Digital tools for the clinical evaluation of medical devices:
A guide to empower regulatory writers

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doi: 10.56012/hmts9332

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Abstract
The implementation of the European Medical Device Regulation (EUMDR) has driven innovation in the digitalisation and the development of artificial intelligence (AI)-powered automations for regulatory writing. This article explores a selection of tools designed for device-related regulatory activities, highlighting their functionalities and use cases. The goals of the article are to demystify the role of AI in medical and regulatory writing, explain the process of developing AI-based automations, illustrate how these tools benefit medical writers, and most importantly enhance the readers' skills in assessing such tools. The article discusses five automation tools: avasis, DistillerSR, Fern.ai, MedBoard, and Nested Knowledge, providing an overview of their features and benefits. The article concludes by emphasising that these automations address certain pain points faced during medical writing, yet they prioritise different features. By doing so, they empower users to improve data quality and streamline tasks in regulatory writing. Since there is no one-size-fits-all tool, the decision-making process is ultimately that of the user, not only on the type of tool to select but also on how best to leverage the software to optimise their technical documentation.

Introduction

The implementation of the European Medical Device Regulation (EUMDR) has played a pivotal role in driving innovation in the development of digitalisation and automations powered by artificial intelligence (AI) for regulatory writing. The role of the EUMDR becomes evident when comparing the timelines of its implementation in May 2021 in parallel with the the number of newly developed tools tailored for medical writing during the same time period (Figure 1).

The surge in software innovation in the medical technology sector was primarily driven by the substantial burden of managing and updating clinical evidence and navigating stringent conformity assessment processes. That resulted in medical device manufacturers encountering unprecedented challenges, both in terms of costs and time, with limited coping strategies at their disposal.[1] These challenges have provided the medical device domain with the long-needed incentive to embrace out-of-the-box technological solutions, ushering the digitalisation industry into a more sophisticated digitalisation era.

However, the emergence of generative AI and its use in the field of medical writing has sparked controversy and raised concerns that could potentially impede the industry's progress and momentum in adopting automated solutions.[2] As a medical writer who worked in the field of software development, I perceive the widespread concern and scepticism surrounding AI-based automations as a threat to the progress achieved as well as an opportunity that has presented itself, to engage medical writers, leveraging their keen inquisitive interest in the matter.

This article is a quest to explore a selection of tools designed for device-related regulatory activities. While they primarily focus on addressing different stages of clinical evaluation and post-marketing surveillance (PMS) processes, these tools can also compile systematic literature reviews of other types. These tools were chosen to illustrate a broad range of capabilities and highlight some unique features intended to streamline the daily tasks of medical writers.
The following are the goals of the article:

- Demystify the role of AI in medical and regulatory writing.
- Explain the process of developing AI-based automations.
- Explore the various functionalities and use cases of automated platforms.
- Illustrate how these functionalities can benefit medical writers.

- Enhance the readers' skills in assessing and evaluating such tools.
- Encourage readers to approach new technologies with scientific curiosity while maintaining a healthy dose of scepticism.
- Foster engagement between all stakeholders, to build a trust-based dialogue that drives technological advancements.

Ultimately, this article should assist you in making informed decisions based on reliable information and in selecting the most suitable tool for your needs. As a disclaimer, I would like to clarify that this article is neither a promotional piece nor a systematic comparison of the showcased tools. The opinions expressed in this article are solely those of the author and are based on research, webinars, and interviews conducted with representatives of these companies.

Behind the scenes of an AI automation in the making

To provide you with a better understanding of the automation development process, I will be using my knowledge of certain aspects of my previous role as a lead medical writer involved in the development process to ascertain some facts. A key aspect of the role of the medical writing team was to actively participate in AI "sanity" verification, conceptualisation of decision-making trees, and validation of their logic. More importantly, as well-trained scientists and clinicians, we gathered high-quality clinical data pertaining to safety and performance of medical devices to ensure the "human-in-the-loop" approach. These datasets were subsequently utilised by machine learning engineers for AI training purposes. Once the models were operational on the platform, the medical writing team created literature review projects to assess and validate their accuracy and sensitivity, two important parameters used in measuring the performance of an AI model.

By underlining the role of medical writers in the process of AI training, some of the prevailing misconceptions surrounding AI automations should be discredited. One such misconception involves the origin and quality of the datasets used for AI training, with many question marks raised regarding the type of checks and quality control processes undertaken to guarantee the robustness of their performance. Given the stringent nature of the regulatory domain, such software solutions go through repeated assessment and validation processes to align with regulatory and legal expectations. The development process involves collaborative efforts between regulatory and medical writing professionals, as well as software and machine learning engineers, who come together to build

optimal products suitable for professionals operating within the intricate regulatory field.

In the following sections, I present five automations to highlight some of the most interesting functionalities currently available to medical writers. The solutions are listed in alphabetical order.

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avasis

As a leader in process digitalisation, avasis offers a comprehensive suite of digital solutions that optimise tasks and facilitate the transformation of information from documents into digital datasets for enhanced reusability, traceability of information, and automated completeness checks, ensuring compliance and enhancing efficiency.[3] These solutions revolve around the core functionalities of Siemen's ALM Polarion software, which ensures the digitalisation of various processes within the medical device life cycle. avasis provides solutions that are particularly relevant to medical writers, enabling efficient management and documentation of content created as part of clinical evaluation, post-market clinical follow-up (PMCF), and PMS activities.

Customers of avasis can select one or more solutions from its portfolio to meet their specific requirements. These solutions can be further adapted to align with the company's specific product portfolio. For example, avaREGULATORY assists in managing regulatory documents and requirements, while avaCLINICAL streamlines reviewing the process of clinical evaluation and literature review, integrating it with risk management and product development. avaPMCF handles the management and documentation of PMCF activities, linking them to clinical evaluation and risk management. The latest addition to their offerings is avaADVERSE/ avaPMS, a tool specifically designed for PMS. Through an integration between these solutions, they allow semi-automated content creation, maintaining consistency, traceability, and improving overall efficiency.

The integration of avaADVERSE with national authorities' databases enables searches and direct access to vigilance data. Subsequently, the relevance and quality of the data can be directly assessed, before sending the information to avaRISK for further analysis. The solution seamlessly integrates with the clinical safety reporting components in avaCLINICAL. The solution provides four readily available templates for creation of safety database review files, safety database search plans, safety database search protocols, and safety database review reports.

Additionally, the avaIMDRF add-on centrally manages International Medical Device Regulators Forum (IMDRF) adverse event (AE) codes digitally, eliminating the need for Excel files. The integration of IMDRF AE terminology library grants users access codes, and the application of these the codes for information in

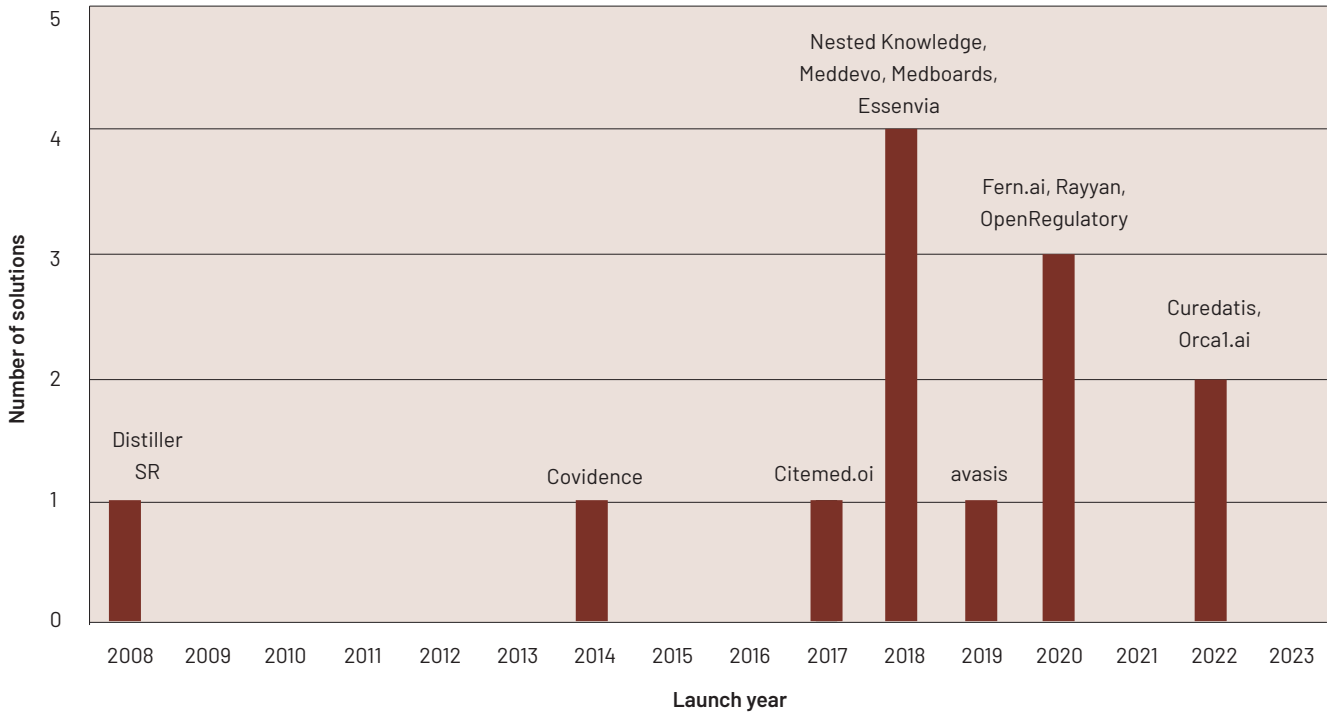

Figure 1. The timeline of the release of regulatory and medical writing tools

This infographic demonstrates the release of tools and platforms aimed for conducting systematic literature reviews and providing assistance for technical documentation of medical device life cycle between 2008 and 2023.

different processes (e.g., for harms in the risk analysis). These codes can be used to identify trends and signals in PMS and to categorise publications identified during literature reviews, ultimately contributing to PMS reporting. The use of IMDRF AE codes for adverse event coding is an international requirement, playing a crucial role not only in vigilance (serious adverse event reporting) but also in various activities such as cause investigation, complaint handling, and clinical evaluation, all of which contribute to effective risk management.

DistillerSR

DistillerSR, one of the pioneers in the field of digitalising literature reviews, optimises the processes of both pre-market approval and post-market compliance evidence management.[4] This platform can be customised to match the complexity of each specific use case, with configuration options available at every key step of the literature reviewing process.

One of the time-saving features of DistillerSR is its smart quarantine functionality, which automates the deduplication process while giving users control over the level of confidence processes at which the AI should consider a reference as a duplicate. Users also have the option to manually review these references at any point.

With its AI capabilities, DistillerSR enables reviewers to find references more efficiently by continuously assessing their relevance and comparing them to pre-screening records. This results in updated rankings and reprioritised order of the reference list. Additionally, DistillerSR plays a role in quality control by double-checking inclusion and exclusion decisions and automatically categorising references.

Workload triage is another aspect of DistillerSR's design that clearly distinguishes the platform. This feature allows project leaders to assign specific portions of the review process to certain reviewers while keeping track of their progress in real time. Through comprehensive traceability, a project leader's task is further facilitated by the access to details of the actions and decisions taken throughout the reviewing process. A specific action or search can be traced back not only to the user, but also to the date and time of execution and is linked to a certain query. This also ensures that any project completed in the platform is audit-ready.

CuratorCR, a recently developed add-on module, serves as a research knowledge centre within the platform. It consolidates and dynamically manages the workflow of evidence-based research, enabling reviewers to continuously curate, share, update, and reuse data across multiple teams, modules, and product portfolios.

Fern.ai

Fern.ai™, previously known as Giotto Compliance, is a comprehensive platform for clinical evidence review that offers an intuitive interface.[5] Fern.ai employs AI models trained by medical writers with a human-in-the-loop approach which deliver recommendations during the title and abstract screening and the extraction steps with high sensitivity and accuracy.

With a literature review-based structure that lends itself well to a wide range of use cases, the platform has built-in features that align with the guidelines set by the EUMDR and EU In Vitro Medical Device Regulation for clinical evaluation and performance evaluation purposes. The platform ensures thorough documentation of all steps, facilitating auditing and ensuring traceability. Users have the flexibility to customise the generated documents, available in various formats, at the end of each step. Academic research, epidemiological studies, and health economics and outcomes research are a few more examples of use cases for Fern.ai.

At the outset of each literature review, Fern.ai allows users to define their research strategy in the project workspace through the Population, Intervention, Comparison, Outcomes and Study (PICOS) framework. These data are subsequently used by the AI as the basis for its recommendations for that specific project. Fern.ai facilitates a seamless transition between the query, screening, appraisal, and data extraction steps through its intuitive workflow.

By leveraging the AI's inclusion and exclusion recommendations, users can optimise their screening process, offering the flexibility to customise the degree of automation in their decision-making. Users can also specify the exclusion reasons on which these recommendations should be applied, giving them greater control over the screening outcomes. Duplication, language type, and missing abstracts are among the common exclusion reasons where a high degree of automation is often used, resulting in significant time reduction during screening. In a similar fashion, Fern.ai plays a central role in improving efficiency and data quality during the data extraction steps. Using natural language processing and customisable data extraction templates, users can directly extract relevant data from selected articles through an intelligent tagging interface. Moreover, users can locate relevant data with the help of the AI's suggestions. The link between the extracted data and their original location in the article allows a "one-click" revision and audit process. The data extraction functionality of Fern.ai is one of the strongest features of the platform.

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MedBoard

MedBoard is a multipurpose platform consisting of six digital modules integrated with a large, curated information portal through a powerful AI search engine for MedTech, Pharma, and Digital Health.[6] These modules include: MedBoard Search, Databases and Analytics, MedBoard profiles, Intelligence (Clinical and regulatory), Systematic Reviews, and Product portfolio and country registrations management.

MedBoard encompasses a wide range of information, covering clinical trials, literature, recalls, adverse events, approvals, guidelines, regulatory news, market news, technical standards, documents, and safety alerts. Equipped with advanced search filters, and an analytics studio, these databases offer the capability to slice and visualise data, providing instant new insights.

MedBoard Search, databases and other trusted data sources are at the core of the platform delivering regulatory, market and clinical intelligence to the other modules. The "Systematic Reviews" module harnesses the extensive database capabilities of the platform. In addition to scientific literature, this module can help users tap into other data resources such as: technical standards, market information, and clinical trials. Furthermore, the Systematic Review module offers features such as automated updates, customisable appraisal criteria, automated PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses), and identification of similar reviews. Additionally, an "AI Reviewer Assistant" is available to assist users in their tasks. In keeping with their strategy of placing the user at the centre of the decision-making process, the role of the AI tool is providing assistance, intelligence, and automating manual, repetitive work.

The platform's modules and functionalities come together to expediate various key activities, including PMS clinical reviews, SOTA (state-of-the-art) analysis, and competitive market analysis by leveraging its extensive database of manufactures and medical product profiles.

Nested Knowledge

Nested Knowledge is an evidence synthesis tool designed to transform the way the scientific community gathers and interacts with clinical data.[7] It offers various functionalities, such as finding, filtering, extracting, and analysing data from diverse sources for different purposes. While its primary use case is health economics and outcomes research, as well as academic meta-analyses, it is also highly effective in early stages of medical device and drug research and development, clinical study design, and compiling data for regulatory submissions.

There are notable differences between publicly available AI platforms and those designed for professional use, particularly in terms of training, testing, and validation.

A significant challenge addressed by Nested Knowledge is the laborious and continuous process of updating existing reviews. Unlike other tools that produce static documentation, Nested Knowledge provides interactive, AI-assisted living systematic reviews and meta-analyses that can be updated in real-time.

Structurally, Nested Knowledge consists of two main modules: AutoLit and Synthesis. The AutoLit workflow serves as the foundation, allowing users to search, screen, and extract content from published studies. AI assistance is available at each step, but an expert review is required for accuracy confirmation. The platform also utilises AI during the screening process, serving as a third reviewer by learning from the user's screening decisions.

Synthesis is a robust analytical component of the platform that provides evidence-based insights into the data collected using AutoLit. These insights are presented through web-based interactive data visualisations that dynamically change as the underlying data are updated. Synthesis offers functionalities such as Quantitative, Qualitative, Manuscript, Critical Appraisal, and PRISMA.

The qualitative Synthesis function of Nested Knowledge enables users to collect and classify data through a tagging hierarchy to review the population and endpoints of trials, and compare interventions and comparators. These data can be used to define the standard of care and compare intervention outcomes when conducting SOTA reviews. On the quantitative side, Synthesis provides a network meta-analysis environment where the data can be reviewed at the summary level using the data elements of interest. Dynamic visual outputs such as forest plots with calculated odds ratios and funnel plots are generated and can be reviewed directly on the platform. Furthermore, heterogeneity and risk of bias are assessed through automatically calculated r-squared value and and risk of bias visual representations.

Conclusion

At the end of this technically packed exploration, I would like to emphasise a key message: Automations are designed to tackle challenges encountered during technical documentation. Despite having a common goal, they employ alternative implementation strategies and thus prioritise different features. As a result, they empower their users through improving data quality, minimising repetitive tasks, and eliminating versioning issues. By providing template and customisable exports and ensuring traceability, they enhance compliance and audit-ready documentation. Digitalisation sets the stage for a highly streamlined collaborative and organisational project management processes. Collectively, these advantages make medical writers more efficient, reduce errors and audit deficiencies, and ultimately alleviate frustration. In the long run, reliable processes foster the delivery of medical devices with enhanced safety and performance profiles, paving the way for innovation and better patient care.

Here are a few additional takeaways:

- Features and functionalities of automation tools can vary significantly. While some focus on content authoring and analytical synthesis, others put more emphasis on data reusability, automated data extraction, and curated global intelligence.
- Considering the diverse profiles of automation tools, there is no one-size-fits-all solution. Users should invest time to determine which tool best suits their specific use cases.
- Not all automation tools incorporate AI and those that do utilise it as an additional feature to facilitate certain activities, while keeping the user in the driver's seat.
- There are notable differences between publicly available AI platforms and those designed for professional use, particularly in

terms of training, testing, and validation.
- When approaching a new tool, it is advisable to employ multiple methods and sources to thoroughly understand its functionalities. Engaging in discussions with long-term users and conducting adequate testing are essential.

As I have only scratched the surface of this group of technologically sophisticated solutions, and given the rapidly evolving nature of this sector with new products and features being introduced regularly, I would like to encourage readers to use this review as a starting point, conduct further research to gain a deeper understanding of the tools covered in the article, and explore additional options that I may not have been able to discuss due to space limitations. Noteworthy automation tools for reviewing clinical evidence include CiteMed.io, Covidence, Curedatis, Meddevo, and Rayyan. For generative AI-based tools in regulatory intelligence, consider Dr.Evidence, Huma.AI, Orca1.ai, and Yseop.

Acknowledgements

The author would like to thank the following people for providing support and technical information about the automations reviewed in the article: Ivan Perez Chamorro (MedBoard), Kevin and Keith Kallmes (Nested Knowledge Inc.) Vivian MacAdden (DistillerSR Inc.), Celeste Maksim (Fern.ai), and Sarah Panten (avasis Solutions GmbH).

Disclaimers

The opinions expressed in this article are the author's own and not necessarily shared by her employer or EMWA. This article is neither a promotional piece nor a systematic comparison of the showcased tools. EMWA and the author do not endorse any specific automation platform.

Disclosures and conflicts of interest

The author was employed by Giotto.ai, the company developing Fern.ai, from April 2021 to June 2023.

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This is called the hash, pound, or number character. A hashtag is a keyword or set of keywords that is preceded by the # character. It is used in social media to create a thread of conversations around a specific theme or topic conveyed in short texts or microblogs. It is commonly used in Twitter, Instagram, YouTube, Pinterest, etc.

A dictionary of most common hashtags can be found at https://www.hashtags.org/definition/~h/.

For your info, EMWA is compiling a list of standarised hashtags for our social media use.

@ This is called the "at" sign or symbol. The @ sign is part of email addresses and social media user names ("handles"). Our EMWA handles are as follows: @Official_EMWA (Twitter), @EMWA (LinkedIn), and @europeanmedicalwritersassociation (Facebook)

The two most important keys on your keyboard