA: RISE AND FALL. Int J Drug Reg Affairs [Internet]. 2015Mar.6 [cited 2020 Sept.19];3(1):1-13. Available from: http://ijdra.com/index.php/journal/article/view/11