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WHITE PAPER

SAFETY SIGNAL MANAGEMENT USING ORACLE EMPIRICA

Abstract

The COVID-19 pandemic has created unprecedented challenges for the medical and scientific community. To protect people from the onslaught of the virus and prevent its spread, bio-pharmaceutical companies are developing vaccines and treatments at a pace never seen before. With patient safety being the main priority, pharmaceutical companies and regulatory authorities have quite a challenge to process data from a wide range of sources for safety monitoring. There is a critical need for a robust process to identify safety signals quickly and accurately.

This white paper provides an overview of signal management using Oracle Empirica and discusses upcoming technological advancements in the field of signal detection.

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Introduction:

The pharmacovigilance landscape is constantly changing. A 30-50% annual increase in adverse event (AE) reports was predicted in the pre-COVID-19 era. With COVID-19 treatments and vaccination programs gaining momentum worldwide, pharmaceutical companies are bracing themselves for a surge in adverse event reports.[1,2] Pharmaceutical companies have a huge task at hand to collect, process and analyze, and report AE data obtained from clinical trials and post-marketing surveillance settings (pharmacovigilance).

Given the complexity of data, variety of sources (structured and unstructured), diversity (multiple geographies and languages) and the volume, traditional methods may prove inadequate in analyzing the data. Therefore, it is imperative that safety and pharmacovigilance teams look at analyzing this data using modern computational methods to identify patterns, trends, and associations. This will speed up the process of identifying potential safety issues (signal) and result in better risk management.

Signal Management in Pharmacovigilance

Signal management is a part of pharmacovigilance and involves identifying and evaluating potential drug safety issues (known as safety signal) from the AE reports of a marketed drug.

A **safety signal** is information derived from one or more data sources, about a new or known risk that may potentially be caused by a medicine. This information is not conclusive as the hypothesis of a risk may change as more data is collected and, hence, necessitate further verification.[3]

Monitoring such information becomes essential to understand if the new information changes the drug's benefit to risk ratio. Once a causal relationship between the drug and adverse event is established, marketing authorization holders need to communicate it promptly to regulatory authorities, healthcare professionals, and consumers.[4]

Data Sources for Safety Signals

Multiple sources are used as data to derive safety signals[5] as shown in Figure 1. Sources include Spontaneous Reporting System Databases, clinical trials data, electronic health records, medical literature, medical insurance claims and post marketing surveillance studies and social media. Along with these traditional sources, companies are now looking at several secondary sources of information like healthcare websites, blogs, social networking sites (e.g., Facebook and LinkedIn), micro-blogging sites (e.g., Twitter) and other internet forums.

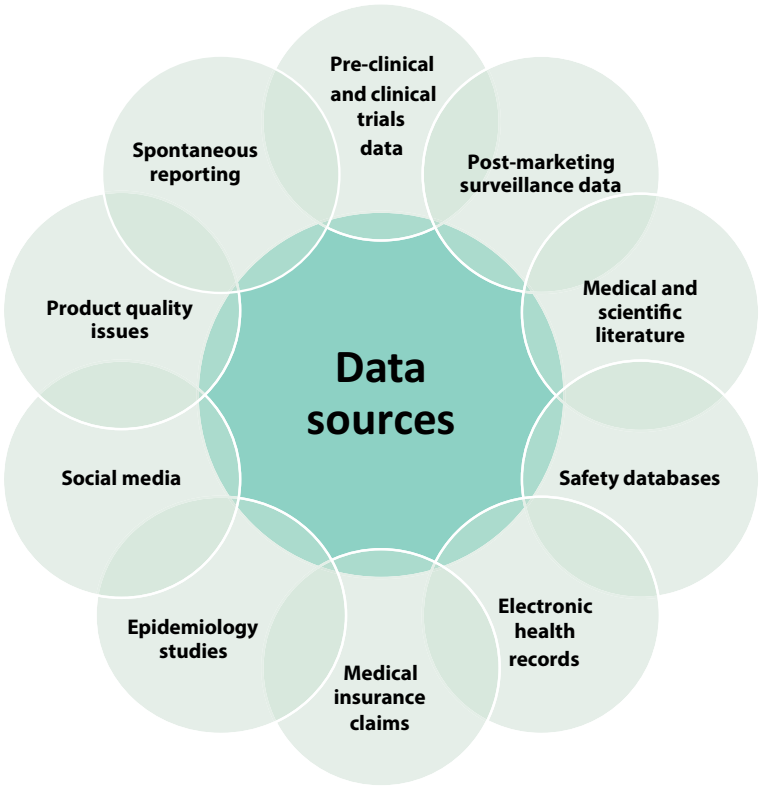

Figure 1 – Data sources for safety signals

Safety Signal Management using Oracle Empirica

Oracle Empirica helps detect, analyze, and manage signals from extremely large and constantly growing datasets using data mining algorithms and statistical methods. Oracle Empirica is compliant with signal management regulation (EU GVP Module IX and CIOMS VIII) and, hence, increases compliance and facilitates better risk management.[6]

As part of the Oracle® Health Sciences Safety Suite, the following products can be used to detect, analyze, document, and manage safety signals[7]:

1. Empirica Study – monitor, detect, and analyze data from clinical trials
2. Empirica Signal – monitor, detect, and analyze data from post-marketing spontaneous reports
3. Empirica Topics – post signal detection, manage signals and activities related to safety issues

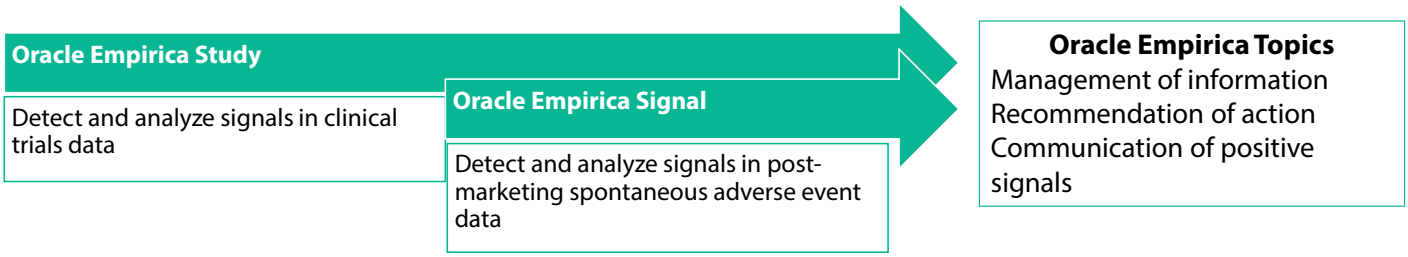

Figure 2 - Signal detection and analysis with Oracle Empirica

Safety Signal Management Lifecycle

Oracle Empirica supports the complete signal management lifecycle as shown in Figure 3.

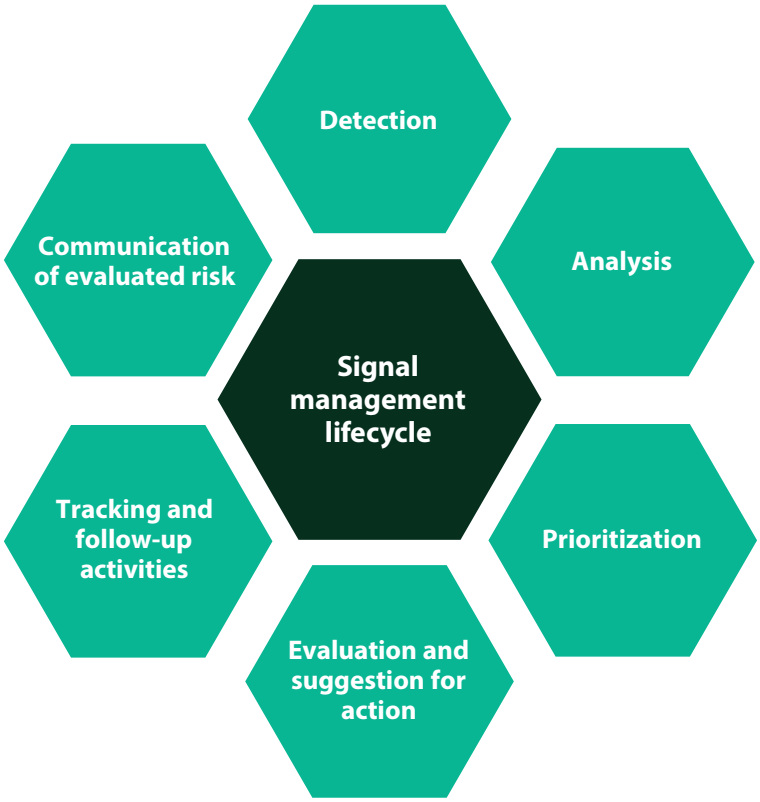

Figure 3 – Signal management lifecycle

1. During clinical trials, Oracle Empirica detects signals in clinical data and tracks them
2. During post-marketing surveillance, Oracle Empirica detects signals in spontaneous reports and tracks them. This information may be new evidence for signals detected during clinical trials or may be new signals
3. Once an issue is identified, it is tagged with an actionable task either for further research or resolution. Eventually, Empirica becomes a knowledge repository of such product risk information and actions related to safety issues

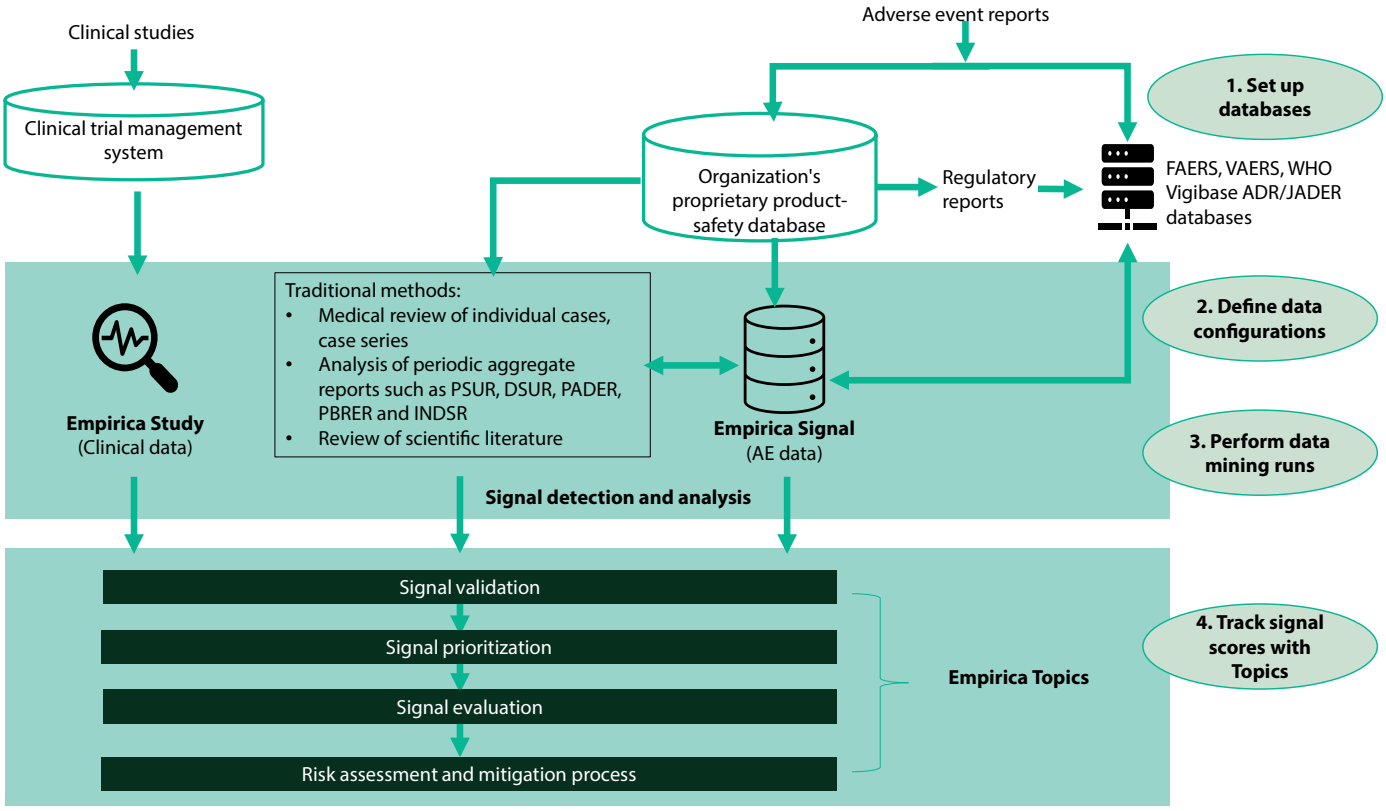

Figure 4 – High-level approach for signal management using Oracle Empirica

Future Roadmap for Signal Detection Methods

The use of artificial intelligence (AI) in signal detection will provide better accuracy of detection, which means more true positives and fewer missed signals, and an improvement in lead time to detection.

Some of the advancements in signal detection are discussed below. While further research is required to address the limitations associated with each of these methodologies, they hold promise as new approaches to signal detection.

1. Neural signal detection

Deep neural network models can be used for the identification and prediction of signals. A neural network, a subset of machine learning, comprises a series of algorithms that can help establish a relationship between datasets. Signal detection using deep neural networks significantly outperforms existing approaches of signal detection (19%-29% improvement in outcome accuracy).[8]

2. Multimodal signal detection

Recently, a multimodal approach for signal detection as shown in Figure 5 has been co-developed by Oracle.[9] The study which evaluated the approach, examined a multimodal system which jointly analyzed 4 different datasets /modalities (each acquisition framework = 1 modalilty).

Computational techniques are used to extract a signal score for drug-adverse event pairs from each data source. The signal statistics from these disparate databases are then transformed into a composite signal statistic or score. This method improves predictive accuracy and lead time to detection.

3. Predictive signal detection[8]

Predictive signal detection uses machine learning to predict the safety profile of a potential drug candidate. Such predictive models compare existing information (pre-clinical data) with various datasets to understand if there is a connection. This will help organizations to identify signals early in the drug development cycle, to make informed choices about investment and, eventually, develop drugs with a safer profile.

Figure 5 – Multimodal signal detection

Conclusion

Signal detection is a critical part of the pharmacovigilance process. Pharmaceutical companies need to have a robust signal management process that will enable them to identify and manage risks during the complete drug development cycle, while maintaining compliance and addressing the growing volume of data (structured and unstructured) from diverse sources.

Oracle Empirica enables life science companies to detect, analyze, validate, assess, and prioritize safety signals in pre- and post-market drugs and provide insights about potential risks, thus leading to better benefit-risk drug profiles.

Advanced signal detection techniques using deep neural networks, multimodal data fusion, and predictive analytics shows promise, and a deeper understanding may help deliver more efficient and effective automated signal detection, leading to the development of safer drugs.

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