A day in the life of a pharmacovigilance case processor

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Abstract

Pharmacovigilance (PV) has grown significantly in India in the last couple of decades. The etymological roots for the word “pharmacovigilance” are “Pharmakon” (Greek for drug) and “Vigilare” (Latin for to keep watch). It relies on information gathered from the collection of individual case safety reports and other pharmacoepidemiological data. The PV data processing cycle starts with data collection in computerized systems followed by complete data entry which includes adverse event coding, drug coding, causality and expectedness assessment, narrative writing, quality control, and report submissions followed by data storage and maintenance. A case processor plays an important role in conducting these various tasks. The case processor should also manage drug safety information, possess updated knowledge about global drug safety regulations, summarize clinical safety data, participate in meetings, write narratives with medical input from a physician, report serious adverse events to the regulatory authorities, participate in the training of operational staff on drug safety issues, quality control work of other staff in the department, and take on any other task as assigned by the manager or medical director within the capabilities of the drug safety associate. There can be challenges while handling all these tasks at a time, hence the associate will have to maintain a balance to overcome them and keep on updating their knowledge on drug safety regulations, which in turn, would help in increasing their learning curve.

Keywords: Causality, coding, duplicate search, expectedness, Medical Dictionary for Regulatory Activities, Suspected Unexpected Serious Adverse, triage

INTRODUCTION

Pharmacovigilance (PV) as defined by the World Health Organization (WHO) is the science and activities relating to the detection, assessment, understanding, and prevention of adverse effects or any other drug-related problem.[1]

The ultimate goals of PV are as follows:

• The rational and safe use of medical drugs
• The assessment and communication of the risks and benefits of drugs, on the market
• Educating and informing of patients.[2]

PV is critical for the pharmaceutical and health-care industries for drug approval, continuance, and to promote safe use of their products. It helps the medical practitioners to enhance and communicate their knowledge in the betterment of therapeutic practices. For patients and the general public, it is the source of all drug safety information and education. Thus, in modern times, PV is a very important instrument for collection, assessment, identification, and communication of all the vital drug safety information that can help patients lead a healthy life.

Data management is a vital part of PV as there is continuous generation of patient safety data. Adverse event information can be generated from various modes, for example, clinical...
trials, post marketing programs, spontaneous reports, and literature or legal reports. This information needs to be collected and reported to the regulatory authorities for analysis. The role of a case processor is to monitor and track all serious adverse events, serious and medically significant adverse drug reactions (ADRs), and other medical-related product information followed by timely processing and reporting of such information in accordance with the company and regulatory reporting timelines. The case processor usually has an educational background in one of the life sciences (e.g., nursing, pharmacy, or other allied health professionals); it is also advantageous to have a working knowledge of medical terminologies.

This article describes the activities a case processor performs every day, during PV data management.

**ROLE OF CASE PROCESSOR**

In some organizations, an associate is expected to work on various activities. In others, the associate works in specific team, for example, case receipt team, triage team, data entry team, and quality control team.

Below is the process flowchart [Figure 1] of the steps required in case processing.

Let’s look at each task in which a case processor is involved on a daily basis.

**Case receipt**

**Mailbox management**

The first thing a case processor will do is to check the email after logging in to the system. This allows the case processor to check the number of cases that have been assigned and also allows the associate to go through any feedback or other communication from the stakeholders.

Once the assigned cases are identified, the case processor starts working on them.

**Acknowledgment**

The case processor will acknowledge the report (every report needs to be acknowledged, more so the valid reports). The reporter may continue to send the same report repeatedly till it is acknowledged; hence, this simple action avoids duplication. Acknowledgment establishes a contact with the reporter for more information, if and when required.

**Data verification and validity check**

**Validity assessment**

After receiving the source document (via email, fax, or phone), the case processor will look for the minimum information which is required for a valid safety report, i.e., an identifiable patient, an identifiable reporter, an adverse event/reaction, and a suspect or interacting drug.[3]

**Triage**

Under this step, the case processor prioritizes all the incoming reports as per the receipt date, seriousness, causality, and expectedness assessment in the triage step. Once the cases are triaged, they can be processed as per the priority assigned to each case.

This is done to ensure that cases which need expedited reporting can be processed and submitted to the regulatory authorities within timelines.

Standard regulatory timelines are as follows:

As per the International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use E2A guideline, fatal or life-threatening unexpected ADRs should be notified to regulatory agencies within 7 days and all other serious, unexpected ADRs within 15 days.[4]

According to the General Reporting Requirements of the Individual Case Safety Reports (European Medicines Agency), all serious ADRs should be notified within 15 days and all non-serious ADRs should be notified within 90 days.

**Duplicate search**

Due to greater awareness, stringent regulations, and multiple reporting sources, the phenomenon of duplicate reports is common. Every safety management software has a facility to identify and delete duplicates. The case processor performs duplicate search for every document received with certain characteristics of a case (gender, age or date of birth, reaction, clinical trial protocol, country, reference number, etc.) to identify whether the same report has been databased previously or not. 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.

**Book-in and registration**

Once the case processor has completed duplicate search for a case in database, there are two ways of processing a case. They are as follows:

- Upon positive duplicate search, i.e., when the processor finds a case in the database, the processor can add a follow-up to the existing case and process the information.
- Upon negative duplicate search, i.e., when the processor does not find any case in the database, the case processor will create a new case to process the information.

**Complete data entry**

Once the case has been triaged, the case processor will perform the complete data entry. The case processor will enter all the details from the source documents into the database, which include reporter information, patient information, patient medical history, laboratory details, family and surgical history, clinical course, and treatment details of the patient.

**Coding the adverse events and drugs**

This step involves coding of the adverse events in the Medical Dictionary for Regulatory Activities (MedDRA). MedDRA is a single standardized international medical dictionary which can be used for regulatory communication and evaluation of data pertaining to medicinal products for human use.[5]

The case processor can auto code the event term (auto code: when the term has an exact match in MedDRA) or code it manually if the exact match is not available in MedDRA. The principle is to be talking the same language across countries, companies, and regulatory bodies.

The case processor will characterize the drug as provided by the primary reporter suspect/concomitant/interacting and will code them in the drug dictionaries which have been configured in the company database.[6]

A suspect drug is the drug associated with the ADR as determined by the initial reporter.[7]

The associate needs to code the company drugs in company product dictionary and the noncompany drugs in the WHO Drug Dictionary (WHO DD). The WHO DD is an international classification of medicines created by the WHO Program for International Drug Monitoring and managed by the Uppsala Monitoring Centre. The associate will also add other information for the suspect drug which includes indication, therapy details, and action taken with the suspect drug in response to the event.

**Causality assessment**

A causality assessment is the relationship between the drug treatment and the occurrence of an adverse event. The case processor enters the reporter’s causality assessment (whether event is related to the drug: yes/no/not reported) in this section.

If the reporter has not provided the causality assessment, the case processor can also assess the case causality. Various approaches have been developed for the structured determination of the likelihood of a causal relationship between drug exposure and adverse events. The case processor can apply the systems which are largely based on the following considerations:

- The chronology or association in time (or place) between drug administration and the event
- Current knowledge of nature and frequency of adverse reactions due to the suspect molecule, or the pharmacology of the drug
- Medical or confounders based on signs and symptoms, laboratory tests, pathological findings and mechanism of action
- Likelihood or exclusion of other causes for the same adverse events, often the disease condition or concomitant medication.[8]

**Expectedness assessment**

The case processor goes through the reference safety documents to check whether the ADR which is reported is listed/expected in the reference safety information (RSI) document or not. The RSI is a list of medical terms detailing the Serious Adverse Reactions (SARs) that are expected for the investigational medicinal products (IMP) and is used by investigators as a reference point when assessing a SAR to determine whether it is a SUSAR. Various sections of the RSI need to be carefully checked, especially the undesirable effect section. An “unexpected” adverse reaction is one, the nature/severity/specificity/outcome of which is not consistent with the information in the relevant source documents.[9]

**Case narrative**

The case processor describes the story of the entire case in this section. The case processor can use predefined templates for writing narratives as per the customer
requirements. The associate provides a summary of the events to the readers, ensure completeness, chronology, and sufficient detail in a narrative so that the reader can come to a conclusion. The inputs given by the medical reviewers can also be incorporated in the safety narrative of the case.

Self-quality check
The associate does a self-quality check for the case before the case is pushed to the next workflow. The associate ensures the completeness and accuracy of the information entered into the database for all the cases. This is a very crucial step, especially when the associate is working on Suspected Unexpected Serious Adverse Reaction or fatal cases.

The associate will also draft queries for the missing information in the case. These queries are sent to the reporter, and once the reply is received, the data is updated in the case. The case processor will also ensure proper follow-up with the reporter if there is no response after sending the first query. Follow-up activities involve contacting the reporter via mail, fax, or phone. Apart from all these activities, the case processor is also expected to take part in audit meetings, training refreshers, ensuring training compliance, and maintaining up-to-date knowledge of global drug safety regulations.

CASE PROCESSING SIGNIFICANCE

For the case processor, every case is different, even within the same study. In fatal cases, the case processor will have to check many things such as the cause of death and autopsy details, whereas in other scenarios, the processor will have to check adverse events of special interests and important medical events and report the same to the stakeholders. The case processor should ensure that there are no grammatical/spelling errors in the case, while routing it to the next workflow. The case processor shares the best practices, which help other associates to do their job efficiently.

It may seem that the case processor’s job could become mundane after a few months; however, for a case processor, every day and every case is a new experience. There is continuous learning from each and every case which will have new information, thereby increasing the learning curve. This experience will also help the processor in future scenarios.

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Disclaimer
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