

TOPICAL FEATURE

Using Innovative Tools and Lean Writing Workflow Processes to Accelerate Regulatory Document Writing*

Robert Panek, PhD; Sara Fernandes, PhD; Mauro Meloni, PhD; Gregory Morehouse, MS, MWC; and Rona Grunspan, MD / Medical Writing, Quality & Editing, and Clinical Trial Transparency ICON plc, Raleigh, NC

ABSTRACT

Lean writing workflow processes can streamline development of complex documents, including protocols and other regulatory submissions.

This paper outlines standard development timelines and describes useful lean writing workflow methods and tools to reduce protocol development timelines without sacrificing document quality.

We present the results of a survey completed by 75 Medical writers (MW) that reveal the strategies used during document preparation and use real case scenarios (protocol development) that illustrate how innovative tools and approaches can be efficiently used to create a lean writing workflow process.

Software tools (e.g., proofreading assistance, citation manager, collaborative authoring and reviewing) were widely accepted and used during protocol development according to the MWs surveyed. Most of the surveyed writers (62%) hypothesized a reduction in production time by about 25%. Efficient collaborative work across different time zones had a marked impact on shortening timelines while maintaining production of high-quality documents.

Real case scenarios were used to illustrate how innovative tools and approaches can positively impact timelines and efficiently create a lean writing workflow process regardless of therapeutic area.

The real case scenarios showed that protocol development time can be decreased by about 26% without compromising the quality of the document. This shows that software tools, templates, checklists, and collaborative writing were more impactful than hypothesized by the MWs included in the survey.

With clear workflow processes, roles, and responsibilities backed by innovative software applications, template guidelines, and collaborative work processes, MWs can overcome common development challenges and improve their lean regulatory writing skills.

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INTRODUCTION

Every clinical investigation begins with the development of a clinical study protocol, which conveys the design and methods for conducting a clinical study. Protocols are written by a multidisciplinary team that normally includes a medical and clinical pharmacology expert, a statistician, a pharmacokinetics expert, regulatory consultants, a study manager, a project manager, and a MW. It is the role of the MW to coordinate the input of all involved experts to compile the protocol.^{1,2}

MWs routinely face accelerated timelines to complete drafts, and realistic schedules are often a luxury. Lack of coordination among team members or any lag during document development could lead to a cascade of events potentially resulting in study delay. Therefore, sufficient time needs to be invested in the development of the protocol to account for multiple reviews, edits, and adjustments after reviews. To produce a document that is clear and concise with a well-organized message, a lean writing process that emphasizes timeliness and quality is beneficial.³ When sufficient time for completing writing processes, particularly lean writing, is not allotted, protocol development is likely to become excessively long. This is because truncated initial timelines require more extensive editing and/or review. Similarly, protocol content could be repetitive, verbose, ambiguous, inconsistent, and riddled with errors, negatively affecting protocol quality.

Given that writing and reviewing compete for time, how can MWs use tools that support both practical timelines and high document quality standards? What can be done to ensure that the time writers spend on protocols is more focused on the quality of the content than on the search for errors and common mistakes?

Here we describe useful lean writing workflow processes and innovative software tools to reduce protocol development timelines without sacrificing document quality.

STANDARD TIMELINES

To effectively manage and coordinate the multidisciplinary

team involved in preparing a protocol, clear descriptions of the roles and functions of each team member are vital. These descriptions are crucial not only so that each team member understands the contribution required of them but also to determine the amount of time necessary to complete their contribution to the protocol effectively. Along with the multidisciplinary team that contributes to the content of the protocol work, the editorial and regulatory publishing teams manage the redactional quality of the final document. Defining a standard, full process timeline streamlines every part of the process: from synopsis preparation to study design; from assessment planning to text, table and figure quality; from the science to published document, a standard timeline guarantees fewer process conflicts (Figure 1).

Standard full-process timelines have evolved over time, with each step further refined by the collective experiences of colleagues across diverse departments and functions. Standard timelines have built-in flexibility to account for variable workloads as each team member may simultaneously work on multiple projects. Each step of the protocol development is divided into rounds. Each step can be fulfilled in the allotted time depending on individual workload. In general, development proceeds from drafting to review and/

or quality control (QC) and then to drafting again, where review comments can be addressed. As mentioned above, standard timelines may require additional flexibility; for example, an ad hoc meeting may be necessary to address any unresolved issues. The drafting step ends with the approval of the protocol, which is followed by the publishing of the common technical document (CTD) in a format consistent with the regulatory submissions (e.g., the ICH CTD format).⁴

Standard ICON protocol development timelines include 10 to 15 days to prepare the synopsis, 47 days for the body of the protocol, and 3 days for the publishing of the CTD-ready document (Figure 2). Synopsis preparation may not always be required, as the client may have prepared the synopsis during conceptual development of the study. Additionally, the client may prefer to publish the protocol using an alternative publishing service. In these cases, our standard timeline would only include the 47-day protocol preparation. The addition of a synopsis and publishing would not change the protocol development process, only the timeline.

In this report, we only discuss the preparation of the protocol and compare our standard timelines with case studies in which we have successfully accelerated protocol writing timelines using the innovative tools described below.



Figure 1. Document preparation process, an outline. QC=Quality control.



Figure 2. Standard protocol development timelines.

We also present the results of a survey completed by 75 MWs that reveal the strategies used during document preparation that illustrate how innovative tools and approaches can be efficiently used to create a lean writing workflow process.

THE SURVEY

A 10-question online survey was designed to understand which timeline-saving tools and approaches are most used by MWs. The survey was administered to 75 writers both internal (54) and external (21) to ICON. Of those who completed the survey, 41% were early phase MWs, 37% were late phase MWs, and 21% were MWs specialized in other areas (ie., manuscript writing).

The majority of MWs surveyed said they required 5 to 7 weeks (49%) or more than 7 weeks (35%) to develop a protocol, including draft preparation, review cycles, administrative tasks, and finalization. For each review cycle, 51% of MWs claimed they allocated an average of 3 to 4 days, while 46% required 5 days or more (Figure 3). Only a small percentage (3%) required 1 to 2 days.

To meet aggressive timelines, 50% of MWs have worked collaboratively across time zones to develop a protocol and

believed that the approach had a positive impact on reduction of development timelines. The key factors for a successful collaborative approach as selected by the writers were: continuous work around the clock, parallel and continuous QC of the work, and a good relationship among the authors (Figure 4). When writers were asked about the factors that could negatively impact collaborative writing, the responses indicated that lack of communication, conflicting opinions, and lack of flexibility were the primary factors.

Software tools are widely accepted by MWs. Most of the surveyed writers at ICON use PerfectIt (91%), EndNote or another reference management software (49%), and PleaseReview (53%) during protocol development. Whereas outside ICON, EndNote is the preferred tool (63%), followed by other software and PleaseReview (37% each), and PerfectIt (16%). These differences likely reflect the different company preferences. Of the MWs who leverage one or more of these tools, 45% believe an application such as PleaseReview is a more helpful tool than the others surveyed for protocol development and reduction of timelines (ICON 52% [50 MW] and outside ICON 29% [21 MW]) (Figure 5). This is likely because when used within a lean workflow process, PleaseReview directly addresses 2 of the

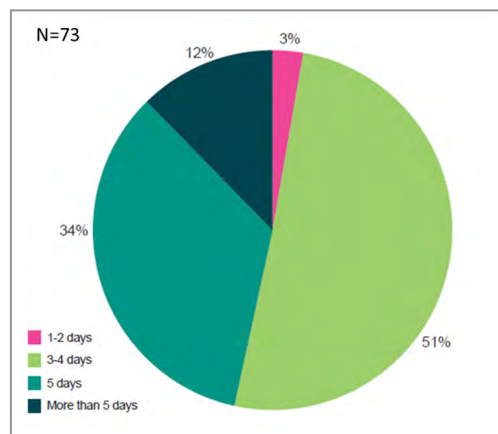


Figure 3. Survey question: On average, how many review days are included in your timelines for each review cycle? Answered, N=73; Skipped, N=2.

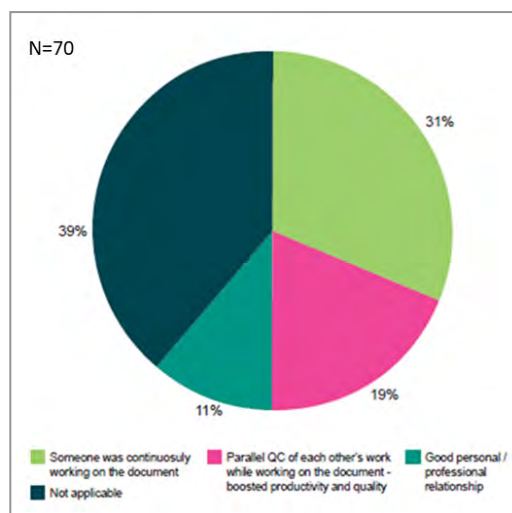
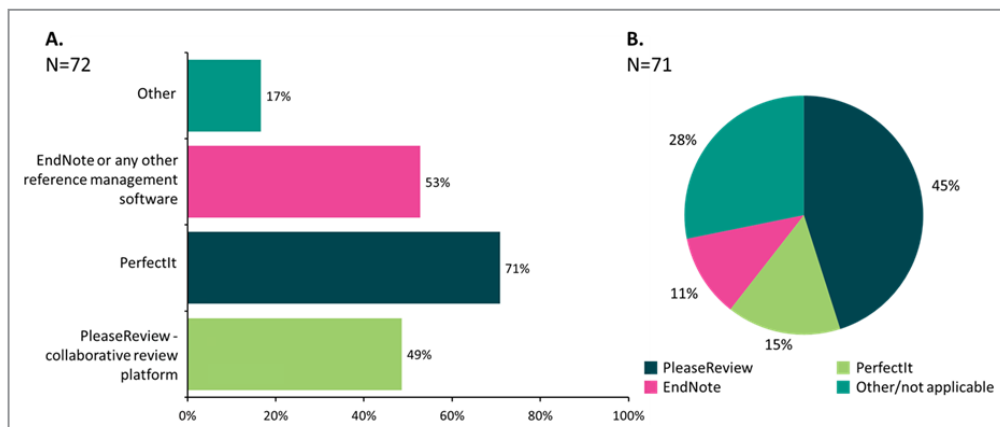


Figure 4. Survey question: If collaborative work positively impacted your timelines, please select the most important factor contributing to timeline reduction. Answered, N=70; Skipped, N=5.

Figure 5. Survey questions:
 A. Do you use any of the following tools for protocol development? Answered, N=72; Skipped, N=3.
 B. Which of the following tools do you consider more helpful for protocol development and reduction of timelines? Answered, N=71; Skipped, N=4.



negative factors identified by MWs: conflicting opinions and communication.

According to the surveyed writers, when taken together, these tools can help to reduce up to 35% of the time required for development of a protocol (Figure 6). The different software tools can efficiently identify grammar, style, and content errors; save time by automating citation updates; and provide a mechanism for simultaneous review and consolidation of reviewer comments.

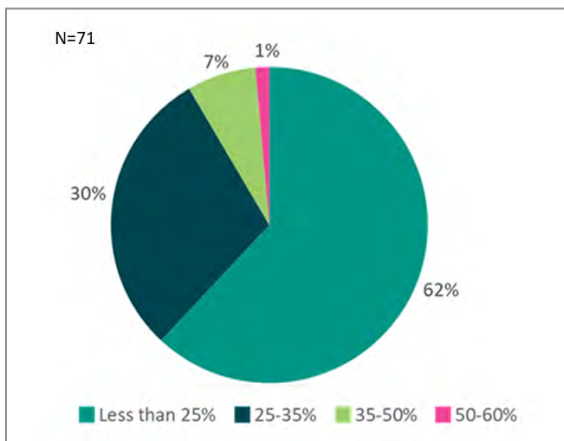


Figure 6. Survey question: On average, how much time can these tools save? Answered, N=71; Skipped, N=4.

REAL CASE SCENARIOS

In ICON’s day-to-day practice, the medical writing team regularly responds to sponsors’ requests to compress standard timelines and deliver high-quality protocols sooner. We use the tools, templates, and checklists described above and work collaboratively across geographically dispersed

teams to expedite development. To demonstrate how these tools and a collaborative approach can positively impact protocol development, we analyzed the results of five real case medical writing scenarios to compare our writing process across standard and reduced timelines with a heterogeneous group of MWs. All scenarios were Phase 1 study protocols of varying study designs: 2 drug-drug interaction studies; 2 single-ascending/multiple-ascending dose studies; 1 food-effect study, and all were of moderate complexity. A collaborative writing approach was used in all the studies. The writers involved in these scenarios had 5 or more years of experience and used 1 or more of the previously described tools.

Our real case scenarios showed that protocol development timelines can be decreased by about 26% without compromising the quality of the document (Figure 7). This shows that software tools, templates, checklists, and collaborative writing were more impactful than hypothesized by the MWs included in the survey. Most of the surveyed writers (62%) hypothesized a reduction in production time by 25% or less; meanwhile, our real case scenarios show a 26% decrease.

MASTERING THE TOOLS FOR LEAN WORKFLOWS

As the number of content contributors on a team increases, so does the potential for inconsistencies and errors, which in turn affects the efficiency of the document review and the overall project schedule. Document review and QC checks can take hours, days or even weeks to complete depending on the complexity and quality of the document. Such checks are typically the most expensive and time-consuming part of the protocol development process. Employing lean writing

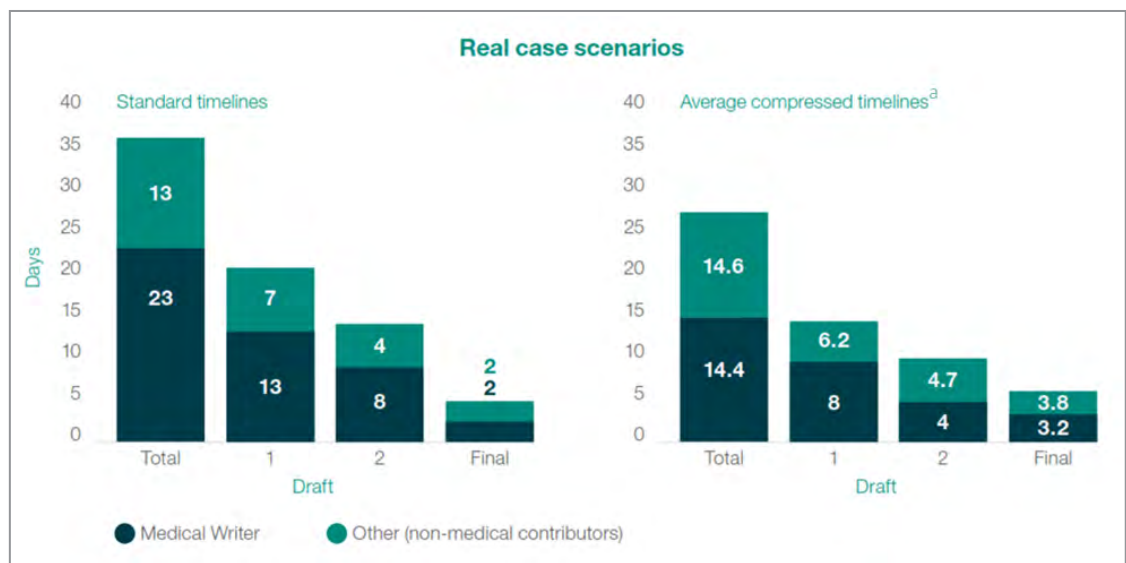


Figure 7. Time required to prepare a protocol under standard and reduced timelines.
^aAverage of 5 reduced timelines was 26.5 days (range 18, 33 days).

workflow processes and innovative software applications can mitigate potential time loss in the document review process without sacrificing document quality.

A variety of software tools are available to help medical writers⁵ streamline the review process, and we will explore the benefits of a few popular tools below. Our study is not intended to promote any software but to highlight the importance of the tools themselves. There are several programs on the market that offer the same or similar tools to the ones referenced in this paper. The programs we mention in our study and survey are simply the software we use at ICON.

The findings of our study may largely pertain to the software applications and tools used by those MWs in the survey and in the case scenarios and may not generalize to other tools or software applications available on the market.

ASSISTED PROOFREADING

As previously mentioned, the more writers and reviewers involved in the development process, the more likely it is that inconsistencies in style appear along with repetition, verbosity, and data and grammar errors. To reduce these errors and optimize our specialists' time, we utilize PerfectIt™, a Microsoft Word add-in, as a proofreading application to manage some of the most tedious and time-consuming editing. It catches inconsistencies in hyphenation and numbers, checks punctuation and capitalization, automatically corrects double spaces, removes spaces after paragraphs and cuts spaces before punctuation. It is particularly helpful with abbreviations, as it ensures that every abbreviation is defined only once at its first presentation.

PerfectIt has saved time in hunting for typographical and grammatical errors and style inconsistencies, resulting in a higher-quality draft and reduced overall QC time.

AUTOMATED REFERENCE MANAGEMENT

MWs often work on large, unwieldy documents with large numbers of references which can be lost, moved, or unlinked from the document body. Style inconsistencies may also be introduced as the document evolves and multiple contributors add on sections.

The citation managing application EndNote™ and its Microsoft Word add-in is used to manage citations of published works and source documents. With EndNote, writers can insert in-text citations while the program automatically organizes references in a bibliography in the preferred style and also updates and crosslinks citations with references throughout document drafting. In EndNote, it is also possible to save bibliographies and literature in libraries that are easily searched and updated. Additionally, EndNote can save references from the major online

scientific databases, such as PubMed or Google Scholar. Like PerfectIt, EndNote comes with default styles and customization options.

EndNote saved time by reducing the MWs referencing workload, including tracking and formatting citations throughout large documents. It has a robust citation library sharing capacity and integrated and up to date referencing to facilitate collaboration.

Box. Software Tools for Medical Writers

PerfectIt

<https://intelligentediting.com>

EndNote

<https://endnote.com>

PleaseReview

<https://www.ideagen.com/products/pleasereview>

STREAMLINED REVIEWING

A multiplicity of authors and reviewers can produce high-quality content, but it can also pose challenges in the review cycle. Reviewers may have conflicting comments and consolidating comments across multiple documents and controlling which edits are made is quite time-consuming.

To facilitate the collaborative review of documents, we use PleaseReview™, an online platform designed for co authoring, reviewing and consolidating comments. It allows teams to achieve faster turn-around times and meet tight deadlines for collaborative document development. Reviewers can review simultaneously, see each other's comments (single interface for all reviewers), and engage in discussion, facilitating comment mitigation.

Additionally, the entire review process is saved in an audit-ready review log. PleaseReview works directly with Microsoft Word, Excel, and PowerPoint documents, PDFs, images, and plain text files. Authorized persons can easily download the reviews and original documents, and the comments and proposed changes can be found in the Word file in tracked-changes.

Authors and reviewers can effectively collaborate and review in real time such that comments can be readily addressed. The author has full control over the proposed edits, and simultaneous review by many authors comes with no risk of losing any of the content, as changes and comments cannot be lost or overwritten by other reviewers. PleaseReview also gives a holistic overview of the process, which includes the review status for each reviewer, reconciliation reports, summaries of all comments and actions taken by the participants.

KNOWING YOUR TEMPLATE

It is the responsibility of the writing team at ICON to find an adequate protocol template to use as a basis for development. There exist several template options such as the TransCelerate common protocol template and National Institute of Health template, which incorporate feedback from multiple industry stakeholders.

Templates may vary depending on the foreseen study design, study population, and/or therapeutic area. A template usually contains already-approved regulatory language, standard laboratory assessments, inclusion and exclusion criteria, a study diagram, and schedule(s) of assessments. Sections are prefilled with the most common and routine assessments and language.

The need for a standardized template has been recognized by the ICH, and one is currently being developed. Most recently, ICH M11 promises similar efficiencies in protocol review and approval to those gained when regulatory approval applications were standardized by the eCTD template within ICH M4.⁴

To save time, it is recommended to develop standard templates that follow the regulatory guidelines. Also, a protocol checklist can be employed to reduce content errors across sections.

This checklist serves as a helpful tip sheet for MWs and peer reviewers working on early clinical protocols. The checklist can help ensure consistency in content across sections of protocols, help identify sections prone to repetition and reduce the likelihood of amendments.

MWs in our group authoring early clinical protocols use a checklist regularly to check their own work before the delivery of drafts for team review and as a last self-check for potential errors before finalization. The use of this checklist has proven to reduce time during document development and quality checks. Many of the tips in this checklist are based on actual inconsistencies that have been uncovered in past company protocols after finalization or raised during Informed Consent Form development.

ENGAGING COLLABORATIVE WRITING

The conventional sequential document development approach, with distinct cycles of authoring and reviews, has evolved toward a more collaborative, asynchronous process. This approach can take advantage of time zone differences for global teams or teams with a wide geographic distribution, thus maximizing development timelines. Instead of a restrictive linear, sequential development, collaborative writing allows authors to work on different sections while writers implement continuous QC checks. Collaborative writing can essentially continue around the clock when conducted across multiple time zones and in

many cases may be the only way to meet aggressive timelines.

Successful collaboration requires effective communication, clear expectations, careful planning, and trust that each member will accomplish their tasks on time and to quality. When executed well, this method helps to build stronger team bonds, as remote teams develop an increased awareness of teammates' cultures, work styles, native language differences, and personalities. Although there are challenges to collaborative writing, the effective use of collaborative authoring tools (including those mentioned above) can enable this activity in ways that would otherwise be impossible.

TIPS FOR A SUCCESSFUL COLLABORATIVE WRITING SYSTEM

- **Effective Communication.** When working with a distributed team, effective communication is the most crucial success factor. Striking the perfect balance between online and offline methods of communication is key. While brainstorming is more effective in real time, using calls or instant messages, an offline approach allows collaborators to work autonomously, uninterrupted, and more productively, giving focused attention to each document section.
- **A Clear Management Plan.** The lead MW must coordinate supporting MWs, direct questions to team members, keep the team informed of key decisions, identify critical updates and sections impacted, and delegate tasks. They must also identify the action steps required to move successfully from project start to finish, outline the various tasks relevant to document production, and clearly define roles and responsibilities to help the team focus on priorities and successfully complete the document.
- **Author Accountability and Cooperation.** Careful planning when assigning each author a section to complete promotes a sense of accountability and cooperation. Important aspects to consider for task allocation are the experience, background, and personality of the writer to maximize their expertise and productivity.
- **Problem-solving.** One of the greatest struggles in collaboration is the potential for disagreement. It is common for collaborating authors to have conflicting approaches to accomplishing work or presenting ideas. Authors must approach these differences collaboratively, with a problem-solving mindset, to share ideas, work toward a common goal, and make decisions together.
- **Embrace the Virtual Processes.** Virtual processes and

collaborative tools improve efficiency in the document development process. For instance, files can be stored in shared repositories for easy retrieval at any time. However, ensuring the team is aligned on the best practices and processes for these tools is crucial. A common version control system and standard naming convention ensures that documents are saved appropriately.

- **Flexibility.** The key to collaborative, asynchronous, and virtual document development is flexibility. The MW should be available to their collaborators to resolve issues and enable continuous progress. Instead of dividing authors into silos, knowledge-sharing among team members helps solve complex problems and enrich content. Similarly, this flexibility in the collaborative approach drives commitment among collaborators and fosters teamwork with a global perspective.

“Great things in business are never done by one person. They’re done by a team of people.”

—Steve Jobs⁶

CONCLUSIONS

Regulatory writing can be complex both in content and development processes, but with lean workflow processes and useful tools, MWs can reduce the amount of time and personnel hours attributed to each step. Software tools are widely accepted by MWs, and many already use the tools discussed above (92%, Figure 6).

Based on the real case scenarios examined, protocol development time can be decreased by about 26%, showing that software applications, templates, checklists, and collaborative writing are more useful than originally hypothesized by the largest group of surveyed MWs (62%).

With clear processes, roles, and responsibilities backed by innovative tools, MWs can overcome common development challenges and improve their lean regulatory writing skills.

Limitations

A limitation of this study is inherent to the survey sample size. Most respondents were ICON employees (54 out of 75 [72%]) and therefore the sample may not be a true representation of the medical writing community. However, this study was exploratory in nature and the results obtained were not intended to be extrapolated to the entire medical writing population. Future research could be undertaken to examine the strategies used by MWs from different backgrounds and levels of experience.

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Author contact: rob.panek@ICONplc.com

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