ISSN 2581-6217

World Journal of Pharmaceutical Science & Technology

Journal homepage: www.wjpst.com

Review Article

PHARMACOVIGILANCE DATA MANAGEMENT AND CASE PROCESSING: CURRENT AND FUTURE SCENARIO

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Received: 15-1-2022, Revised: 29-1-2022, Accepted: 31-1-2022

ABSTRACT

Pharmacovigilance is defined by the World Health Organization (WHO) as "the science and practises relating to the detection, evaluation, understanding, and prevention of adverse drug reactions and other medicine-related problems." Pharmacovigilance's definition and scope have developed as a result of a systems approach. As a result, pharmacovigilance is a delicate field. It involves keeping an eye on the safety of drugs and taking steps to limit risk while maximising benefit. The management of pharmacovigilance data is not only inefficient, but it is also ineffective. As a result, establishing a comprehensive pharmacovigilance data management system that conforms with severe regulatory criteria, worldwide pharmaceutical conventions, and ultimately protects the pharmacovigilance end users, the patients, is critical. Implementation of business management software would be an ideal approach for improved data management, process harmonisation, data security, and time savings due to excessive manual labour dependency. In pharmacovigilance, case processing is a fundamental activity. It provides data for the analysis of adverse effects that allows to detect new safety concerns and to periodically assess the benefit to risk ratio associated with the use of a pharmaceutical product. The precision and quality of safety data processing, also from the medical point of

view, is crucial for ensuring correct analysis and undertaking corrective actions in timely manner, which in turn helps to safeguard the health of the patients and allows safe use of the drug. Consequently, every company that markets even a handful of products across many countries, gathers thousands of reports per year. The only way to manage this data load is using latest software and automation

KEYWORDS:- ICSR, causality assessment, benefit-risk profile, safety database, automating case processing

INTRODUCTION:-

Pharmacovigilance is the pharmacological science relating to the detection, assessment, understanding and prevention of adverse effects, particularly long term and short term side effects of medicines. Generally speaking Pharmacovigilance is the science of collecting, monitoring, researching, assessing and evaluating information from healthcare providers and patients on the adverse effects of medications, biological products, herbalism and traditional medicines with aims :

- Identifying new information about hazards associated with medicines
- To improve patient care and safety
- To improve public health and safety
- Contributing to assessment of benefit,harm, effectiveness and risk of medicines
- To promote rational and safe use of medicines

Pharmacovigilance starts from the clinical stage and continues throughout the product life cycle of the drug, mainly divided as pharmacovigilance during clinical phase and post-marketing. The process of collection of such information about a drug begins in Phase I of the clinical trial, before approval of the drug, and continues even after approval; several post-market safety studies are conducted, with many made mandatory by drug regulatory agencies around the world.

Pharmacovigilance is particularly concerned with adverse drug reactions, or ADRs, which are officially described as:

*"*A response to a drug which is noxious and unintended, and which occurs as doses normally used for the prophylaxis, diagnosis, therapy of disease, or for the modification of physiological function." understanding, and prevention of adverse drug reactions and other medicine-related problems.

Pharmacovigilance is gaining importance for doctors and scientists as the number of stories in the mass media of drug recalls increases. Because clinical trials involve several thousand patients at most; less common side effects and ADRs are often unknown at the time a drug enters the market. Even very severe ADRs are often undetected because study populations are small. Post marketing surveillance uses tools such as data mining of spontaneous reporting systems and patient registries, and investigation of case reports to identify the causality, relationship between drugs and ADRs.

The initial phase in pharmacovigilance data management is data collecting, which includes addressing the report's origin, triaging cases, entering information into a drug safety database, doing medical

assessments, requesting report follow-up information, and submitting reports on time. All of these processes require a high and sophisticated degree of technical expertise and judgement to ensure that proper decisions are achieved during the formulation of a product's benefit-risk profile. Then data flows to database for processing. Then medical evaluation, analysis of processed data and signal identification is done. The safety monitoring of data is gaining more importance due to:

- Capture of complete safety data
- To fulfill ethical requirement
- To avoid serious consequences due to to non compliance.

MATERIAL AND METHODS:-

SAFETY DATA MANAGEMENT

A Serious Adverse Event for a molecule could be generated during the preregistration or postmarketing phase. They could occur during clinical trials or be reported spontaneously by a patient, caregiver, relation, doctor, nurse or pharmacist. Another regulatory body or a licencee company could also be the informant. It could be received on phone, mail, fax, journals, newspapers or the latest social media.

Unexpected adverse events could arise anytime in the life of a product. These could put the user to serious risk and could curtail the life of the product. As part of the risk management plan, safety data is gathered throughout the life of a product.

The steps in safety data management are as:

- **Data collection and verification**
- **Validation**
- **Duplicate search**
- **Triage**

DATA COLLECTION AND VERIFICATION

Competent authorities and marketing authorisation holders should take appropriate measures to collect and collate all reports of suspected adverse reactions associated with medicinal products for human use originating from unsolicited or solicited sources. The system should be designed so that it helps to ensure that the collected reports are authentic, legible, accurate, consistent, verifiable and as complete as possible for their clinical assessment.

Sources of data

A: Unsolicited reports

A.1 Spntaneous reports :

A spontaneous report is an unsolicited communication by a healthcare professional, or consumer to a competent authority, marketing authorisation holder or other organisation (e.g. regional pharmacovigilance

centre, poison control centre) that describes one or more suspected adverse reactions in a patient who was given one or more medicinal products. It does not derive from a study or any organised data collection systems. With regard to this, the following situations should also be considered as spontaneous reports:
stimulated reporting that occurs consequent to a direct healthcare professional communication

- Publication in the press, questioning of healthcare professionals by company representatives, communication from patients' organisations to their members, or class action lawsuit; unsolicited consumer adverse reactions reports irrespective of any subsequent "medical confirmation"
- Reports of suspected adverse reactions, which are not related to any organised data collection
- Systems which are notified through medical enquiry/product information services and which are consequen0t of the distribution of information or educational materials, unsolicited reports of suspected adverse reactions collected from the internet or digital media
- ICSR; an individual case notified by different reporters, and at least one notification is done
- spontaneously; reports of suspected adverse reactions from non-interventional post-authorisation studies related to specified adverse events for which the protocol does not require.

A.2 Literature reports :

The medical literature is a significant source of information for the monitoring of the safety profile and of the risk-benefit balance of medicinal products, particularly in relation to the detection of new safety signals or emerging safety issues. Marketing authorisation holders are therefore expected to maintain awareness of possible publications through a systematic literature review of widely used reference databases (e.g. Medline, Excerpta Medica or Embase) no less frequently than once a week.

The marketing authorisation holder should ensure that the literature review includes the use of reference databases that contain the largest reference of articles in relation to the medicinal product properties . In addition, marketing authorisation holders should have procedures in place to monitor scientific and medical publications in local journals in countries where medicinal products have a marketing authorisation, and to bring them to the attention of the company safety department as appropriate. Reports of suspected adverse reactions from the medical literature, including relevant published abstracts from meetings and draft manuscripts, should be reviewed and assessed by marketing authorisation holders to identify and record ICSRs.

A.3 Reports from non-medical sources :

If a marketing authorisation holder becomes aware of a report of suspected adverse reactions originating from a non-medical source, for example the lay press or other media, it should be managed as a spontaneous report. Every attempt should be made to follow-up the case to obtain the minimum information that constitutes a valid ICSR. With regard to the submission of those ICSRs, the same modalities and time frames should be applied as for other spontaneous reports.

A.4 Information on suspected adverse reactions from the internet or digital media :

In line with ICH-E2D, marketing authorisation holders should regularly screen the internet or digital media under their management or responsibility, for potential reports of suspected adverse reactions. With respect to this, a digital medium is considered to be company sponsored if it is owned, paid for and/or controlled by the marketing authorisation holder.

The frequency of the screening should allow for potential valid ICSRs to be submitted to the competent authorities within the appropriate regulatory submission time frames based on the date the information was posted on the internet site/digital medium. Marketing authorisation holders may also consider utilising their websites to facilitate the collection of reports of suspected adverse reactions

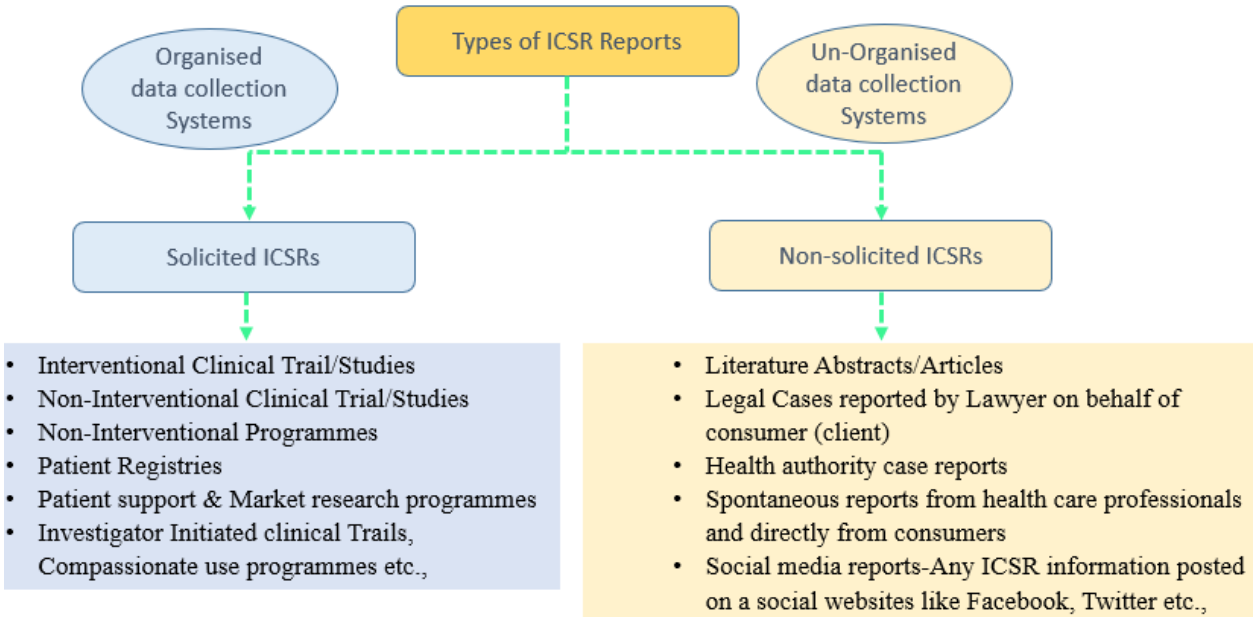
B. Solicited reports:

As defined in ICH-E2D, solicited reports of suspected adverse reactions are those derived from organised data collection systems, which include clinical trials, non-interventional studies, registries, post-approval named patient use programmes, other patient support and disease management programmes, surveys of patients or healthcare professionals, compassionate use or name patient use, or information gathering on efficacy or patient compliance.

Reports of suspected adverse reactions obtained from any of these data collection systems should not be considered spontaneous. This is with the exception of: reports of suspected adverse reactions from non-interventional post-authorisation studies related to specified adverse events for which the protocol does not require their systematic collection

for EU guidance on this type of non-interventional post-authorisation studies, and for EU guidance on the electronic submission of these ICSRs, reports of suspected adverse reactions from compassionate use or named patient use conducted in countries where the systematic collection of adverse events in these programmes is not required. With regard to the submission as ICSRs, solicited reports should be classified as study reports. They should have an appropriate causality assessment to consider whether they refer to suspected adverse reactions and therefore meet the minimum validation criteria. Valid ICSRs should be submitted in line with the time frames and modalities.

Fig.1 TYPES OF ICSR REPORTS



VALIDATION OF REPORT

Every report needs to be acknowledged, more so the valid reports. Acknowledgement establishes a contact with the reporter for more information whenever required . It builds company image with the stakeholder and also protects from litigation. A consentious reporter may continue to send the same report repeatedly till it is acknowledged, hence this simple action avoids duplication. Only valid ICSRs qualify for submission. In accordance with ICH-E2D, all reports of suspected adverse reactions should be validated before submitting them to the competent authorities to make sure that the minimum criteria are included in the reports. Four minimum criteria are required for ICSRs validation:

a. **one or more identifiable reporter** : characterised by parameters such as qualification (e.g. physician, pharmacist, other healthcare professional, lawyer, consumer or other non-healthcare professional), name, initials, or address (e.g. reporter's organisation, department, street, city, state or province, postcode, country, email, phone number). Local data protection laws might apply. In line with ICH-E2D, the term 'identifiable' indicates that the organisation notified about the case has sufficient evidence of the existence of the person who reports the facts based on the available information.

   When the information is based on second-hand or hearsay, the report should be considered nonvalid until it can be verified directly with the patient, the patient's healthcare professional or a reporter who had direct contact with the patient

b. **one single identifiable patient** : characterised by at least one of the following qualifying descriptors: initials, medical record number (from general practitioner, specialist, hospital, or investigation), date of birth, age, age group, gestation period, or gender. The information should be as complete as possible in accordance with local data protection laws. An ICSR should not be considered valid for submission unless information is available for at least one of the patient qualifying descriptors

c. **one or more suspected substance/medicinal product :** Interacting substances or medicinal products should also be considered suspected.

d. **one or more suspected adverse reaction :** If the primary source has made an explicit statement that a causal relationship between the medicinal product and the reported adverse event has been excluded and the notified competent authority or marketing authorisation holder agrees with this assessment, the report does not qualify as a valid ICSR since the minimum information for validation is incomplete (there is no suspected adverse reaction). The report also does not qualify as a valid ICSR if it is reported that the patient experienced an unspecified adverse reaction and there is no information on the type of adverse reaction. Similarly, the report is not valid if only an outcome (or consequence) is notified and (i) no further information about the clinical circumstances is provided to consider it as a suspected adverse reaction, or (ii) the primary source has not indicated a possible causal relationship with the suspected medicinal product.

DUPLICATE SEARCH:

A duplicate case refers to the same individual reported by different senders, through different routes to describe suspected adverse reaction/s related to administration of one or more medicinal products to an individual patient at a particular point of time.

Common causes of duplicate reports are:

- A consumer and healthcare professional reporting the same event/reaction occurrence
- Multiple healthcare professionals treating the same patient reporting the same event/ reaction occurrence
- An event/ reaction occurrence being reported by the original reporter to both MAH and the NCA
- Literature reporting of the same event/ reaction occurrence for generics

Due to, greater awareness , stringent regulations and multiple reporting sources, duplicate reports is a common phenomenon. Every safety management software has a facility to identify and delete duplicates. . Certain characteristics of a case (sex, age or date of birth, dates of drug exposure, clinical trial code, country, etc.) may be used to identify duplicate reporting. This action is of significance for further processing of the case. The duplicate could actually be follow up information that could alter the seriousness and hence reporting timeline of the case. Missed out duplicates could send misleading information to signal detection systems.

TRIAGE:

Once the is received at PV department of company, it must be properly classified for processing. The initial triage should be to determine the report needs urgent processing in order to be transmitted to the regulatory authorities, or business parterners. Experienced and qualified personnel should always supervise triage.

Triage means to review, assess and prioritize received information and to record minimal information required, to quickly and reliably establish the case priority regarding expediated requirements. Triage applies to all reported adverse events, special situations, and product complaints associated with adverse events from

both solicited and unsolicited reports. So, it helps to prioritize ICSRs in the safety database and placing them in correct regulatory reporting section for submission.

Triage should cover atleast, the following:

- ADRs
- Product quality complaints
- Product quality complaints associated with ADRs
- Medical inquiries
- legal

ADRs can further be triaged using the following criteria:

- Seriousness or non seriousness
- Expected or unexpected
- Causality (specially for SAEs from clinical trials)

Collins dictionary defines triage as:

(Medicine) the principle or practice of sorting casualties in battle or disaster or other patients into categories of priority for treatment

(Government, Politics & Diplomacy) the principle or practice of allocating limited resources, as of food or foreign aid, on a basis of expediency rather than according to moral principles or the needs of the recipients

Triage in safety means prioritizing the case for reporting to authorities. An oversimplification of triage would be to report deaths and life threatening unexpected reports in 7 days and other adverse reactions in 15 days as there are also other occasions where expedited reporting is required.

CASE PROCESSING

Case processing is an important part of pharmacovigilance. It provides data for the investigation of adverse effects, allowing new safety concerns to be detected and the benefit-to-risk ratio associated with the usage of a pharmaceutical product to be assessed on a regular basis. From a medical standpoint, the precision and quality of safety data processing are critical for assuring correct analysis and implementing corrective actions in a timely way, which helps to protect patients' health and ensure safe drug usage.

Case processing comprises following steps:

- **Data entry**
- **Case narrative**
- **Coding of adverse drug reaction/event**
- **Coding of drug**
- **Causality assessment**
- **Reportimg to authority**

DATA ENTRY:

A seemingly repetitive and inconsequential step in the process but something that forms the basis of good reporting. The quality of data entry affects the further processing of the case. The safety database softwares are made in such way that end user can enter data very easily and more accurately. These systems generally require additional mandatory fields like date of receipy of ADR, source country, type of source.

Details of the four pillars of a valid case have to be reported meticulously. Patient information has to follow the HIPPA code for confidentiality. Reporter information has to clear and detailed enough to be able to contact the person if necessary. Drug identifiers like name, formulation and dose, duration of exposure have to be captured correctly. Event report has to be detailed enough for the evaluator to decide on the cause of the adverse event. This would include chronological description of the event or events, nature, localisation, severity, characteristics of the event, results of investigations and tests, start date, course and outcome, concomitant medications and other risk factors .

CASE NARRATIVE:

A narrative is brief summary of specific events experienced by patient, during the course of a clinical trial/treatment. Narrative writing involves multiple activities such as generation of patient profiles, review of data sources and identification of events for which narratives are required.

The purpose of case narrative is to provide summary of identified/specific adverse events occurring in a patient to conclude casual relationship between the drug and event. During the course of safety data management, it is seen and used by various groups like case reviewers to decide seriousness, upgrade etc, affiliate companies to triage for their countries, during preparation of PSURs and other summary reports and also by regulatory authorities. One should ensure completeness, chronology and sufficient detail in a narrative so that the reader is able to come to a conclusion.

CODING OF ADVERSE REACTION:

Adverse event coding is the process by which information from an AE reporter, called the "verbatim", is coded using standardized terminology from a medical coding dictionary. The purpose of medical coding is to convert adverse event information into terminology that can be readily identified and analyzed.

This step ensures that everyone is talking the same language and the data can be shared internationally, Most commonly used system is the MedDRA(Medical Dictionary for regulatory Activities). Use of MedDRA has lead to a global standardization across regulatory agencies, across companies & across countries. This step usually needs oversight by a medically qualified person.

CODING OF DRUGS:

Both the suspect drug and concomitant medication have to be coded. The principle is again to be talking the same language across countries, companies and regulatory bodies. Most common dictionary is the WHO Drug Dictionary enhanced. This is provided as a product by the Upsala Monitoring centre of the WHO. Entries are updated 4 times a year. The majority of entries refer to prescription-only products, but some over-the-counter

(OTC) preparations are included. The dictionary also covers biotech and blood products, diagnostic substances and contrast media. For chemical and therapeutic groupings the WHO drug record number system and ATC classifications are considered.

CAUSALITY AASESSMENT:

Causality assessment is the assessment of relationship between drug and the occurrence of an adverse event. Non spontaneous case reports usually indicate whether an adverse drug reaction is suspected due to the administered drug. In these circumstances and even otherwise, a causality assessment is required to be conducted. Various approaches have been developed for the structured determination of the likelihood of a causal relationship between drug exposure and adverse events. These systems are largely based on following considerations:

- the chronology or association in time (or place) between drug administration and event
- current knowledge of nature and frequency of adverse reactions due to the suspect molecule; or the pharmacology
- medical or pharmacological plausibility based on signs and symptoms, laboratory tests, pathological findings, mechanism of action
- likelihood or exclusion of other causes for the same adverse events; often the disease condition or concomitant medication.

Data required for performing casuality asessessment in ICSRs:

- Medicinal products- All medicines that patient receiving during the time of event onset, including start date, stop date, doses and indications
- Adverse event- The detailed event description including date of onset , duration of onset and outcome of event
- Dechallenge and rechallenge information
- Patient medical history- Including past diseases of importance and other current diseases

TIMELY REPORTING TO AUTHORITIES:

This is the end goal for which all the above has to be done in a timely manner. The reporting could be by sending data back to the sponsor or by a click of a button based on the software used. Case distribution is nothing but submission of ICSRs to Regulatory Authorities.

Safety database is configured to allow automatic scheduling and generation of expediated and non expediated reports. Safety data entry associate responsible for monitoring the database worklist reports regularly to ensure appropriate and timely submission.

Safety data management is the most basic step in pharmacovigilance. This is often outsourced so that internal company resources can focus on the domain related, mentally stimulating activities like signal detection, regulatory responses, information to stakeholder.

INDIVIDUAL CASE SAFETY REPORT:

Pharmacovigilance is an important part of any healthcare system due to its ability to protect patients from harm or death caused by drugs, vaccines, and other products used in healthcare settings. ICSRs are a type of report that can be submitted on behalf of an individual patient as opposed to a group; these reports are stored in VigiBase.

What is icsr in pharmacovigilance?

The ICSR (Individual Case Study Report) is the source of data in pharmacovigilance. WHO developed a global individual case safety report database, VigiBase, and it is maintained by UMC on behalf of WHO. In this article we will discuss what an ICSR is and why they are important to the process. One purpose that pharmacovigilance provides to the public is to help understand any possible risk associated with medicines or medical devices that have been approved for use and how they should be used safely and effectively. An ICSR is the source of data in pharmaco vigilance process – it helps provide understanding about risks related to drugs/medical devices approved for usage;

ICSR Format

ISO ICSR aims at establishing the same format for the reports on individual cases of suspected side effects in patients due to a medicine across the world. It also is expected to include better information on medicines that might be associated with an adverse drug reaction and on the therapeutic uses of those medicines. In addition, the standard also strengthens personal data protection in the records of ICSRs collected by pharmaceutical companies and regulatory authorities.

This will improve the quality of data collected, and increase the ability to search and analyse them. Regulatory authorities will be able to detect and address safety issues with medicines more quickly, and therefore better protect patients.

The Importance of ICSR to Pharmacovigilance

ICSRs are important because they provide a different perspective than adverse event reports, which can be collected from multiple patients. ICSR is an individual case safety report that includes **data** on individuals who have had experience with the medical treatments or products we want to know about. These types of cases may not always represent the same information as other studies.

The individual case study report (ICSR) is an adverse event report for an individual patient and is the source of data in pharmacovigilance. The main focus of ICSRs are reports from healthcare providers and patients in member countries of the WHO Programme. A WHO global individual case safety report database (VigiBase) is maintained and developed on behalf of the WHO by the UMC.

VIGIBASE

VigiBase is the single largest drug safety data repository in the world. Since 1978, the Uppsala Monitoring Centre (UMC; established in Uppsala, Sweden) on behalf of WHO, have been maintaining VigiBase. Vigibase is used to obtain the information about a safety profile of a medicinal product. These data are used by

pharmaceutical industries, academic institutions and regulatory authorities for statistical signal detection, updating periodic reports, ICSR comparisons with company databases and studying the reporting patterns. The data is collected from each of its 110 member states. About a hundred thousand ICSRs are added each year.

COMMON ERRORS IN CASE PROCESSING AND HOW TO AVOID THEM

There is a number of quality issues that pharmacovigilance personnel performing case processing activities encounter. The most frequent issues are:

- Incomplete reports
- Discordant data
- Coding errors
- Narrative: incomplete information, spelling errors and types
- Missing or inconsistent medical assessment

Incomplete reports

In our experience, there are three main types of Incomplete Report errors:

- Missing adverse events/special situations;
- Missing co-suspect drugs, medical history, lab data;
- Missing medical review and assessment;

One of the most effective ways to avoid the problem of data incompleteness is to conduct regular training. Trainings should involve not only the pharmacovigilance staff who may receive reports from patients/HCPs, but also other company departments (e.g. marketing, legal, QA), investigators, and clinical research assistants. Moreover, it is important to ensure the quality of AE/SAE report forms in order to capture as much important information as possible. Finally, it is helpful to request the missing data directly from the reporter, especially for serious unexpected ADRs. We advise to use checklists to collect missing follow-up information in order to ease daily work of pharmacovigilance team.

Discordant data

Another common error regards the inconsistency of data. One of the most common examples is the error in the gender of the patient. In this case, the structured field can feature “female” as gender, while the narrative has a reference to a male patient or vice versa.

In order to avoid such mistakes, we advise to configure automatic data check in the security database. In this way all inconsistencies are automatically detected and reported. It is possible to set automatic control to prevent the user from continuing the work until the inconsistency is resolved.

Coding errors

Medical coding is essential for preventing spelling errors, incorrect abbreviations or non-standardised terms, but its most relevant function is to standardise and organise scattered terms into a standard parent category, which is essential for effective safety data analysis.

An appropriate and clear source of data allows to avoid coding errors. However, pharmacovigilance professionals can sometimes receive inaccurate or unclear information and abbreviations:

- Congestion – the type of congestion is not clear (nasal, liver, sinus, pulmonary…)
- Pain – the type of pain is not clear
- MI – it is not clear whether MI stand for myocardial infarction or mitral incompetence

In such cases, we advise to request clarifications directly from the reporter. If the clarifications are not exhaustive, it is advised to consult the "MedDRA Points to Consider" document, as it contains many useful examples grouped by type coding errors.

Narrative

Another common error type in narrative is inconsistency between key information present in the case narrative but missing from the structured database fields. It is crucial that all information in the narrative is correctly captured and coded in the relevant structured fields. This approach allows pharmacovigilance professionals to assess the cases quickly and facilitate consistent data retrieval. A way to avoid inconsistencies is to use the auto-narrative function of safety database. Moreover, personnel who works on case narrative should have a good knowledge of English language and should also turn on spell check in their text editor while they are writing the case narrative. Finally, it is important to involve a second person to perform a Quality Control.

Missing or inconsistent medical assessment

Clinical medical assessment of cases is a vital integrated process that is performed in order to identify a diagnosis, ensure that diagnostic procedures have been carried out, identify a suspect drugs and consider alternative causes of adverse events. Therefore, clinical medical assessment should always be consistent and complete.

HOW TO ACHIEVE QUALITY CASE PROCESSING

Case processing is a vital activity that serves as a base for decision-making in pharmacovigilance. If it is performed with precision, it allows pharmacovigilance team to analyse the safety data correctly and take corrective actions in timely manner, making sure that the drug benefits the patients in the best possible way.

There are several strategies that can help to increase the quality of case processing:

- Clear written Standard Operating Procedures.
- Additional trainings for personnel who may receive or process safety reports (e.g. clinical development, sales, medical information, legal, quality control).
- Clear and well-designed safety data collection forms.
- Quality Control performed by a second person of all data entered in database.
- Periodic checks on random samples of cases entered in database. This can be either a complete check or a check of the selected critical fields.
- KPIs monitoring and CAPAs in case of deviations.

WHY SMART CASE PROCESSING IN PV NEED AUTOMATION MORE THAN EVER BEFORE

Numerous safety databases available in the market like Oracle Argus, ARIS-G etc. are used by the industry to process and report adverse events (AEs) to local regulatory authorities.

Usually, thousands of AEs are processed manually every month by ICSR (Individual case safety report) case processing teams at pharmaceutical companies or their outsourcing partners that are involved in case intake, triage, booking, data entry, quality review and medical review of individual case safety reports in the safety database. Some of these cases are reported to regulatory authorities on an expedited basis by submission teams.

Need for transformation to smart case processing

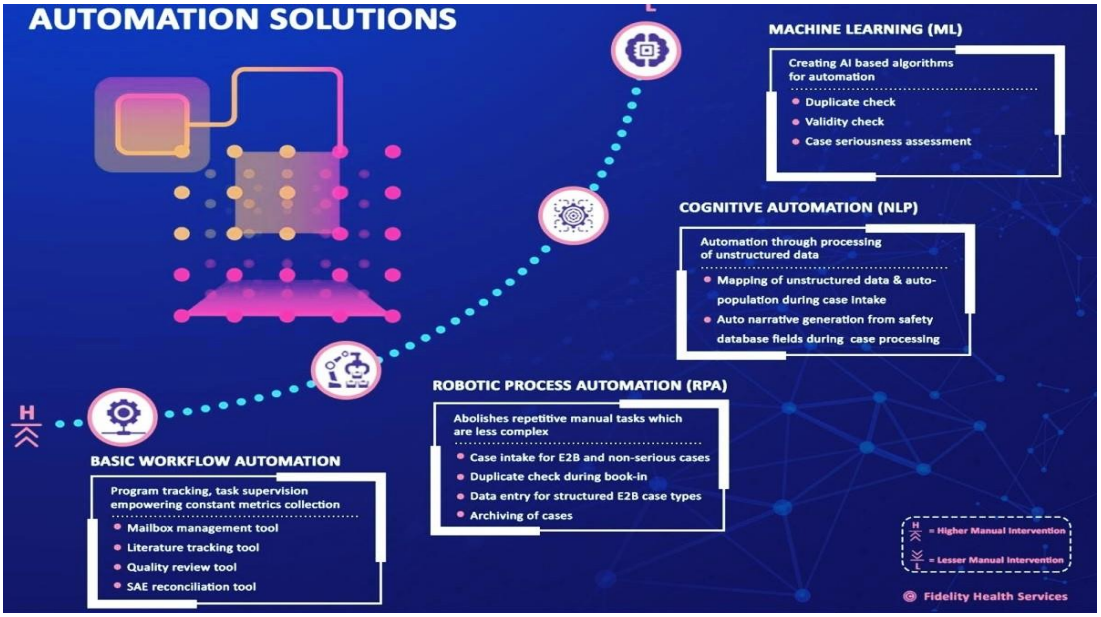
With the evolving regulatory environment and increased regulatory scrutiny, increasing disease complexity and number of drugs getting approved, growing awareness with patients and providers about reporting of adverse events, social media connectivity resulting in a huge influx of data and source documents with multiple templates or formats, there is increasing need for pharmaceutical companies to deploy and maintain more complex PV systems and manage safety surveillance activities more meticulously and proficiently than ever.

It's a need of the hour to revisit the traditional manual methods of case processing due to both the reduced supply of safety talent vis-à-vis demand and pressures on the companies to reduce the costs of manual case processing due to the increasing number of adverse events getting reported year on year.

As per the report published by Deloitte, pharmaceutical companies are allocating 40-85 % of PV budgets on case processing, and case volumes are increasing at a rate of 10-15 per cent per year.

As mentioned in the report, reducing the cost of case processing was the primary goal for 90% of respondents and survey respondents expected automation to deliver the cost savings of 30% per ICSR.

Fig.2 SMART CASE PROCESSING: AUTOMATING SOLUTIONS



Automating case processing: technologies and benefits

Automation strategy implementation roadmap would start typically with process mapping and assessment to drive improvements in process, making end-to-end case processing leaner and superior and eradicating repetitive steps in current processes.

Artificial Intelligence technologies starting with basic automation through RPA (robotic process automation) to cognitive automation with NLP (natural language processing) and finally taking to ML (machine learning) can be applied in the transformation of pharmacovigilance case processing to make it smarter at every stage with lesser human intervention.

Even though there are current cloud-based platforms like Oracle Argus, ARIS-G etc. automating case processing and reporting activities, the process still requires a lot of manual work in case intake and data entry.

The rules-based, recurring and generalised nature of these processes marks them an ideal fit for automation by using RPA/AI technologies through identification of patterns in unstructured data.

The whole process, from case receipt to reporting, can be automated, thereby reducing manual intervention to certain tasks like handling exceptions, quality control and medical review.

Strategies of standardisation and automation of PV processes designed with combined skillsets of pharmacovigilance domain experts, data scientists and IT engineers have the capability to enhance the case process efficiency by 20-30% ultimately contributing to significant cost reduction, reducing manual errors thus improving the quality deliverables to >99% and ensuring 100% regulatory compliance due to the improved turnaround time.

Adoption of these novel technologies thus can bring a new level of speed and intelligence to the pharmacovigilance process and can be achieved through clear vision and well-defined strategies and plans of implementation with mileposts to track the progress at each step and metrics to track the effectiveness and benefits.

Companies that understand the significance of integrating these novel disruptive technologies and harnessing them would essentially transform the drug safety landscape and would be more effective in managing the growing case volumes with better quality and ultimately complying with the regulatory obligations related to safety surveillance of their products.

RESULT AND DISCUSSION:-

In pharmacovigilance data management and case processing it is critical to address the report's origin, triage cases, enter information into a drug safety database, perform medical assessments, request report follow-up information, and submit reports in a timely manner. All of these are to ensure that precise conclusions and correct decisions are reached, phases necessitate a high and sophisticated level of technical competence and judgement are produced during the creation of a product's benefit-risk profile. Case processing is a critical activity that serves as the foundation for decision-making. If done correctly, it helps the pharmacovigilance

team to correctly analyse safety data and take remedial actions in a timely manner, ensuring that the drug benefits patients as much as feasible. There are numerous ways that can aid in improving case processing quality.

Strategies of standardisation and automation of PV processes designed with combined skillsets of pharmacovigilance domain experts, data scientists and IT engineers have the capability to enhance the case process efficiency by 20-30% ultimately contributing to significant cost reduction, reducing manual errors thus improving the quality deliverables to >99% and ensuring 100% regulatory compliance due to the improved turnaround time.

According to a Deloitte analysis, pharmaceutical companies spend 40-85 percent of their PV budgets on case processing, and case volumes are growing at a pace of 10-15% each year.As stated in the report, 90 percent of respondents wanted to cut the cost of case processing, and they expected automation to save them 30% per ICSR.

CONCLUSION:-

Data management and case processing are a vital activities in pharmacovigilance because it allows different stakeholders like patients, healthcare professionals and competent authorities, to exchange huge amounts of safety data. Ensuring the quality of data during case processing is vital. Correct performance of case processing activities is the basis of successful data analysis, scientific assessment and decision-making which in turn allows to effectively protect public health. The good quality of data is important key to:

- Optimal communication between Competent Authorities, Sponsors, Marketing Authorisation Holders regarding safety of medicinal products
- Regulatory compliance
- Effective analysis of safety data that is used for benefit / risk assessment and signal detection activities in order to safeguard patients' health in effective manner.

Artificial Intelligence technologies such as RPA (robotic process automation), NLP (natural language processing), and ML (machine learning) can be used to modify pharmacovigilance case processing to make it smarter at every level with minimal human participation. Adoption of automation of PV process and these technologies can bring a new level of speed and intelligence to the pharmacovigilance process and can be achieved through clear vision and well-defined strategies and plans of implementation with mileposts to track the progress at each step and metrics to track the effectiveness and benefits.

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