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Review Article

Global scenario of Medical Device vigilance system

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Abstract

Patient all over the world depend on wide array of medical devices for diagnosis and management of diseases. Medical devices are considered as crucial component for patient care. It is difficult to establish a global definition of medical devices, as different countries have numerous regulatory bodies overseeing the market of medical devices. As per Global Harmonization Task Force (GHTF) definition, the term medical devices means any instrument, apparatus, implement, machine, appliance, implant, in vitro reagent and calibrator, software, material or other similar or related article intended by the manufacturer to be used alone or in combination for human beings for diagnosis, prevention, monitoring, treatment or alleviation of disease. Pharmacovigilance system is a branch of pharmacological science dealing with reporting of adverse reaction events which are caused by medicines and medical devices. Adverse event can have a major effect on population and hence is one of the potential concerns of public health which requires continuous recording, evaluation and monitoring. To achieve uniformity among the national medical device regulatory systems and increase the access to safe, effective, and clinically beneficial medical technologies, the Global Harmonization Task Force (GHTF) was conceived in 1992 by five members: European Union, United States, Australia, Japan, and Canada. All regulated countries have clearly defined medical devices, as has the GHTF. Although GHTF has tried to achieve harmonization with respect to medical devices, some differences still exist in the national laws of the countries of GHTF. Further, regulated countries have classified medical devices on the basis of their associated risk. India is lagging behind in medical device regulations, although now it is moving towards harmonizing its medical device regulations with those of regulated countries, this study aims to identify vigilance system of medical devices in various countries.

Keywords: Medical Devices, Vigilance, Regulatory Systems, GHTF

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1. Introduction

The term "medical device" comprises a wide variety of products from wound covering, cutting of tissues, or holding up open clogged arteries to computerized highly sophisticated diagnostic devices and medical equipment. Manufacturing, distribution and sale of devices need to be regulated in order to ensure their safety, quality and efficacy as they include a broad category in type and most vital for patient care. United States initiated the post marketing surveillance of medical devices under section 522 for class II and class III devices with sanction of Food and Drug Administration Modernization Act 1970. (1-3)

Table 1 Medical device act and history

Year	Act
1970	Food and Drug Administration Modernization Act (FDAMA) for post market surveillance
1989	Therapeutic Goods Act (TGA) that focused on harmonization of medical devices
1993	Council Directives: 90/385/EEC(MD) 93/42/EEC (IVD) Amended in 2007 Council directives: 2017/745(EUMDR) 2016/746(EUIVDR)

2015	Materiovigilance Programme of India (MvPI) under Central Drug Standard Control Organization (CDSCO)

To achieve uniformity between the national medical device regulatory systems and to increase the access to safe, effective, and clinically beneficial medical technologies, the Global Harmonization Task Force (GHTF) was conceived in 1992 by five members: European Union, United States, Australia, Japan, and Canada wherein the vigilance of devices was among the study groups.

All regulated countries have distinctly defined medical devices, but GHTF defined a medical device as any instrument, apparatus, implement, machine, appliance, implant, in vitro reagent or calibrator, software, material, or other similar or related article, which is thereby intended to be used by the manufacturer for human beings for one or more of the specific purposes of:

- Diagnosis, prevention, monitoring, treatment, or alleviation of disease or compensation for an injury
- Investigation, replacement, modification, or support of the anatomy or of a physiological process
- Supporting or sustaining life
- Control of conception
- 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 and which does not achieve its primary intended action in or on the human body by pharmacological, immunological, or metabolic means, but which may be assisted in its function by such means.

The Medicines and Healthcare products Regulatory Agency (MHRA) has excluded materials used for disinfecting medical devices from the definition, whereas the Therapeutic Goods and Administration (TGA) has excluded tampons and hospital, household, and commercial grade disinfectants. However, to date, India has considered medical devices as drugs.

2. Materiovigilance Programme of India (1,3,4)

Materiovigilance programme of India (MvPI) was approved by Ministry of Health and Family Welfare on 10/02/15 as National Collaborating Centre and National Health System Resource Centre (NHSRC), New Delhi is the technical support and resource center. The MvPI was formally launched on 6th July 2015 at Indian Pharmacopoeia Commission (IPC) Ghaziabad by DCG India. Presently, MvPI is having 10 dedicated functional medical device adverse event monitoring centers (MDMCs) all over the country. All the Adverse Drug Reaction Monitoring Centers (AMCs) under PvPI has also been entrusted to report adverse events due to use of medical devices. It aims to monitor the safety of medical device in country.

Objectives of MvPI

- Create a system for monitoring safety of patient.
- Helps in risk-benefit assessment of medical devices.
- Assist CDSCO in decision making process on use of medical devices.
- Generate data based on evidence for safety of medical devices.
- Convey medical devices safety information to various stakeholders in order to reduce the risk.
- Evidence based data generation on safety of medical devices.
- To upsurge as a national center of excellence for materiovigilance activities.
- Promote collaborations with other international agencies and healthcare organizations for exchange of information and data management.

List of institutions under MvPI

- Department of Biomedical Engineering PGIMER, Chandigarh
- Department of Biomedical Engineering, CMC Vellore
- Department of Biomedical Engineering, AIIMS Trauma Centre, New Delhi
- Department of Biomedical Engineering, PGIMS, Rohtak
- Department of Biomedical Engineering, DMCH, Ludhiana
- Department of Biomedical Engineering, SGSM College & KEM Hospital, Mumbai
- Division of Health Care Technology, National Health System Resource Centre, New Delhi
- Department of Biomedical Engineering, AIIMS, Patna
- Department of Biomedical Engineering, NIMS, Hyderabad
- Department of Biomedical Engineering, KMCH, Kolkata

Data Flow (3)

After the enrollment of medical institute as AMC/MDMC then the Adverse Drug Monitoring Centers starts sending Medical Device Adverse Event (MDAE) Reports to NCC-MvPI. If found valid then they are evaluated and put up to the Core Technical Committee (CTC) for any recommendation to the national regulatory authority. In case if data is not valid or complete then reports are sent back to concerned AMCs/MDMCs. Additionally, to this query or necessary

comments are also made so that respective report can be corrected or completed and sent to NCC again for evaluation.

3. Organizational Structure

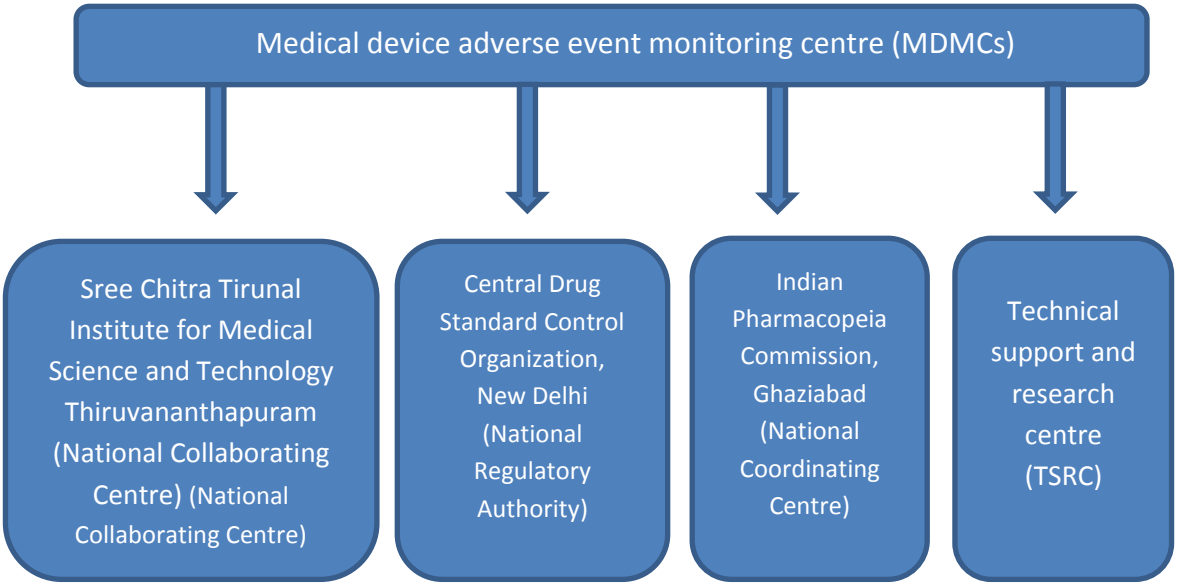

Figure 1.1 Medical device adverse event monitoring centre (MDMCs)

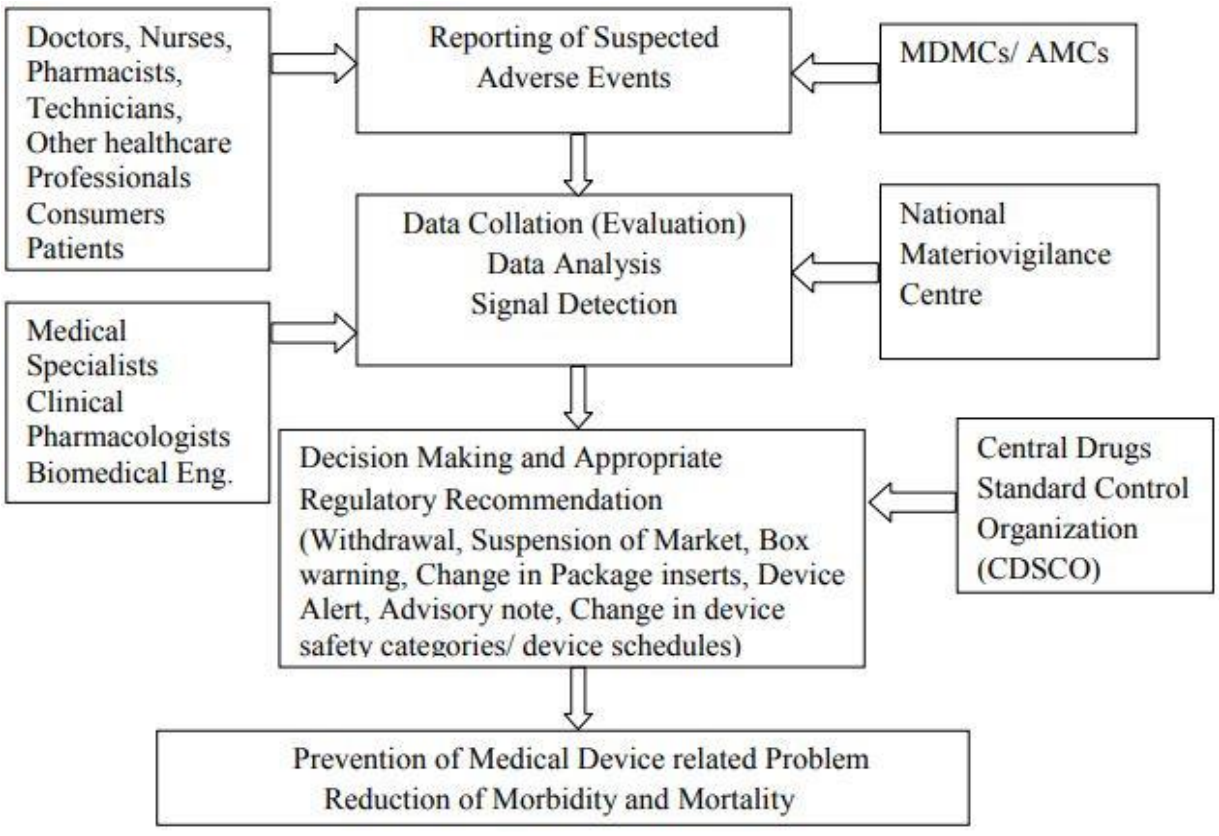

Figure 1.2 Medical device adverse event monitoring centre (MDMCs)

MvPI Communications: Key for successful functioning of MvPI is efficacious program communication. The given chart demonstrates continuous transfer of data information and knowledge

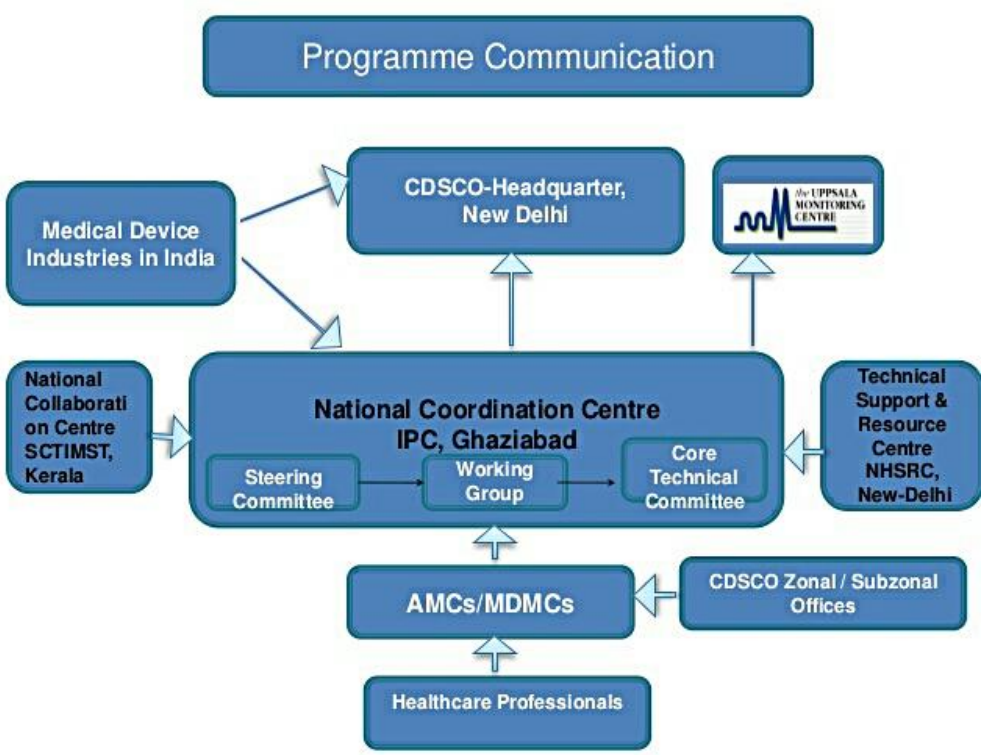

Figure 2. MvPI Program Communication

Table 2 Roles and Responsibilities of each unit

Centre	Responsibilities
Medical device adverse event monitoring center (MDMCs)	• Monitor completeness of adverse events • Analyze failure and access causality • Send monthly report to National Collaborating Centre
Sree Chitra Tirunal Institute for Medical Science and Technology Thiruvananthapuram (National Collaborating Centre)	• Communicate the outcome of report to NCC (National Coordination Centre) • Conduct awareness programs
Indian Pharmacopeia Commission, Ghaziabad (National Coordinating Centre)	• Coordinates with all stakeholders • Recognize new MDMCs • Prepare SOP, guidance doc etc • Formulates data from SCTIMST and recommend to CDSCO
Central Drug Standard Control Organization, New Delhi (National Regulatory Authority)	• Formulates regulatory decisions and communicates to different stakeholders
Technical support and research centre (TSRC)	• Provides technical support to NCC and National coordination Centre for preparation of SOP, guidance doc, newsletters and training manuals • Helps in identifying new adverse event monitoring centers

4. Reporting System (4)

Medical devices have several adverse effects. It is responsibility of stakeholder to report adverse events associated with use of medical devices to safeguard public health. Materiovigilance Programme of India includes reporting of all types of medical devices related adverse events. They can be known as unknown, serious and non-serious, frequent or rare. Under MvPI clinicians, biomedical engineers, pharmacist, hospital technology, nurses, technicians, medical device manufacturers or traders can report medical device related adverse events to National Co-ordination Centre ie NCC-MvPI, IPC Ghaziabad. Adverse event can be reported on "Medical Device Adverse Event (MDAE) reporting form" which is available at www.ipc.gov.in

US Regulatory System *(5,6)*

Medical device reporting is one of the tools used by FDA to access risk benefit ratio of the product, to monitor device performance and to detect potential device related safety issues. Annually, several hundred thousand medical device related issues are reported to FDA which includes device associated deaths, serious injuries and malfunctions. As per the Center for Devices and Radiological Health (**CDRH**) report the current system of medical device post market surveillance in United States rely primarily upon the given sources for identifying potential issues with medical devices:

- **Medical Device Reporting (MDR):** FDA annually receives several hundred thousand reports of confirmed or possible medical device related malfunctions, serious injuries, and deaths. Limitations of this passive surveillance system include incomplete, inaccurate, and/or delayed data reporting; underreporting of events; and lack of information on the total number of devices on the market in clinical use.
- **Medical Product Safety Network (MedSun).** FDA receives about 5,000 higher quality reports each year on device use and adverse outcomes from a network of 280 U.S. hospitals. The network "can be used for targeted surveys and clinical research" and has specialty subnetworks that focus on particular device types (HeartNet), laboratories (LabNet), or patients (KidNet).
- **Post-Approval Studies:** Such studies may be ordered by FDA as a condition of approval for a PMA device. These studies are typically "used to assess device safety, effectiveness, and/or reliability including longer-term, real-world device performance."
- **Postmarket Surveillance Studies**: FDA may order a manufacturer of a Class II or Class III device to conduct a 522 study (FFDCA Section 522) if failure of the device is reasonably likely to have serious adverse health consequences, if it is expected to have significant use in pediatric populations, or if it (1) is intended to be implanted for longer than one year or (2) has life-supporting or life-sustaining use outside a device user facility. Approaches used in 522 studies "vary widely and may include nonclinical device testing, analysis of existing clinical databases, observational studies, and, rarely, randomized controlled trials."
- **FDA Discretionary Studies:** In addition to those mentioned above, FDA "conducts its own research to monitor device performance, investigate adverse event signals and characterize device-associated benefits and risks to patient subpopulations." Sources of privacy-protected data for these studies include "national registries, Medicare and Medicaid administrative and claims data, data from integrated health systems, electronic health records, and published scientific literature."
- **Other Tools:** Identified in the appendix of the September 2012 FDA report

Postmarket Surveillance Studies ("522 Studies") (6)

While the term postmarketing surveillance refers to a wide range of programs, the term postmarket surveillance refers to a specific activity defined in law. For certain class II and class III devices, FDA may order a manufacturer to conduct a postmarket surveillance study also called a 522 study once the device is approved or cleared for marketing in order to gather safety and efficacy data. A postmarket surveillance study may be ordered if

- device failure would be reasonably likely to have serious adverse health consequences;
- the device is expected to have significant use in pediatric populations;
- the device is intended to be implanted in the body for more than one year; or
- the device is intended to be a life-sustaining or life-supporting device used outside a device user facility.

Mandatory medical device reporting *(7,8)*

21CFR Part 803 is the regulation for medical device reporting. MDR reportable events is defined as an event that a user facility become aware of that reasonably suggests if a device has or may have caused or contributed to a death or serious injury of a patient. It contains mandatory requirements for manufacturers, importers and device user facilities to report certain device related adverse events and product problems to FDA

Table 3 Mandatory reporting requirements (9)

Reporter	What to report	Report form	To whom	When
Manufacturers	30 day report of deaths, serious injuries and malfunctions	Form FDA 3500A	FDA	Within 30 calendar days of becoming aware of event
	5 day report for an event designated by FDA or an event that requires remedial action to prevent an unreasonable risk of substantial harm to public health	Form FDA 3500A	FDA	Within 5 working days of becoming aware of an event
Importers	Reports of death and serious injuries	Form FDA 3500A	FDA and manufacturer	Within 30 calendar days of becoming aware of event
	Reports of malfunctions	Form FDA 3500A	manufacturer	Within 30 calendar days of becoming aware of event
Device user facilities	Device related death	Form FDA 3500A	FDA & manufacturer	Within 10 working days of becoming aware of an event
	Device related serious injury	Form FDA 3500A	manufacturer FDA only if manufacturer	Within 10 working days of becoming aware of an event

			unknown	
	Annual summary of death and serious injury reports	Form 3419	FDA	Jan 1 of the preceding year

Medical Device Tracking *(10)*

"Manufacturers are required to track certain devices from their manufacture through the distribution chain when they receive an order from [FDA] to implement a tracking system for a certain type of device." Device tracking ensures that manufacturers of these devices can locate them quickly, if needed once in commercial distribution, to facilitate notifications and recalls if serious risks to health are associated with a particular device. FDA may issue a tracking order for any Class II or Class III device:

- the failure of which would be reasonably likely to have serious adverse health consequences;
- which is intended to be implanted in the human body for more than one year; or
- which is intended to be a life-sustaining or life-supporting device used outside a device user facility.

FDA has issued orders to track a number of implantable devices (including silicone-gel filled breast implants, certain joint prostheses, implantable pacemakers, implantable defibrillator, mechanical heart valves, and implantable infusion pumps) and various other devices that are used outside a device user facility.

Electronic Medical Device Reporting (eMDR) *(11)*

Specific requirements for the submission of postmarket MDRs to FDA are in 21 CFR Part 803.eMDR submission is a file containing one or more medical device reports in an electronic format that FDA can process, review, and archive. The MDR regulation (21 CFR Part 803) specifies the types of reports and the data elements required in an MDR. An eMDR contains the same data elements. Importers must include the information specified in 21 CFR 803.42. Manufacturers must include the information specified in 21 CFR 803.52. User facilities must include the information specified in 21 CFR 803.32. Although the eMDR Final Rule permits user facilities to continue to submit MDRs on paper, user facilities may instead choose to submit MDRs in an electronic format.

Table 4 Difference in vigilance system of United States and India (1)

Parameters	US	India
Definition	includes all instruments, appliances, materials, machines, in vitro diagnostic agents, implants, software, accessories, and disinfectants	10 device category regulated as drug
Medical device classification	3 classes: class i, class ii, and class iii	
Basis of classification	Level of control Medical specialties	NA
Postmarketing surveillance activities	Medical device tracking MDR MDR event files, records, and written procedures complaint handling Recall procedure and seizures	Adverse event reporting For Importers Complaint handling Adverse event reporting Procedure for distribution of records
Medical device tracking	Have established tracking system since 1993	in labeling provisions, the lot number/batch number for device is mandatory for easy traceability
Who need to report AE	Manufacturers, importers, user facilities, users, distributors, and health professionals	Manufacturers only
Criteria for reporting	Death or serious injury Device malfunctions User error injury / illness requiring medical intervention	Event has occurred Medical device's association with the event that might lead to death/ serious injury
Not-reportable incidents/events	Manufacturers can apply for RAE, eg, Erroneous information When other manufacturer makes the device	Root cause of the adverse event is due to the patients' preexisting condition. Exceeded service life of device Likelihood of adverse event is acceptable after risk assessment Side effects clearly identified in the manufacturer's labeling and documented in device master record.
Reporting time frame	Manufacture: death, serious injury,	Unanticipated death or serious injury

	and malfunctions – 30 calendar days, and events requiring immediate remedial action – 5 working days User facility: death and serious injury – 10 working days Distributors and importers: death, serious injury, and malfunction to manufacturer – 10 working days	within 10 days All other reportable events not later than 30 elapsed calendar days.
Types of report	30-day reports 5-day reports Baseline reporting supplemental reporting	Initial reporting Trend reporting Final reporting
Applicable forms	Form 3500 – online Form 3500A for manufacturers, importers, and distributors Form 3419 Form 3417 Form 3381	Adverse Event Reporting Form
Records	AE records Evaluation records Records for follow-up and inspection investigation protocol copies of test, laboratory reports, and service records	A mandatory specification for importers only
Recall	Manufacturers need to initiate recall	A mandatory specification for importers only
Recall communication	Telephone calls, telegrams, and mailgrams First class letters approved by FDA General public warning Public warning through specialized news media	

5. Conclusion

Even after several efforts by founding members of GHTF, in order to achieve uniformity for regulations of medical devices however differences still occur. Similar to ICH major differences are required to be eliminated to enable the introduction by manufacturer both in developing and developed nations. By considering these differences the aim of harmonization should not only improve the health of patient but also promote international trade. For this India has started an adverse event reporting system which is in uniformity with that of regulated countries. Therefore CDSCO should support the adaptation of existing vigilance system to maintain a national system of controls thereby introducing timely amendments. For example

- Medical devices should clearly be defined and classified on basis of risk involved.
- Similar to United States, reporting time frame should not only consider manufacturer but also user facility and distributors.
- Distinct tracking provisions for tracking of devices must be included in regulations.
- Vigilance exchange program need to be incorporated by CDSCO.
- Like United States eMDR, CDSCO should also establish an online reporting system.
- Establishment of specific format for FSCA and FSN.
- Unlike the FDA, CDSCO should define distinctly the enforcement actions including a recall system in case of breach of regulations.

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Conflict of Interest

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

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