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TECHNOLOGY TALK

Generative AI in Clinical Research: Regulatory Submissions, Clinical Data Management, and Beyond

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ABSTRACT

Artificial intelligence and its subsets, such as generative artificial intelligence, have been making headlines due to their potential to accelerate the growth and expansion of various industries, including healthcare. However, the majority of application areas in healthcare revolve around diagnosing diseases, finding lead molecules for potential treatments, optimizing hospital operations, and other related aspects. This means that there are areas where the potential of these technologies is still to be realized. Examples of where such technologies could produce a significant impact across multiple elements are clinical research and its related domains, including regulatory submissions, clinical data management, clinical documentation, and other closely related areas. When artificial intelligence and its related technologies are utilized in these areas, they yield unparalleled outcomes regarding efficiency, consistency, and reproducibility. This, in turn, supports professionals involved in clinical research, like medical writers, statistical programmers, and other stakeholders, to drastically improve the speed by which they produce the initial drafts of various outputs, reduce the risk of errors that could lead to submission rejection, and optimize the overall clinical research workflow. Despite the potential of this area, the number of available solutions that support the aforementioned domains remains low. This is further complicated by the fact that there are even fewer numbers of working solutions.

The release of the generative pre-trained transformer 3 (GPT-3) language model in 2020, and more recently, the chatbot ChatGPT, have sparked considerable interest in the potential applications of artificial intelligence (AI) in various fields, including health care.[1,2] Despite the vast uses of AI in this area,[1,3] its potential in automating regulatory submissions, such as those submitted to the Food and Drug Administration (FDA), remains underrepresented. Other growth areas in which generative AI and its related technologies could provide significant value include clinical data collection, management, analysis, postmarketing surveillance, pharmacovigilance reporting, and other areas.

Automating regulatory submissions, such as clinical study reports (CSRs), which are part of the electronic common technical document (eCTD), is challenging because large clinical studies generally yield incredibly complex and copious amounts of data points around participants. This is where the current GPT-3 and -4 technologies fail because they were not designed nor optimized to understand this specific activity and how those particular data sets relate to each other. Moreover, they are not clinically trained; they are prone to errors and hallucinations, negatively impacting their validity. Indeed, such challenges are evident in complex therapeutic areas, like oncology and studies with a higher number of subjects.

For example, patient narratives,[4] a key component of CSRs, examine serious adverse events that are fatal, life-threatening, or of special interest, among others. Usually, medical writers (MWs) could spend days preparing drafts of a few patient narratives because these narratives could be tens of pages long in treatments that address rare or difficult-to-treat conditions. This would require additional effort in studies with a higher number of participants. Before getting to the writing step, statistical programmers and other stakeholders involved in clinical research are required to prepare the files that MWs will use. This job could take weeks or even months of work and is prone to human errors due to the vast sizes of the data sets that need to be handled.

With the use of AI, the first step to preparing the initial draft of patient narratives requires establishing relationships between the proper data points within complete databases. Only then may the creation of narratives incorporating all the aforementioned types of adverse events be automated using natural language processing (NLP) and natural language generation (NLG) models. NLP and NLG are subsets of AI, and when combined with a well-structured data modeling technique, they work not just to process the data, but to also highlight interdata relationships and highlight key components within the data that afford higher accuracy for the narratives. This approach may save MWs hundreds (or even thousands) of hours and cut submission cycle durations significantly.

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It is important to note that the use of AI and its related technologies, such as NLP and NLG, in automating regulatory submissions like CSRs is meant to augment the potential of MWs by helping them reduce the time spans needed to create initial drafts and modify them in a much shorter time frame. Otherwise, MWs would spend a significant amount of time preparing the drafts and updating their content upon request from the sponsor.

In addition to generative AI potential in CSR authoring, other automation tools have also shown significant value in accelerating regulatory submissions. For example, automating Tables, Listings, and Figures (TLFs), which are documents created by statistical programmers and other stakeholders and are used by MWs to populate CSRs, have proven to be of significant value to MWs and programmers alike. TLF automation reduces the time needed to author CSRs and improves the quality assurance process by flagging potential errors, inconsistencies, or missing data in the databases used. By automating TLFs, documents submitted to the FDA will inherently have higher data quality and be devoid of errors, resulting not only in faster approval times but also significantly lessen the chances of rejections due to errors.

When viewed from the perspective of time and quality, adopting AI in creating, validating, authoring, and submitting regulatory documents decreases the man-hours spent across the spectrum of these processes by at least several months or more. The quality of the submitted documents is also much improved. Ultimately, this translates into cost and time savings. In addition, it would increase the availability of personnel resources, such as MWs, statistical programmers, and other stakeholders involved in creating eCTDs, freeing them up to attend to more critical processes that require substantial human input.

Currently, there are only a handful of AI-driven regulatory automation solution providers. Those with actual working and proven solutions are even less common. Notwithstanding, organizations that have managed to perfect CSR automation have witnessed increased demand for services from parties involved in clinical research.

The potential of generative AI and related technologies extends beyond the realm of regulatory submissions. For instance, in clinical research—more specifically clinical trial data collection, management, and analysis—the use of AI can potentially flag inconsistencies related to the same entry across multiple databases. For example, recorded information concerning adverse events in a patient is captured in both the safety and efficacy databases. Although the former mostly holds serious adverse events, the efficacy repository contains both serious and nonserious adverse events, plus more. The use of two separate databases has been shown to cause inconsistencies in entries due to human error. This could negatively affect the evaluation of the safety and efficacy of a biopharmaceutical or medical device product. Another example of a challenge in which generative AI and related technologies can help is one in which case report forms do not have cross-form consistency. For instance, the concomitant medication used to treat an adverse event could be written manually, making it liable to typos, nonstandard abbreviations, or include terms that are not necessarily aligned with those in the Medical Dictionary for Regulatory Activities. Moreover, dates entered in the "date" field might appear like actual dates, but there are no time-consistency checks, leading to the loss of the cause–effect link. When implemented, AI could flag such inconsistencies in entries, helping stakeholders correct these errors beforehand. In this area, the use of AI not only ensures consistency but also upholds quality because the human eye could easily miss such errors due to the sheer size of the databases.

Automation of data analysis with AI could offer significant value across other areas in clinical research conduct and reporting. In postmarketing surveillance, the use of AI could help scan, collect, and organize safety signals from various sources like clinical studies, adverse event reporting forms, scientific literature, and other sources. Additionally, generative AI and related technologies could help automate pharmacovigilance efforts by identifying and tracking safety trends and generating reports that revolve around those safety signals. Similarly, the same technology could be utilized in cross-reporting, allowing standardization, efficient data collection, analysis, and reporting.

In conclusion, the use of AI in regulatory submissions, cross-reporting, and the other aforementioned areas is still marginal, even in the literature. Nevertheless, pharmaceutical companies, clinical research organizations, and other stakeholders could gain substantial advantages through AI adoption—most notably with regard to time saved. This ultimately allows for the introduction of life-saving treatments sooner than would otherwise transpire.

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