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Short Literature Review on Pharmaceutical Regulatory Affairs with Significance of Artificial Intelligence, Machine Learning and Big Data for Clinical Trial Validation Process Automation

Mr. Rushikesh V. Jagtap
Clinical Research Associate,
DiagnoSearch Life Sciences Pvt. Ltd, Thane, Maharashtra, India

Abstract
Regulatory Affairs are umbrella activities for drug discovery, medical devices discovery and clinical trials throughout the world. There are diversified rules and regulations for the validation of criteria among them. However, as a post-covid-19 pandemic scenario, automation in the field of pharmaceutical is promoted worldwide. One of such upcoming research domain is artificial intelligence for process automation. Hence, this paper presents the empirical literature review where similar to pharmaceutical expert as a medical coder; there is a need of artificial intelligence strategy and big data storage facility provider with the knowledge of pharmaceutical domain. The validation of compliances processes in regulatory affairs is crucial and multidisciplinary research is necessary. This review presents the need of artificial intelligence, machine learning and big data analytics for fast and precise execution of validation process of clinical trial data.
Keywords: Clinical trial, drug discovery, pharmaceutical regulatory affair automation, artificial intelligence, machine learning, big data

1. Introduction

Current constrain of Regulatory Affairs reveals diverse countries need to follow different regulatory requirements for Marketing Authorization Application (MAA) approval of new drugs. Every country has its own regulatory authority which is responsible to enforce the rules and regulations and issue the guidelines to regulate the marketing of the drugs [1]. Most clinical studies were carried out in the United States, Europe, and Japan up until 1995. In 1995, the first assessment of research in India was completed. A 2004 article suggested that

India lacked the ideal research environment that the majority of clinical researcher's demand. Clinical trials carried out in India significantly increased in 2009. A public interest litigation (PIL) was filed in 2012 accusing government, non-governmental, and independent investigators of conducting clinical studies improperly [2].

By the Drugs and Cosmetics Act, Central Drugs Standard Control Organization (CDSCO) oversees approving drugs, conducting clinical trials, setting standards for drugs, monitoring the quality of drugs imported into the nation, and coordinating the efforts of state drug control organizations by offering professional advice to ensure uniformity in the application of the Drugs and Cosmetics Act. The US Food and Drug Administration (FDA), a single agency, oversees the regulation of a trillion dollars' worth of goods, or about 25 cents of every dollar

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spent, including 80 percent of the food supply in the US, all medical devices, and prescription drugs, animal products, cosmetics, and even the production of tobacco products [3]. (Refer following Fig.1)

Fig. 1: Components of Pharmacovigilance: Regulatory Affairs

The field of regulatory affairs deals with the regulatory requirements for marketing authorization of therapeutic products. This field is facing a myriad of forces impacting all aspects of the development, regulation and value proposition of new therapeutic products. Changes in global megatrends, such as geopolitical shifts and the rise of the green economy, have emphasized the importance of manufacturing and supply chain security, and reducing the environmental impacts of product development. Rapid changes due to advances in science, digital disruption, a renewed focus on the centrality of the patient in all stages of therapeutic product development and greater collaboration between national regulatory authorities have been accelerated by the COVID-19 pandemic [4].

Artificial intelligence (AI) refers to the ability of a computer to carry out tasks associated with human intelligence, including thinking, discovering, and learning from prior experience. AI can be integrated to simplify the complexity of pharmaceutical regulatory affairs. AI tools can be applied to automate regulatory processes such as administrative work, dossier filling, data extraction, auditing, the implementation of regulations, and quality management. AI creates process links and reduces complexity, resulting in a more efficient management system. Human–AI interaction opens up new opportunities in regulatory affairs. This article explores the potential role of AI in pharmaceutical regulatory affairs [5].

In 2013, the Global Coalition for Regulatory Science Research (GCRSR) was established with members from over ten countries (www.gcrsr.net). One of the main objectives of GCRSR is to facilitate communication among global regulators on the rise of new technologies with regulatory applications through the annual conference Global Summit on Regulatory Science (GSRS). The 11th annual GSRS conference (GSRS21) focused on “Regulatory Sciences for Food/Drug Safety with Real-World Data (RWD) and Artificial Intelligence (AI).” The conference discussed current advancements in both AI and RWD approaches with a specific

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emphasis on how they impact regulatory sciences and how regulatory agencies across the globe are pursuing the adaptation and oversight of these technologies [6].

2. Literature Review

Artificial intelligence (AI) aims to automate human decision-making behavior and is therefore also considered the next phase of the industrial revolution. We have previously reviewed the state of the art and challenges of AI applications in healthcare. This book provides a forecast of how AI and other technologies are likely to skyrocket healthcare in the foreseeable future. The European Commission published proposed regulation in April 2021 (European Commission, 2021) that intends to create a uniform legal framework for AI within the European Union (EU) [7]. In addition to its investment in Natural Language Processing (NLP) technologies, the FDA has launched initiatives to restructure its data operations and reshape its technical data infrastructure, such as INFORMED (Information Exchanged and Data Transformation), which tasked entrepreneurs-in residence, engineers, and data scientists with medical/pharmacy subject-matter expertise to strategize how the FDA should invest in big data analytics capabilities [8].

Several factors, including advances in computational algorithms, the availability of highperformance computing hardware, and the assembly of large community-based databases, have led to the extensive application of Artificial Intelligence (AI) in the biomedical domain for nearly 20 years. AI algorithms have attained expert-level performance in cancer research also [9]. Through extensive research, it was confirmed that very few studies have attempted to review existing works to analyze the implementation of Big Data in the pharmacology, toxicology, and pharmaceutics fields. Thus, the present study is expected to greatly contribute to upcoming research, by providing clear knowledge regarding the implementation of Big Data in the field of drug development, and will also encourage the development of different big data-based models to serve the medical community [10].

Regulatory affairs professionals can be found in all sorts of companies, for example, biotech, pharmaceuticals, medical devices, diagnostics, and even nutritional products. They play critical roles in the health product lifecycle, from development through post-market approval. It is crucial for regulatory affairs professional to be adaptive and believe in continuous learning. The regulatory affairs professional must also be able to capture intelligence from a variety of sources [11].

A regulatory affair is a unique synergy of internal departments of an industry with the regulatory bodies, which starts with the conceptualization of the product to be developed by that industry, till the marketing of that product. It is a very important and salient feature of pharmaceutical product development. Author(s) provided insight into the importance of regulatory affairs, regulatory requirements for product approval, and documentation in pharmaceutical industry, with a special mention of the master formula record, drug master file, and distribution records [12].

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Recent improvements and innovative approaches in the field of artificial intelligence promise high potential for the diagnosis and treatment of patients. The sub-area of ML in which selflearning algorithms are trained on large datasets and used to make predictions independently when exposed to new data, is particularly advancing. More and more research is showing that newly developed algorithms can process specialized tasks just as well as experienced health professionals or can increase their efficiency and performance in daily care. A crucial factor for the successful development of ML-based software and assistance systems is besides medical and technological expertise in particular, the testing and use of these applications in daily clinical routine [13].

Big data has gradually become a fundamental national strategic resource and a cornerstone factor in production. However, increasing big data security problems are exposed and the number of big data security incidents occurring around the world is on the rise [14]. The efficient development of personalized medicine is largely dependent on the tools, sequencing techniques used and regulatory policies related to the personalized medicine products, tests and companion diagnostics. The uncertainties in the regulations governing personalized medicine should be eliminated and specific guidelines should be laid down by the respective regulatory authorities to bridge the emerging tools and technologies with the regulatory policies. Also, proper regulatory approval pathways for companion diagnostics will resolve the complications of organized development of therapeutic products and diagnostic tests [15]. Registration of pharmaceutical drug products in emerging market is maximum worrying task. Although the requirements are harmonized in regulated international locations by way of CTD (Common technical document) submitting, yet others have considerable diversity in necessities. International conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) has brought regulatory authorities and pharmaceutical industries of US, Japan and Europe collectively for various factors of drug registration. But there is no such harmonized guideline for rising marketplace besides Association of Southeast Asian Nations (ASEAN) and Gulf Co-operation Council (GCC) where harmonization exists in clusters with their mutual situation [16].

3. Methodology

This study has been undertaken as a systematic literature survey of data analytics of internet of things architectures and algorithms for understanding of IoT middleware. In this case the goal of the survey is to assess systematic literature reviews, so this study is categorized as a bi-directional literature review. The steps in the systematic literature review method are documented below.

3.1. Research questions

To address the methodology of proposed research, few pilot research questions are formulated as below which can be evaluated at the stage of research methodology development:

RQ1. Is the significance of artificial intelligence for enhancement of regulatory affairs beneficial?

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RQ2. Is citation is in line with collaborative future scope for artificial intelligence, machine learning and big data?
RQ3. Are pharmacy expert needs to collaboratively work with artificial intelligence, machine learning and big data?

4. Database Search Process

We followed systematic method to generate literature database. Initially, we identified significant electronic databases as: Springer, ACM and Elsevier for publications search with phrase "pharmaceutical regulatory affairs". Following search string is developed and applied: (((Drug discovery and Compliance Report *) OR (Clinical trial validation documents) OR (Drug approval process) OR))) AND ((CTD) OR (Regulatory affairs SAS*))) The outcomes of the above query over the selected databases are given in Table 1.

Table 1: Domain Specific Literature Papers

Input String	No. of papers (Primary Search)			
	Springer	Elsevier	eBooks	Other Journals
Drug discovery and Compliance Report	21	14	1	12
Clinical trial validation documents	25	16	1	9
Drug approval process	19	19	1	17
CTD	15	14	0	5
Regulatory affairs SAS	16	18	1	4

4.1 Data Extraction Criteria

In the second stage, we physically examined overall 127 conference and journal paper titles (eBooks, publications prior to year 2023 and miscellaneous are omitted). Publications analyzed from rest of libraries as an introductory search, rejected any which are not related to our domain of research and also multiple abstract similarity data rejected if published on more than one database. We filtered the unique data as per our domain of proposed research and finalized 16 documents with an immediate significance to our work.

4.2 Quality assessment

We evaluated shortlisted papers for following aspects, Q1:
Is author cited high impact factor publications?
Q2: Is information provided by author is cited by other researchers?
Q3: Is drug discovery regulatory processes and SAS is used and promoted artificial intelligence, machine learning and big data?

The quality assessment answers are synchronized as follows:
Ans.1: Yes.
Ans.2: Yes. Research citation record till 2023 is available with each e-article and many crossreferences used in original cited article.
Ans.3: Yes. Most commonly preferred inclusion of pharmacy expertise with artificial intelligence, machine learning and big data.

4.3 Data collection Strategy

The present data is gathered from high indexed journals, conferences and transactions for study purpose, stored in Microsoft excel sheet. The information is separated as:

- Title of research
- Author name of research paper
- Publication Date &Year, Volume, Issue, Page numbers, ISSN/DOI

5. Conclusion

As per the literature review conducted, it is necessary to incorporate the pharmaceutical regulatory affairs with artificial intelligence, machine learning and big data to minimize the risk of manual validation of drug discovery data. It is the responsibility of pharmaceutical experts to coordinate the drug dataset for validation of compliance reports in line to national/international regulatory guidelines. As per the interdisciplinary research domain, to achieve the automation of the pharmaceutical regulatory affairs both medical and computational proficiencies are required. As SAS software, medical code compilation is carried out by the pharmaceutical experts' similar way artificial intelligence model strategies can be developed by the pharmaceutical experts. This will bring a new domain in practice for the battement of the healthcare systems.

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