AMERICAN MEDICAL WRITERS ASSOCIATION AMWA JOURNAL V39 N2 / 2024

REGULATORY INSIGHTS

# Say the Right Thing: Developing a Program Lexicon for Cross-Functional Teams

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## ABSTRACT

Achieving consistency in terminology and speaking with one voice in clinical documents is challenging for several reasons. Cross-functional team members, including medical writers, may use different terminology to describe the disease, condition, and study features, as well as to compare and interpret clinical data. Inconsistent use of terminology in clinical documents can negatively impact the overall quality, efficiency of development, and clarity of messaging and may lead to longer regulatory reviews, extensive questions from regulators, delays in approval, and the possible rejection of a regulatory submission.

The development and use of a program lexicon can alleviate some of these challenges. The lexicon is created by the lead medical writer with input from all involved functional areas. The purpose of the lexicon is to provide detailed program-specific guidance for appropriate terminology to create accurate and consistent content within and across documents for use by all contributing authors and reviewers from document initiation to finalization. For regulatory medical writers, a lexicon is an integral part of the focused authoring approach in using consistent comparison language. The lexicon identifies the terminology that should be used, should not be used, if any exceptions are allowed, and examples.

Medical writers often drive the development, implementation, and periodic updates of the lexicon to maintain it as a living document. Once developed and used, the lexicon can facilitate faster authoring, review, and quality control of regulatory documents, and meeting tight timelines for regulatory responses or submissions. By standardizing terms and definitions, the lexicon also facilitates automation, structured authoring, and content reuse. Finally, the lexicon can be included as a source file for artificial intelligence tools to produce first drafts of documents that meet regulatory requirements.

Regulators have identified poor document quality as an issue that negatively impacts review of submitted clinical documents, and they specified a "lack of clarity" as one of the most frequently identified document quality issues.[1] Using consistent terminology and style conventions within and across clinical documents supports the development of clear, high-quality documents.[2-4] A program lexicon is a valuable tool that assists medical writers and cross-functional teams to effectively use consistent terminology and speak with one voice across clinical documents.

## IMPORTANCE OF CONSISTENT TERMINOLOGY IN CLINICAL DOCUMENTS

Clinical documents are an integral part of the development process for pharmaceutical products (drugs, biologics, and devices). The complex content of these documents is often developed by diverse authoring teams under condensed timelines to support a regulatory submission.[4] Developing high-quality clinical documents that are consistent, concise, clear, accurate, well-organized, and specific to their indication(s) and audience is critical in supporting a smooth regulatory review.

Consistent terminology in clinical documents helps the reader focus and comprehend the overall purpose and key messaging while avoiding distraction. This is especially important for complex studies with multiple comparisons for multiple treatment and age groups, time points, end points, statistical approaches, and other variables.

Inconsistent use of terminology in clinical documents can negatively impact the overall quality, efficiency of development, and clarity of messaging. Poor quality documents impede regulatory reviews and may lead to longer reviews, extensive questions from regulators, delays in approval, and the possible rejection of a submission.[1,4] Poor quality documents in a submission from an applicant may impact the review of other documents in subsequent submissions from the same applicant.[1] Additionally, if an applicant is developing submission documents that will be translated into various languages, ensuring that the initial documents are of


ISSN 2163-5315

high quality and using consistent terminology is critical for successful translation.[5]

## CHALLENGES TO USE OF CONSISTENT TERMINOLOGY

Achieving consistency in terminology and speaking with one voice in clinical documents is challenging for several reasons. Medical writers and other lead authors use materials from various sources of differing quality and combine all relevant information into clinical documents. These sources may use different terms to describe the same thing and accepted terminology may change over time.[6]

Medical writers work in cross-functional teams with many different authors, contributors, and reviewers who use different terminology to describe the disease, condition, and study features, as well as to compare and interpret clinical data. Cross-functional teams may struggle to find detailed and appropriate terminology for their program documents.

## USE OF A LEXICON

### What is a Lexicon?

A lexicon is a set of conventions that help facilitate consistent terminology use across a variety of clinical documents. The purpose of the lexicon is to provide detailed program-specific guidance for appropriate terminology to create accurate and consistent content within and across documents for use by all contributing authors and reviewers from document initiation to finalization. The lexicon identifies the terminology that should be used, should not be used, if any exceptions are allowed, and provides specific examples (Table 1). The lexicon may include the following

- terms for products, formulations, disease, and indications;
- standard terms for clinical trials;
- definitions for endpoints, assessments, and abbreviations; and
- cut-offs or rules for data interpretation and comparisons.

Lexicons are part of scientific communication platforms to provide the foundation for all communication around a product or disease and to ensure accurate and consistent language and terminology.[7] For regulatory medical writers, a lexicon is an integral part of the focused authoring approach in using consistent comparison language.[8] A lexicon should be a living document and reviewed and updated regularly as new guidelines and data emerge throughout the project or program's lifecycle. It can be developed to be specific to a document, regulatory submission, or program, or apply to several related programs.

**Table 1.** Example of a Lexicon

| Term to Use | Do Not Use | Examples/Rationale/Notes |
|---|---|---|
| Treatment | Intervention | eg, Study treatment. Also use treatment groups. |
| Study | Trial | eg, Clinical study. |
| Participant | Subject, patient | Use to describe participants in clinical studies.[a] |
| Comparable | Similar | Use comparable to describe results for endpoints in which statistical comparisons are made (ie, *P*-values and/or 95% CI). Usually for primary or key secondary endpoints for efficacy and safety.[b] |
| SARS-CoV-2 infection | COVID-19 infection | Use to describe the infection caused by the virus (SARS-COV-2), not the disease (COVID-19). |
| Viral error catastrophe | Viral error induction | eg, Drug A inhibits viral replication by inducing viral error catastrophe. |
| *Clostridioides difficile* | *Clostridium difficile* | Exception: Clostridium genus is used for all other species except difficile, eg, *Clostridium perfringens* bacteria causes food poisoning. |

*CI, confidence interval; COVID-19, coronavirus disease 2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.*

*[a]Patients may be used when describing results of real-world evidence or data studies.*

*[b]For results pertaining to objectives with hypothesis testing, use superior, noninferior, or other language as specified in hypothesis.*

### Standard Operating Procedures/Templates/Style Guides Compared With Program-Level Lexicons

Cross-functional team members may ask the medical writer why another guidance document or convention sheet is needed if the team has standard operating procedures, overall style guides, and standard document templates. Although these tools are invaluable in providing high-level guidance for the authoring of clinical documents, they are not intended to provide specific guidance for documents at the program level. Ensuring that an updated program-specific lexicon is available before initially drafting a regulatory document for a clinical development program will save time and effort downstream during document authoring, review, and at team consensus meetings.

## DEVELOPMENT OF A LEXICON

Medical writers often drive the development, implementation, and periodic updates of the lexicon to maintain it as a living document (Figure 1). The medical writer should meet with the project team early on in a project to explain the value of a lexicon, and if available, provide examples from other programs. The medical writer can then lead a discussion with the project team regarding what terminology, definitions, rules for data interpretation, and any exceptions to these should be included in the initial draft program lexicon. The team developing the lexicon can identify appropriate terminology from various sources such as guidelines, clinical conventions, previous program documents (eg, protocol,

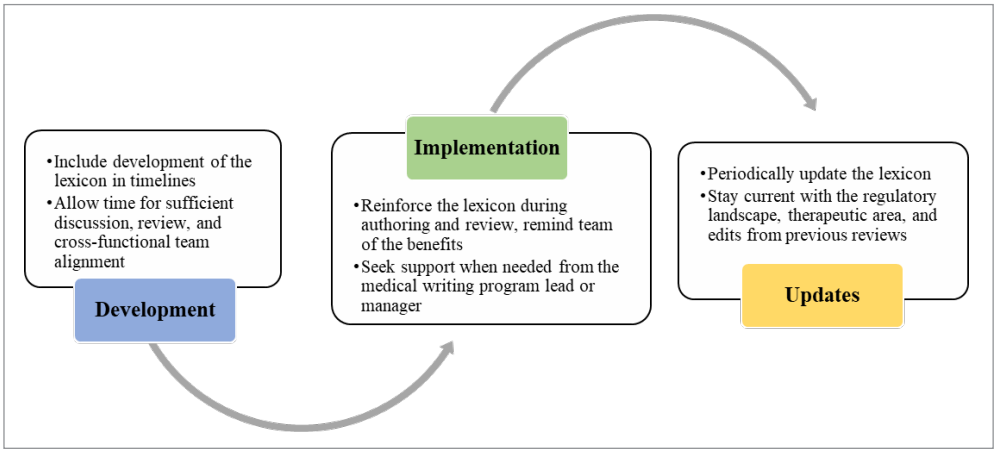


**Figure 1.** Development, Implementation, and Updates of Lexicons

investigator brochure), literature, statistical rules, etc. The draft lexicon can be in whatever format is best for the team (Word document, Excel document, PowerPoint, etc) and be stored in a central location (team site, OneDrive, OneNote, etc) accessible to cross-functional team members.

The medical writer should allow time for sufficient discussion, review, and cross-functional team alignment of the lexicon. Once the initial draft is produced, it should be reviewed by the project team and any other individuals that the project team would like to consult. The program lexicon can be used for development of multiple types of documents during the lifecycle of the program (eg, protocols, investigator brochures, diversity plans, clinical study reports, common technical documents, product label, response documents, publications, marketing materials, etc). Because there may be different teams working on different regulatory documents, the medical writer may need to continue to remind new team members of the benefits of a program lexicon and reinforce the use of the lexicon before initial document development. The medical writer should seek support when needed for implementing the lexicon from the medical writing program lead or manager. It is also important during quality control (QC) review to inform the editor that the team has used a program-level lexicon for authoring the document and provide the lexicon as one of the sources for the review.

The team should review and update the program lexicon on a periodic basis throughout the program life cycle. For example, the lexicon may be reviewed at the initiation of development of documents for each new regulatory submission. The medical writer should manage the review cycles for the program lexicon. Depending on the clinical landscape in the product's specific therapeutic area, the lexicon may be static or may change on a regular basis over the lifecycle of the program.

## BENEFITS OF A LEXICON

The program lexicon is a tool that supports teams in creating accurate and consistent content within and across documents in a program. The development and use of a lexicon can alleviate challenges with lack of consistency for clinical documents. Once developed and used, it can proactively avoid conflict within an authoring team over terminology, data interpretation, and presentation. Thus, the team can focus their attention on including meaningful study results and interpretation and the right level of detail. The lexicon can facilitate faster authoring, review, and the QC of regulatory documents and meeting tight timelines for regulatory responses or submissions.

Regulators have recognized the value of medical writers in improving the quality of clinical documents that they write.[1,9] The lexicon empowers the medical writer as the document leader during authoring in using preferred terminology that has been aligned on within the team. For multiple submissions occurring over time, different medical writers and others may be involved in developing the documents and having an up-to-date program lexicon can help ensure consistency. Finally, by standardizing terms and definitions, the lexicon also facilitates automation, structured authoring, and content reuse.[10,11] With many teams using tools for artificial intelligence, the lexicon can be included as a source file for data ingestion to produce first drafts of documents that meet regulatory requirements.[10,11]

***Author declaration and disclosures:*** *The authors note no commercial associations that may pose a conflict of interest in relation to this article.*

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