



TECHNICAL BULLETIN

Optimizing pharmaceutical document reviews

Health Inspired, Quality Driven.

Pathways to enhanced productivity and quality.

Documents are the motor of the pharmaceutical industry. Clinical study approvals, participant safety, the collection of reliable and useful data and, ultimately, market approval, are all driven by the creation of multidisciplinary, interdependent, strategic and scientific documents. Fundamental to the quality of these documents is clear, well-structured writing, from the study protocol to the proposed labeling text.

Equally important is the review process. Many clinical research professionals fail to realize that effective and efficient reviews contribute no less to the quality of the document's content than the writing. However, because the review process is labor-intensive, it often engenders frustration in participants and may be less productive than it seems.

It is one thing to generate comments but what does it take to generate true document improvements?

Why review your review process?

Reviewing is simple, no? The reviewer reads the document and provides input. All of us in the industry can read and evaluate text, providing comments as we go, so why should we dedicate time and effort to assessing and improving something that seems to be straightforward?

Cost and effort is one important reason.

When developing a document, roughly 70-80% of the total effort goes into reviewing. If this seems incredible, consider the fact that for each document there is usually one writer but between six and ten reviewers. In most cases, these reviewers will be involved in multiple review rounds and, as we shall explore, productive reviewing means more than just reading the document from cover to cover.

70-80%

of the total effort goes into reviewing

Several publications have described the document review process as time-intensive and frequently suboptimal. It is often perceived by both reviewers and writers as inefficient and frustrating (Bernhardt, 2003; Cuppan & Bernhardt, 2012; Fiebig, 2015). So how do we take this costly and potentially frustrating activity and refashion it into an efficient and effective process that respects everyone's time and effort?

This article focuses on clinical study reports (CSRs), but the principles can be applied to structured review of all clinical research-related documents. We will start by determining some important attributes of a productive review and then ask questions to determine what barriers may exist to achieving those desired attributes. From there we can map a practical route to improvement.

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Destination

The goal of any writing and review process is the creation of a high-quality document.

WHAT DOES A HIGH-QUALITY DOCUMENT LOOK LIKE?

A good quality document is one that is fit for purpose. It must effectively target its audience and be clear, concise, complete and consistent with the sources.

The last two points are self-explanatory: no information should be missing and all information should be correct (i.e. match the source). Whether text is clear and concise becomes slightly more subjective, but a writer can achieve this without much input.

Nevertheless, these four aspects are typically what reviewers naturally focus on. They are also the easiest aspects to address during a review, captured by a simple and chronological read-through of the document.

However, input from clinical team members through review is vital for finetuning the document so that it is tailored to its intended audience (e.g. health authority assessors as the ultimate audience of a CSR) and fit for purpose (e.g. does the CSR answer the questions that formed the rationale behind the study?). These goals will shape the common thread throughout the document, without which it can easily get bogged down and become a featureless enumeration of data.

Reviewing these larger-scale aspects of a document is more difficult and may require multiple or non-sequential read-throughs. The additional effort is warranted though, because the risks from badly conducted or consolidated reviews can go beyond wasted time to include the introduction of new errors and inconsistencies (Nürnberg, 2014). In addition, a survey of health authority reviewers revealed poor explanation of rationale, lack of transparency and excessive length/repetition/verbosity were the most important issues that negatively affected health authority assessment (Cooper et al., 2022).

WHAT DOES PRODUCTIVE REVIEW LOOK LIKE?

Productive clinical document review is a concerted team effort of writers and reviewers that moves the document through a predetermined process from first draft to final document in an efficient manner. Effective improvements will be made along the way with respect to the time and effort invested by everyone involved.

The review process is efficient and effective if:

- Each reviewer focuses on the aspects that need his or her attention, as determined by his or her function in the team and the document's stage and purpose
- Review comments are useful, ie, each comment suggests true improvement communicated in a way that allows the writer to act on it
- Writing and review occur with agreed and realistic timelines

Possible barriers to productive review

DO ALL REVIEWERS KNOW THE PURPOSE AND GOAL OF REVIEW?

There is a common misconception that the purpose of review is correction. This is not the case, and editing, proofreading and quality control checks are not (or should not be) part of the reviewer's role. It is simply inefficient for multiple reviewers to perform this type of error inspection when it is more effectively done by one person (usually a second writer or dedicated quality controller).

The reviewer should focus on whether the document is fit for purpose and therefore view it from the perspective of the intended audience. This is usually not the document signatory, the clinical team or the sponsor company, but the health authority assessors.

Reviewers should ask themselves if the text will convince assessors that:

- The study was rigorous and well-controlled, and the data trustworthy?
- The selected dose is the best one to continue with?
- The two drugs can be safely administered together?
- The formulation change is acceptable?
- The product is effective and safe?
- ...

If the current text does not answer these questions satisfactorily, then it is the task of the reviewer to determine why not and what can be done to improve it, given the study is complete and the data immutable. Every expert contributing to the review should look at these questions from the perspective of their own field and the collective input of all experts in the team will result in a convincing case.

So, rather than an error inspection, the review should entail the reading of the text for logic threads and overall message. This requires a different mindset to reading the text for editing.

The focus should not be on the flow of the text itself, but on the flow of the ideas and arguments that underlie it. It is not safe to assume that all reviewers are aware of these expectations, which means training could be required.

IS THE REVIEW ON TARGET, I.E. AS PLANNED AND AT THE REQUIRED STAGE?

A document may pass through the reviewer's hands multiple times, but these review rounds are not interchangeable (see Table 1). The investment in repeated reviews is not redundant or wasteful and it is important that reviewers understand that correctly applying focused effort at each stage, especially during the early stages, will result in a more effective and efficient process.

Proofreading and quality control (QC) are most efficient when done later in the document development process. This can avoid rework (e.g. effort invested in editing text that is later removed or changed). It also helps to prevent possible new errors being introduced through changes made after QC.

Critical comments on document content or structure should be made early in the process, when there is still time to adequately address them. All too often, these comments are received on later drafts because reviewers postpone the review effort ('This is only the first draft, I will get another chance to review it.'). The consequence of late inputs is that either the comments can no longer be addressed, or the timelines will need to shift to accommodate the additional work.

Table 1: Staged clinical study report review

What are you reviewing:	Focus of review:	Considerations for review:
Pre-writing meeting = discussion of content (as opposed to the kick-off meeting, which is about timelines and practicalities)	<ul style="list-style-type: none"> • Large-scale structure • Key messages 	<ul style="list-style-type: none"> • Help the writer build a logical information flow • Get the team aligned on key messages • Discuss intext data presentation
Shell/methods = protocol and statistical analysis-based methods text including outline of results, intext tables and figures	Large-scale structure: does it support the logical flow of information?	At this stage, there is room for large-scale changes without serious impact on workload or timelines
	Content reflects actual trial conduct	Where did things not go as planned? What was done instead?
	Content is complete	Is all information included that is necessary to evaluate whether the study data are scientifically sound and can support the key messages?
	Appropriate allotment of space and priority to various topics	For example, are there parts of the planned analysis that do not need intext representation in the CSR? Or parts that need more representation, or need to be in the forefront?
	Appropriate choice of text vs tables/figures for data presentation	Sometimes, output tables are too large to include in the CSR body. If a summary table or figure is needed, it is best if this is known with plenty of time for it to be produced, undergo quality control, be approved and included, so it can be reviewed in situ
Draft 1 = the writer's best approximation of the team's expectations as initially communicated	Does the structure facilitate navigation & easy localization of specific content?	Review from the assumption that most users of a CSR will not read the document cover-to-cover but instead will look for specific information
	Are there gaps or redundancies in data presentation?	These need to be identified as early as possible so they can be adequately addressed with minimal impact on workload and timelines
	Are data presented & interpreted correctly?	Do the conclusions match the objectives? Are the conclusions rooted in the data?

Draft 2 = first consensus of the writer's and team's input	Were comments from the previous review round satisfactorily implemented?	If any were not, consider providing additional context and information to make it clear to the writer what your expectations are (rather than repeating the previous comment)
	Does the document answer the research question logically and sufficiently?	Do the conclusions match the objectives and the key messages?
	Is the document fit for purpose?	Is a health authority reviewer likely to accept the conclusions drawn from the data or are there concerns that have not been sufficiently addressed?
	Does the document content align with the development strategy?	Do the document's key messages support the product development strategy?
Final draft = consolidated version containing input by the writer, team and the team's line management	Were comments from the previous review round satisfactorily implemented?	If any were not, consider providing additional context and information to make it clear to the writer what your expectations are (rather than repeating the previous comment)
Final	Check for appropriate implementation of comments from previous rounds before approval and signature	New comments at this stage will have significant impact and should only be given if they are critical

Also, late-stage versions that are typically under greater time pressure may not be reviewed by all reviewers who were involved in the earlier stages, so information that is added later in the process may escape critical review.

Comments coming in after the agreed deadline are disruptive to efficient implementation (see Table 2).

If they supplement or contradict comments that have already been implemented, the writer will need to go back and redo or undo work that has already been completed. This could then mean other reviewers need to be contacted outside of the designated review period to get agreement on any proposed change. If comments regularly come in late, it is worth examining possible causes.

Table 2: Impact of a structured review process

Element of structured review process	Impact on reviewers	Impact on writer(s)	Impact on the document
Focused review (not corrective or stylistic, within reviewer's area of expertise)	<ul style="list-style-type: none"> Only invest time where it is truly needed Reducing the volume of comments makes important comments more visible Reducing the volume of comments means less work reading and responding to comments from colleagues 	<ul style="list-style-type: none"> No time lost on unnecessary editing or stylistic changes Reducing the volume of comments means more time to invest in the important ones 	<ul style="list-style-type: none"> Improved quality Leaner document Better tailoring to audience
Consolidated comments	<ul style="list-style-type: none"> Reduced communication traffic (whether via email or other channels) Comment resolution meetings can efficiently focus on cross-functional issues 	<ul style="list-style-type: none"> No need to contact reviewers with questions either via email or during a comment resolution meeting More time focused on comment implementation rather than comment management 	<ul style="list-style-type: none"> Shortened timeline because of reduced effort

Staged review	<ul style="list-style-type: none"> • More efficient reviews because some sections may not need to be revisited in later drafts if there is early consensus on their content (e.g. CSR methods sections) • Reduced review effort because of early communication of expectations to the writer (document more tailored to expectations from the start) • Reduced likelihood of additional (unplanned) drafts needed to accommodate the review of late-coming new text/tables/data/etc. • Reduced risk of introducing errors due to late-stage revisions 	<ul style="list-style-type: none"> • More focused writing effort because of early communication of expectations • Fewer reworks and less wasted effort implementing comments on text that is later altered or removed • Reduced risk of introducing errors because of late-stage revisions • Reduced likelihood of additional (unplanned) drafts needed to include late-coming new text/tables/data/etc. 	<ul style="list-style-type: none"> • Improved quality • Leaner document • Better tailoring to audience • Shortened timeline because of reduced effort
Review tool (ideally allowing live collaborative review)	<ul style="list-style-type: none"> • Version control: no doubts or mistakes about which version is for review • Real-time reading of and ability to respond to comments from colleagues in context • Easy navigation & tracking of comments 	<ul style="list-style-type: none"> • Version control: all changes from review traceable, nothing lost or missed because changes were not tracked • No need to manage and reconcile comments from multiple sources • Reduced risk of comments being lost or missed • Easy navigation and tracking of comment status (in progress, resolved, declined) 	<ul style="list-style-type: none"> • Improved quality • Shortened timeline because of reduced effort



Timely review	<ul style="list-style-type: none"> • Live team interaction in the review tool • Reduced email traffic, especially outside designated review periods • More efficient comment resolution meetings 	<ul style="list-style-type: none"> • Less duplication of effort or wasted effort due to impact of late comments on already implemented changes • No disruption of comment tracking or need to reconcile comments from multiple sources • No need to contact reviewers with questions outside the designated review period 	<ul style="list-style-type: none"> • Improved quality • Shortened timeline because of reduced effort
Actionable comments (unambiguous, specific, constructive and relevant)	<ul style="list-style-type: none"> • Reduced communication traffic because writer will not need to come back for clarification or additional information • More efficient comment resolution meetings (fewer comments to discuss) 	<ul style="list-style-type: none"> • Reduced effort to manage and clarify comments before they can be implemented • Reduced need to contact reviewers with questions, either via email or during a comment resolution meeting 	<ul style="list-style-type: none"> • Shortened timeline because of reduced effort

Reviewing is a strenuous mental activity. As described above, we don't need the reviewer's attention to go to the word, sentence or paragraph, we need it to go to the section, how content flows within each section and across sections throughout the document. Reviewing should entail contemplation of the overall building of arguments rather than reaction to the local text. It requires the reviewer to spend a continuous block of time focused on one task.

Do team members have the leeway to block out time in their calendar, or is reviewing routinely treated as an ad hoc, 'on-top-of-my-actual-job,' activity?

Do conflicting priorities lead to rushed reviews of reduced quality?

ARE REVIEW COMMENTS USEFUL, THAT IS, CAN THE WRITER ACT ON THEM TO MAKE IMPROVEMENTS TO THE DOCUMENT?

A good review comment is unambiguous, specific, constructive, actionable and relevant (Fiebig, 2015; Radovan, 2018).

If the writer cannot act on the comment or misunderstands it, the time and effort that went into its delivery, discussion and implementation will not contribute effectively towards a true document improvement.

When asked to self-evaluate, most reviewers indicated that their comments complied with the above-listed requirements (Bernhardt, 2003; Cuppan & Bernhardt, 2012).

However, when evaluated by consultants based on a set of objective criteria, only a minority of comments were found to meet these criteria (Bernhardt, 2003; Cuppan & Bernhardt, 2012). This implies providing comments that meet all the above criteria is less straightforward than it may seem and is, for a lot of people, a skill that needs to be taught.

Where multiple reviewers from each functional area contribute to a review, consolidation of these comments is important. When there are conflicting opinions, the functional area should discuss the comment internally to present a unified opinion that is then documented. Ideally, the previous conflicting comments will be removed. Consolidation increases efficiency because it prevents issues that pertain only to one functional area (be it clinical, regulatory, statistical, etc.) from taking up the time of the entire team as they read and respond to comments.

The least labor-intensive comments to implement as a writer are those that clearly identify a problem and offer a solution (Radovan, 2018). Too often, comments ask further questions, are unclear or read as notes to self for the reviewer. At best, the writer can puzzle out the reviewer's goal and make changes based on their assumption of the reviewer's intent. At worst, the writer needs to reach out to the reviewer for additional information or clarification. It is often the case that small additional effort on the part of a reviewer can save hours of additional work for multiple other team members.

In her 2018 publication, Diana Radovan presents an overview of ineffective comments, identifying issues and suggesting improvements (Radovan, 2018).



Most writers are only too familiar with comments that ask questions (e.g. why is this here?), are vague (e.g. please rephrase), don't provide sufficient information (e.g. please elaborate), or lack any request for action (e.g. I don't agree with this). A simple trick reviewers can use to enhance the usefulness of their comments is to put themselves in the writer's shoes and re-read their comment from an implementation point-of-view (e.g. if I had to change the text based on this comment, would I know what to change?). For instance, a comment like 'please elaborate' can become effective if the reviewer takes a moment to specify what information they would like to add – for example, 'please add AE severity, relatedness, duration and resolution'.

IS REVIEWING BY MULTIPLE REVIEWERS OCCURRING SERIALY OR CONCURRENTLY?

How are documents distributed for review?
How is version control ensured?

Serial review, where a copy of the document is distributed and passed from one reviewer to the next, often leads to multiple circulating files and a loss of version control (Fiebig, 2015). The writers will then have to either find a way to transfer all comments into one document without creating gaps, duplication or artefacts, or they must rigorously track and implement comments from multiple sources, consolidating as they go to ensure nothing is missed, because reviewers cannot see each other's comments during the review.

Current technology allows for a live, interactive and concurrent review by multiple reviewers. Working independently, they can leave comments and read and react to other's comments without the need to walk through the document in a meeting. Use of such technology has increased the efficiency of comment management and implementation by writers. Everything is in one place and comments are consolidated in situ by the team.



Review tools also have advantages for reviewers. It is a lot more convenient to react to questions if you see them live and in context while you are working on the document, as opposed to receiving the question via email when you are in the middle of another task. Different time zones don't have to impact interaction because everyone can see all previous comments. To get the full benefit of this in-document interaction, reviewers may need to return to the document multiple times to stay abreast of the latest changes.

A review tool will also provide a convenient record of all comments, resolutions given to conflicting comments, and meeting outcomes. This may be important for future meetings to avoid rehashing or even the reversal of previously made decisions without good reason. In the event a previously dealt with issue resurfaces, the writer can refer to the record to support a request for adherence to previous decisions.

ARE COMMENT RESOLUTION MEETINGS CONDUCTED EFFICIENTLY?

Where multiple solutions are offered or conflicting views are voiced in the comments, the team will need to gather to discuss and achieve consensus on document content. Such comment resolution meetings can easily become lengthy, especially if explanations are required or the discussion gets side-tracked into debates that are not relevant to the document under review.

In some cases, even lengthy discussions will fail to result in a decisive action that improves the document.

Common problems with comment resolution meetings include:

- Non-participation of reviewers
 - i.e. functions not represented
- Unprepared reviewers
 - unaware of others' relevant comments or even expecting the document to be reviewed during the meeting
- Inability to achieve consensus
 - no decision taken

The recipe for efficient comment resolution meetings isn't complex. The writer should prepare the topics for discussion and then guide the team through the meeting. It is generally more productive to focus on topics in a descending order of importance, impact or priority, rather than chronologically working through the document.

It is also more efficient to only bring topics to the meeting that are truly cross-functional, i.e. requiring the input of more than one functional area. Clarification for other comments is better dealt with through different communication channels. It is also good practice to mandate someone to take a decision on document content if the team is unable to reach consensus.

Road maps for improvement

STRUCTURED REVIEW GUIDANCE

In this highly regulated industry, the review process is likely to already be part of the standard operating procedures (SOP). It will often be integrated into document development SOPs (e.g. protocol development, CSR writing) and be limited to which functions are reviewed at which stage of a document's development. This may not be sufficient to drive company-wide effective and efficient reviews.

A procedure or work instruction covering aspects of the review that are independent of the document type may go a long way to improving review efficiency and reducing frustration. These could include the difference between review and quality control, the use of a collaborative review tool (Fiebig, 2015), staged review (Fiebig, 2015; Radovan, 2018), review focus for each functional area (Radovan, 2018), best commenting practices, etc.

This is particularly effective if the instructions are practical and accessible. Reviewers need to understand that reviewing is an iterative endeavor for the entire team, where the guidelines help prevent duplication or wasted effort.

TRAINING

Training the procedure or work instruction is a prerequisite for success. Following initial training, every reviewer should undergo regular refresher training sessions to ensure the desired outcomes are achieved. A summary sheet can be presented at the kick-off meeting or distributed by the writer along with the call for review.

Writers are uniquely placed to detect areas where standards are slipping. These writers are uniquely placed to detect where standards are slipping. Repeated micro-learning via email are a flexible way to remedy this and this loop can be reinforced by positive feedback from writers to improved review practices.

Helpful practices can flow back to improve the review guidance. A short summary of the review guideline's main points should be available to each individual to refresh their knowledge as required.

ENFORCEMENT

The next step is guidance enforcement. The benefits of guidance will only be felt if all participants honor the process. This should be non-negotiable.

If only one reviewer deviates from the correct process (e.g. not consolidating comments, providing them outside the review tool or outside of the agreed time window), it will have a significant impact on the timeline and the workload of the writer and other reviewers (see Table 1). If no impact is observed, this is probably an indication others are compensating by investing extra time to keep the deliverable on track.

The review guidance might include the steps to be taken if review comments are repeatedly not returned within the allotted time or the designated review tool is not used. This could include mandatory refresher training.

In some cases, rather than policing bad practice, it can be more effective to reward and showcase good practice while providing support to solve practical issues that may arise. Once a reviewer gains firsthand experience of the benefits of good practice, feedback within and across teams can create a self-reinforcing positive loop that encourages continued good practice.

EMPOWERING MEDICAL WRITERS

Writers are important cornerstones in the building of an effective and efficient review process. Since they are in constant communication with the reviewers, they can drive training and improvements on a per-project basis.

Any experienced writer will have a solid grasp on what high-quality reviewing looks like and where bottlenecks may develop that can cause issues.

They are ideally situated to advocate good practice, for instance by communicating review roles and expectations during the project's kick-off meeting or when each draft is sent for review.

This will only have the desired effect if the writer is empowered by support from cross-functional management.

Writers can also make a significant difference in the managing and moderation of comment resolution meetings. They can reinforce an efficient format where only comments needing cross-functional input are brought up for discussion. Ideally, they will work in tandem with the assigned lead per document (document owner), who has the mandate to take decisions if the team can't achieve consensus.

STIMULATING POSITIVE COLLABORATION

Review is communication between the reviewers and the writer (Radovan, 2018).

This implies review is not only a cognitive, but also a social endeavor. As with any form of communication, misunderstandings may arise that can be costly and frustrating. Fostering a culture where writers and reviewers perceive themselves as one team working towards the common goal of a quality document engenders a shared responsibility to make the whole process as smooth and efficient as possible.

Positive and constructive communication goes a long way towards reducing miscommunication and frustration. If either the text to be reviewed or review comments are not within expectations, it helps to communicate from the assumption that this stems from a lack of information or knowledge, rather than ill will.

Did the other party know what the expectations were? Were they not clear or did a misunderstanding arise? Does the other person know everything you assume is known? Do conflicting priorities require a reshuffling of resources?

Kind and constructive communication throughout the whole process, from kick-off meeting to document finalization, will reinforce the sense of one team working towards one goal. It is a true privilege to experience the effectiveness and efficiency that such a team spirit can achieve, even under extreme time pressure.



Conclusion

Since marketing approval dossiers are built on the foundation of CSRs, dossier work starts when the first CSR is being written. Although review accounts for a large part of the time and effort invested in creating high-quality documents that are fit for purpose, training for reviewers seems to be rare.

Effective training and a well-structured review process can drive significant gains in time and effort, not only for reviewers but also for writers. If writers are empowered to guide document reviews, they can be a strong driving force for the building of an effective and efficient review process.

References

- Bernhardt SA. Improving document review practices in pharmaceutical companies. *Journal of Business and Technical Communication*, 2003;17:439-473
- Cooper J, Chamberlain James L, Affleck J, et al. Value of medical writing: the regulator's perspective. *Medical writing*, 2022;31:72-78
- Cuppan GP and Bernhardt SA. Missed opportunities in the review and revision of clinical study reports. *Journal of Business and Technical Communication*, 2012;26:131-170
- Fiebig D. Back to the future...or the amazing lack of progress in effective document review. *Medical Writing*, 2015;24:169-172
- Nürnberg A. Organizing the review process in Microsoft Word®. *Medical Writing*, 2014;23:13-16
- Radovan D. Help reviewers tell you what they want. *Medical Writing*, 2018;27:69-74

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The logo for SGS, consisting of the letters 'SGS' in a bold, sans-serif font, with a vertical line to the right of the letters.

When you need to be sure