INTUITIVE ANALYTICS PLATFORM FOR APPROVED DRUGS

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Abstract : Once a drug approved by regularity bodies, it comes into the market. Then we come to know about their significance and consequences at real time environment with the help of news and articles published into different geographical locations and on different platforms. Those published artifacts are critical to be considered for ongoing research and development work for the same drugs. Scientists from different area of drug development life cycle are struggling to find out these sensitive information at a centralize platform. So, that they can consider those artifacts for their analysis into ongoing research and development works.

Intuitive Analytics Platform for Approved Drugs (IaPAD) is going to provide scientist and researcher a centralize portal, where they can easily lookup into the adverse events reported across the globe, analyze the information and take an important decision in their ongoing research.

IndexTerms - **Artifacts, Analytical platform, Adverse events.**

I. INTRODUCTION

Each year many new prescription drugs are approved by the Food and Drug Administration (FDA). The process of developing and bringing new drugs to market is important for primary care physicians to understand.

The Food and Drug Administration (FDA) is responsible for assuring that foods and cosmetics are safe and that medicines and medical devices are both safe and effective. To carry out this responsibility, the FDA monitors more than $1 trillion worth of products, representing about $0.25 of every $1.00 spent annually by American consumers. Balancing the efficacy and safety of these products is the core public health protection duty of the FDA. This mission requires examining efficacy as determined from well-controlled trials, effectiveness as determined from actual use in uncontrolled settings, and safety for both prescription and over-the-counter pharmaceuticals before approving a medication for market. During the past decade alone, more than 500 new prescription drugs have been approved by the FDA.

Physicians face the continual challenge of learning about new products approved by the FDA. The process of developing new drugs and bringing new drugs to market has important practice implications yet is poorly understood by most primary care physicians. Understanding how clinical trials are conducted is important when physicians consider the use of a new medication for patients in their own practices.

Primary care physicians who might receive invitations to participate in clinical trials need to understand the risks involved for patients and the importance such investigations play in determining efficacy and safety issues of newly released medications. Finally, physicians who challenge the cost of new medications might benefit from a more complete understanding of the time, cost, and complex issues involved in having a new product approved by the FDA.

Results: The process starts with preclinical testing. For drugs that appear safe, an investigational new drug application is filed with the FDA. If approved, clinical trials begin with phase 1 studies that focus on safety and pharmacology. Phase 2 studies examine the effectiveness of the compound. Phase 3 is the final step before submitting a new drug application (NDA) to the FDA. An NDA contains all the information obtained during all phases of testing. Phase 4 studies, or post marketing studies, are conducted after a product is approved.

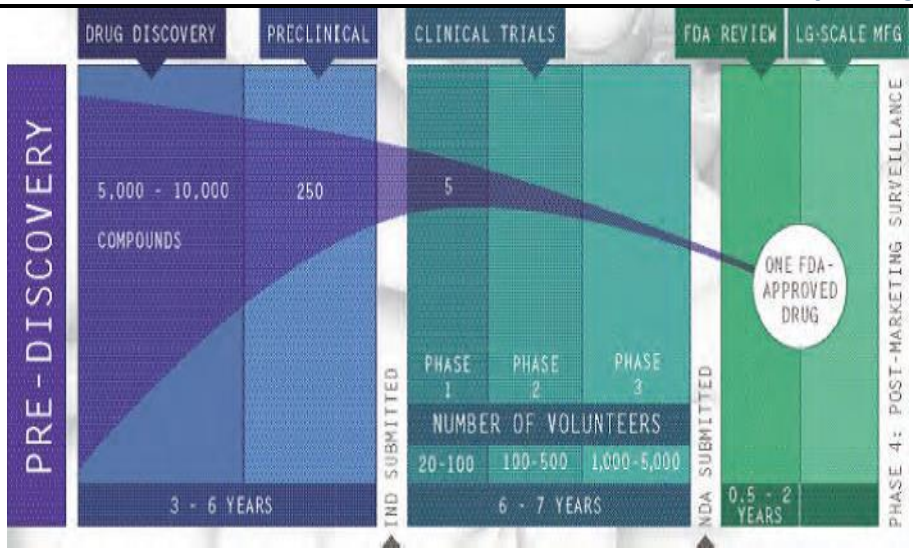

Figure 1 Drug discovery process timelines

The objective of this dissertation work is to prepare an efficient and an intuitive analytics platform for approved drugs with their current and historical significance and consequences happening across the globe.

This platform will help different scientific groups, who are working in different phases of drug research and development. Motive of this platform is to reduce efforts and cost disburses during drug research and development life cycle. Scope of work comprises of preparing a digital analytics platform for mining artifacts for approved drugs.

II. DRUG DEVELOPMENT AND APPROVAL PROCESS

It takes about 10-15 years to develop one new medicine from the time it is discovered to when it is available for treating patients. The average cost to research and develop each successful drug is estimated to be $800 million to $1 billion. This number includes the cost of the thousands of failures: For every 5,000- 10,000 compounds that enter the research and development (R&D) pipeline, ultimately only one receives approval.

The new drug approval is of two phase process - the first phase for clinical trials and second phase for marketing authorization of drug. Firstly, non-clinical studies of a drug are completed to ensure efficacy and safety, and then application for conduct of clinical trials is submitted to the competent authority of the concerned country. Thereafter, the clinical trials can be conducted (phase I to phase IV). These studies are performed to ensure the efficacy, safety and optimizing the dose of drug in human beings. After the completion of clinical studies of the drug, then an application to the competent authority of the concerned country for the approval of drug for marketing is submitted. The competent authority review the application and approve the drug for marketing only if the drug is found to be safe and effective in human being or the drug have more desirable effect as compare to the adverse effect .

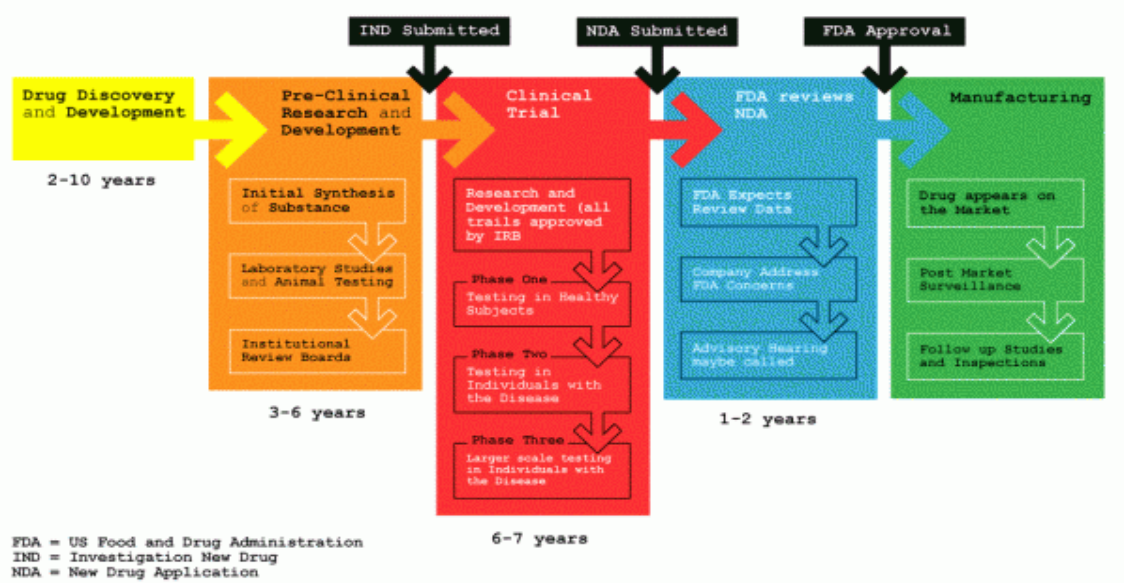

Figure 2 Drug development lifecycle

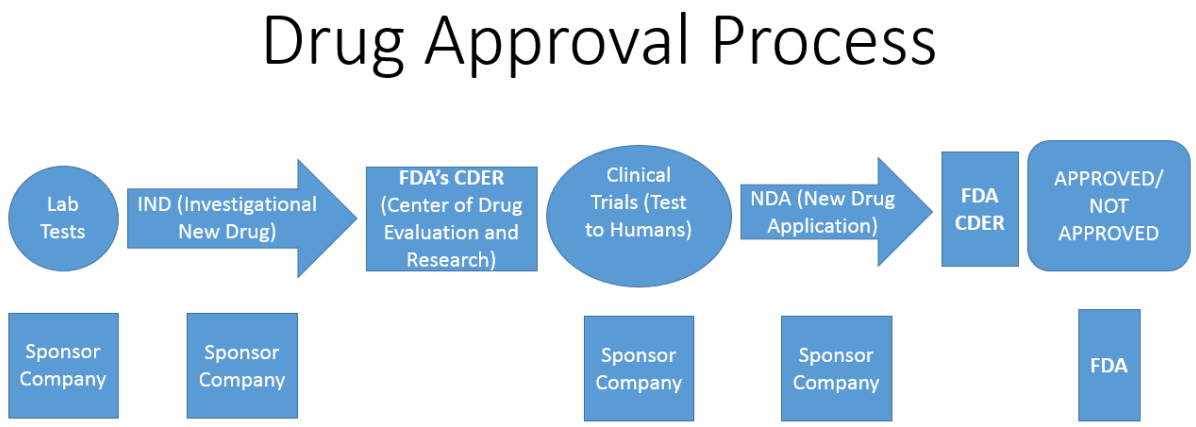

Figure 3 Drug approval process

Even after the approval of new drug, government should monitor its safety due to appearance of some side effects, when it is used in larger population. The interactions with other drugs, which were not assessed in a pre-marketing research trial and its adverse effects (in particular populations) should also be monitored.

III. ADVERSE EVENT ANALYSIS

The understanding that adverse events are common and often result from the poor design of health care delivery systems (Institute of Medicine, 2000) has led to the development of institutional adverse event systems. These systems are used to collect data on adverse events that make it possible to learn from such events and identify trends that may reveal organizational, systemic, and environmental problems.

With few exceptions, existing studies each report data for different populations, and they frequently differ in the way they define, count, and track adverse events. Major variations in nomenclature with no fixed and accepted consensus hamper further research and application.

Adverse event systems have two fundamental components—methods for detecting adverse events and methods for analyzing such events.

There are many sources of adverse event data. These include the following:

- Voluntary and mandatory reporting from internal hospital systems, state and federal systems, and patients themselves and their relatives.
- Document review, including patient charts, medical–legal documents, death certificates, coroners' reports, complaint data, and media reports.
- Automated surveillance of patient treatment data, including clinical patient records, hospital discharge summaries, and Medicare claims data that may be a response to a patient injury.
- Monitoring of the progress of patients to anticipate conditions that could lead to adverse events or to identify adverse events and implement corrective actions.

Reporting and chart review approaches identify adverse events that have already occurred. The focus is on the analysis of a subset of adverse events to determine root causes and identify improvements in care processes, ultimately improving patient safety.

Automated surveillance of data and monitoring of patient progress, referred to as concurrent surveillance methods, are prospective in that they start with a clinical care process and seek to identify critical points in that process at which failures are likely to occur (e.g., when medication is prescribed). These approaches aim to prevent adverse events from happening in the first place or to quickly identify an adverse event once it has happened.

IV. IAPAD: AN ANALYTICS PLATFORM

Different FDA bodies saturated in different countries have their own AERS(Adverse vent Reporting System). They use to have a standardize process of reporting adverse events identified in patients.

Once, those AERS confirm the news about adverse event identified at a specific geographical location then they use to publish that information on public portal in the interest of general awareness and knowledge sharing, which is a useful source of information for many researcher, scholar, & scientist. That information can be crucial some time to take impulsive decision.

Intuitive Analytical Platform for Approved Drugs (IaPAD) is going to be an independent system, which can be integrated within existing database driven application own by our organization. This system is an effort to make adverse reporting and analysis process easier and user friendly.

IaPAD (Intuitive Analytics Platform for Approved Drugs) system is going to be an add-on for those databases driven application to strengthen their rich feature list. This system is going to interact with different AERS APIs to collect information about adverse event happened for a specific compound. It can be integrated in a different search area of existing application which will provide intuitive information about adverse event reported for a specific indication or a compound.

IaPAD will create a visualization and analytical platform for approved molecules and drugs with their existing database records to provide in-depth information about compounds, drugs and indications historical performance and its significant.

The methodology section outline the plan and method that how the study is conducted. This includes Universe of the study, sample of the study,Data and Sources of Data, study's variables and analytical framework. The details are as follows;

*4.1*Architecture for IaPAD

IaPAD is a UI Driven System, which is going to interact with different AERS APIs. This system will have three main component as given below:-

- Adverse event reporting system / APIs
  These are a publically available reporting system, where adverse event information use to capture and verified.
- Data computation
  It is responsible for performing a IaPAD data computational algorithm.
- Visualization & Reporting
  A visualization component, consist of various kind of graphs and reports which can be link with other application.

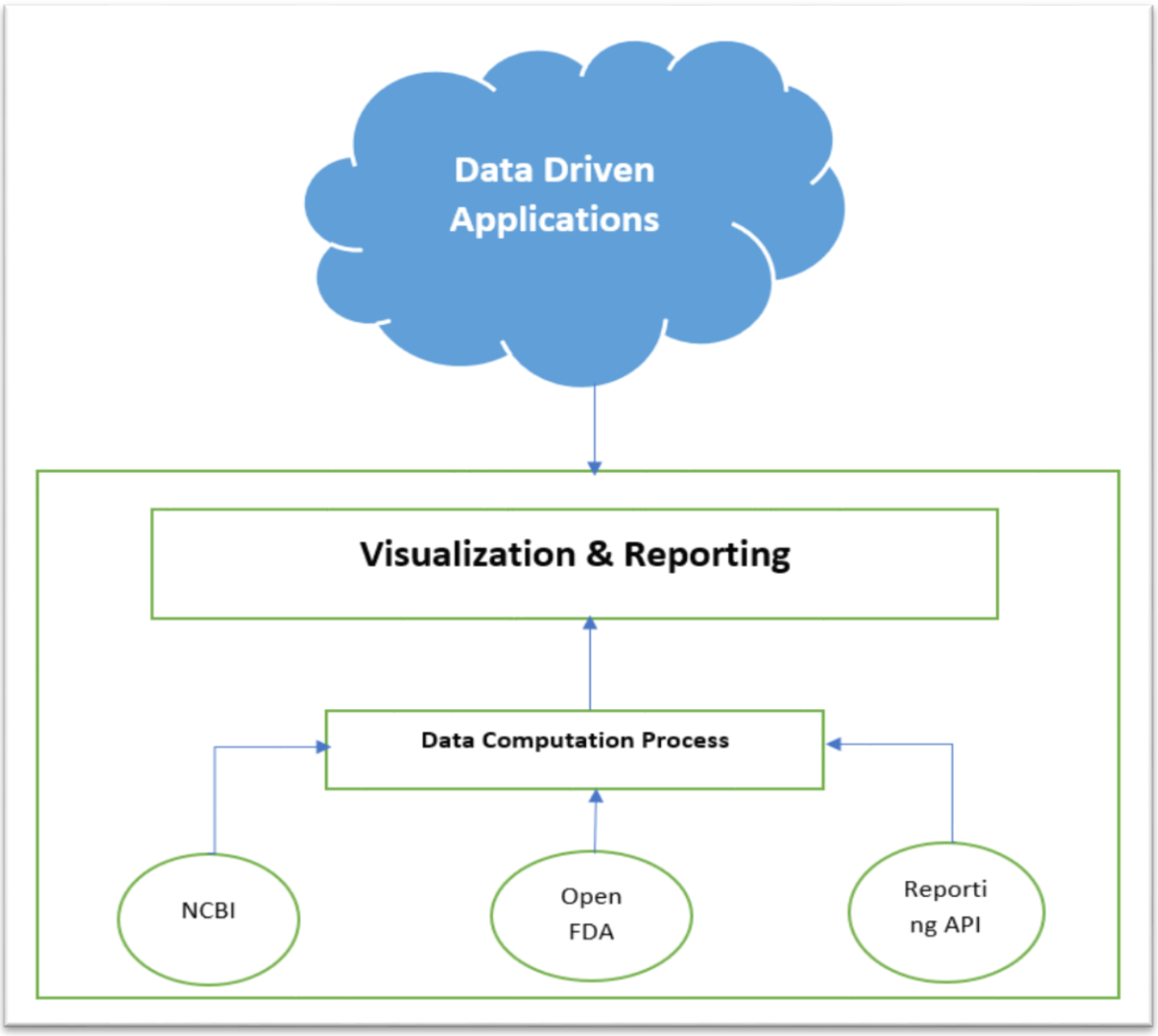

Figure 4 IaPAD Architecture

4.2 Technology specification for IaPAD

IaPAD is going to be a very lightweight, pluggable system. It has designed in a way that it can be mapped with existing database driven application for our organization.

Proposed system will consist different type of attractive graphs and statistics information. Which will presented on a UI. Thus a major technology stack for this system will carry a UI driven technologies. Since, our motive to design a system within a tightly coupled cost boundaries and provide a highly customized solution. That is why most IaPAD has been developed with latest open source technologies.

Below are the technologies used in iPAD system:-

- HTML5 & CSS3 : For designing a UI stack
- AngularJs: For defining a well-defined MVC framework.
- React.Js : For defining a data computation component
- D3.js : For designing different kind of graphs
- Webpack: For bundling application
- Web server: For developing and testing server.

4.3 Technical Flow for IaPAD

IaPAD application will be accessible by web and mobile browser over the internet. As per the current scope of this application, it will be deployed on a centric server location. Which can be easily accessible by client browser.

This application is going to be designed in such a way that it can be accessed individually or can be plugged in into any of the other application.

Base of this application is completely written in AngularJs and HTML & CSS technologies. Application work flow is completely managed by MVC architecture provided by AngularJs. All request coming from client browser use to handle by Angular route and it redirect to angular controller for further process.

A Typical angular controller process the request further and bind a data back to HTML view with angular model view binding mechanism. This process always make sure that data binding work at the run time with an optimize performance. It makes IaPAD dynamic data driven, flexible and easy to access platform.

IaPAD application is a typical web app. Which can be easily run on desktop, tablets and mobile devices with the help of HTML5 & CSS3 compatible web and mobile browsers.This application is an easy to use and flexible platform to do analysis on reported adverse events across the globe.

This application contains rich analyzed information for different approved drugs such as drug indications, drug classes, drug infections, AE reported geographical location, Patient information and general information etc.

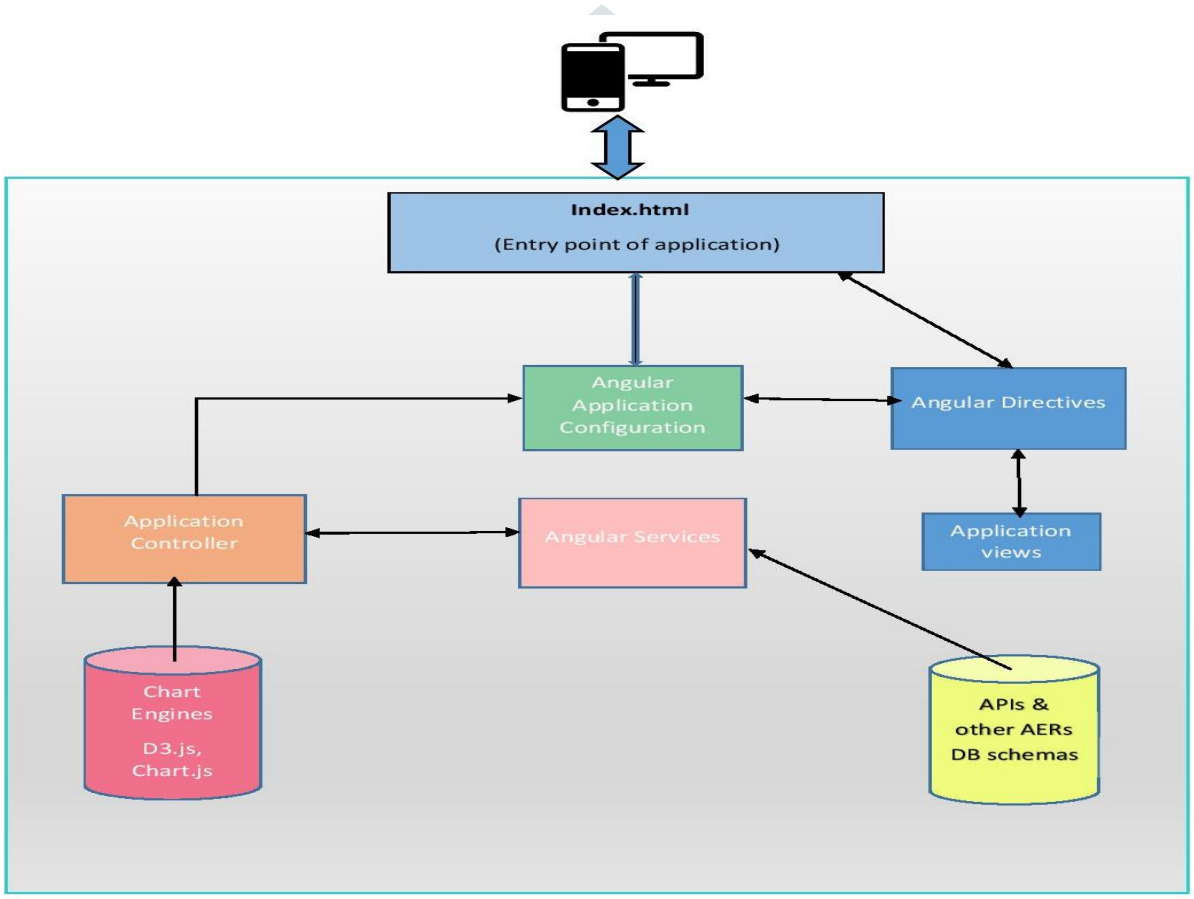

Figure 5 Technical flow for IaPAD Application Features

Below are the main features available in current IaPAD application:-

- Drug adverse event general information,
- Drug adverse event indications,
- Drug adverse event pharmacologic classes,
- Drug adverse event infections.

4.3.1 Drug Adverse Event General Information

General information about drug adverse event is an initial information captured in AERs. It gives us a basic information about the adverse event happed across the globe, reported by, medium of adverse event report, patient general information etc.

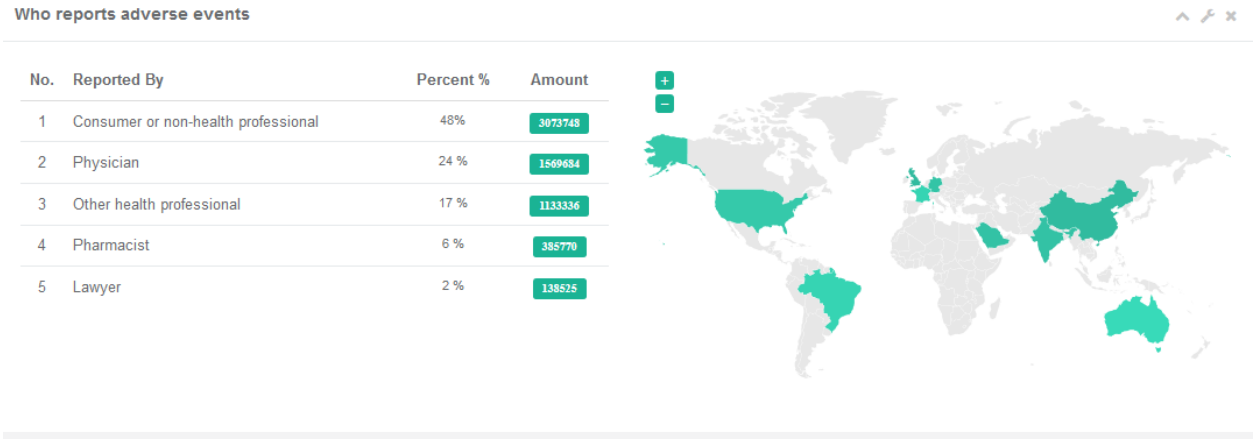

Figure 6 who reported adverse events

As show in Fig. 6, IaPAD application inform use about the reported adverse events general information such as

- Who has reported the adverse event
- Where did adverse event identified
- Is patient male or female
- How old the patient was
- Other general information

This sort of general information gives an idea to scientist to narrow down their research based on outcome reported during AERs. It used to be a crucial analysis to for efficacy and safety information about the disease on which they are working on.

4.3.2 Drug Adverse Event Indication

Drugs listed in adverse event reports often have an indication for use specified—a disease being treated, or a certain therapeutic goal.

Figure 7 Indication identifies AE

It gives a detail information about an indication, which can be research centric information for scientist. So that they can define a research flow for a specific therapeutic class.

4.3.3 Drug Adverse Event Pharmacologic Class

The seriousness of reported adverse events varies with the associated drugs. This information shows the drug classes most often associated with adverse event reports.

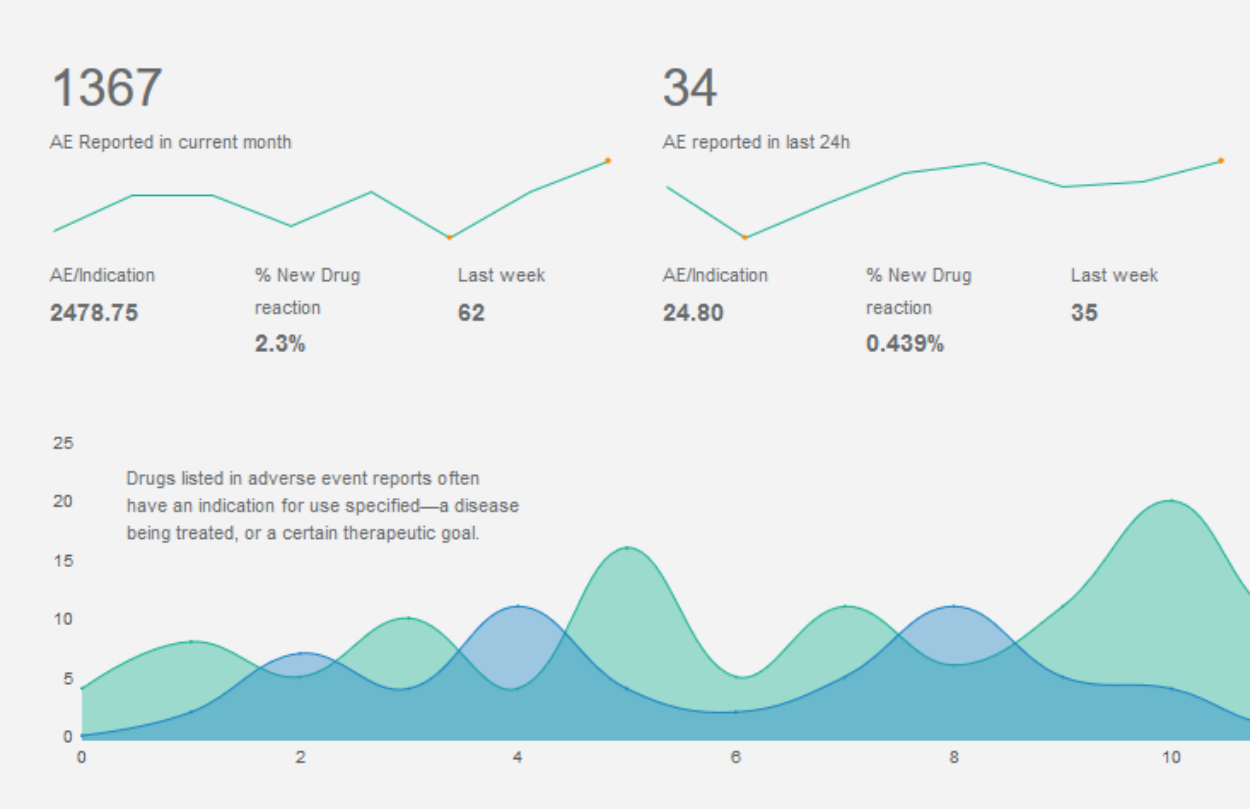

Figure 8 Drug class information

Reported adverse event help to identify the information about drug class, which have been reported such cases. So that scientist can take a crucial decisions about that specific drug class and accordingly shift their coordinates to find out an alternate or a similar drug class to improve that specific drug.

4.3.4 Drug Adverse Event Infection

Adverse reactions range from product quality issues to very serious outcomes, including death.There is no certainty that a reported event (adverse reaction or medication error) was actually due to a product. Generally, FDA does not require that a causal relationship between a product and event be proven, and reports do not always contain enough detail to properly evaluate an event.

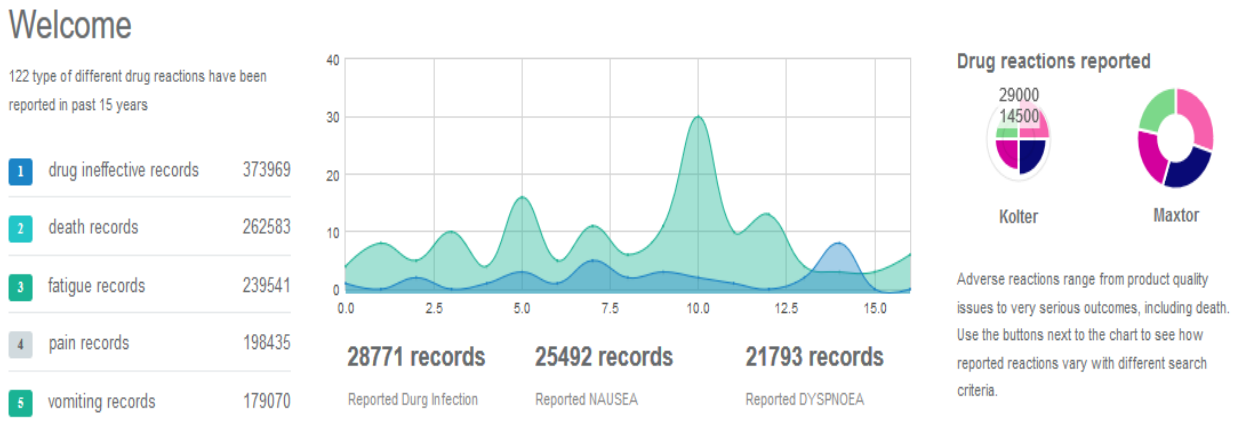

Figure 9 Drug infection reported due to adverse event

This feature gives a cumulative information about different infections happen due to adverse event of drugs. Thus, this outcome information can be crucial for efficacy and safety level studies on therapeutic classes.

V. SUMMARY

Use of adverse event systems is also aimed at identifying improved health care processes through the analysis of adverse event data. This process involves selecting and defining the adverse events to survey, defining the analysis population, collecting surveillance data, analyzing surveillance findings (identifying causal factors), and using the findings to develop interventions. The process requires standard definitions of adverse events, minimum datasets for describing the events, standard definitions of dataset variables, and standard approaches for collecting and integrating the data.

Researcher and scientist can use IaPAD for identifying potential cause of reported adverse event and can direct their research work with the help of available analytical information. It will help them to strengthen their decision making process.

IaPAD is going to be a milestone contribution towards to society for making people life safer.

VI. CONCLUSION AND RECOMMENDATION

IaPAD is an informative system, which will plug-in with our existing database driven applications or it can be use an independent web component too. It can be an add-on feature for these applications. It will provide an analytical view for existing drugs related search.

Since, this system has developed with open source data and available latest open source technologies. Thus, this solution is a low cost and a potential revenue generation source for the organization.

VII. DIRECTION FOR FUTURE WORK

We have already analyzed about a potential market for IaPAD system. Our plan is to release a dev version of this system by the end of Dec 2016 and will plan for a beta testing with internal scientific users and researcher.

We will work on the feedback/ suggestion given by internal user and will plan to incorporate those changes into the existing system. After that we will plan for a beta version test with UAT groups of our potential clients.

As per the UAT feedback, we will package this system for final amendments and roll out in market as a first version of IaPAD.

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