

Manuscript Writing

Section Editor:

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How to start writing a scientific manuscript

Getting started writing a manuscript – or any other document for that matter – can be difficult. Manuscripts are large projects, sometimes taking hundreds of hours and many months to complete.

Faced with a blank page or screen, one might be tempted to simply start typing, attacking the project by the path of least resistance, but working in this way can lead to a poorly defined text that may even stray into tangential or irrelevant areas. Having a clear, organised plan of attack can save a manuscript writer a lot of time and avoid many headaches.

In this article, I explain how to start writing and organise the early stages of a manuscript in the best manner.

Step 1: Write a problem statement

In my experience working on manuscript projects and teaching medical writing, I have seen that the biggest problem for most writers is clearly defining what the manuscript is about. In a September 2012 article in MEW, Marina Hurley calls this process defining the ‘problem statement’.¹ Briefly, the problem statement is one or two sentences describing the purpose of the manuscript. The problem statement is directly related to the objective, aim, hypothesis, or central question. Distilling these ideas into a single statement can be difficult, especially for less experienced writers, but going through the process is an excellent way to start writing a coherent, effective, and interesting text. Two typical examples of problem statements are shown below. In both examples, the first sentence describes the overall problem and the second describes the specific problem for the manuscript:

Many candidate HIV vaccines have been developed but results in animals have not been predictive of efficacy in humans. *A reliable animal model for predicting the efficacy of HIV vaccines is needed.*

Despite several initiatives to improve the treatment of epilepsy in low- and middle-income

countries, in many countries, as many as 95% of people with epilepsy remain untreated. *Clear, simple goals that can be immediately put into action are needed to reduce the epilepsy treatment gap.*

Both examples directly and succinctly describe the problem and will enable the writer to define a clear and simple process for the article.

Step 2: Prepare a concept outline

With a well-defined problem statement, outlining is the essential next step in building a manuscript. As asserted by Robert Taylor, also in the September 2012 issue of MEW, ‘Using outlining to organise your writing project can help keep you on a straight path and avoid wandering into the wastelands of irrelevance’.² I would add that outlining saves a lot of time and is therefore critical for meeting time and financial budgets. Like Dr Taylor, I have found that outlines reduce problems in collaborative projects because they can be used to get the contributors to comment and agree at an early stage.

I like to use two kinds of outline, which I call ‘concept’ and ‘detailed’. The concept outline is a first step and is a skeleton on which to build a detailed outline. A concept outline contains the main sections of a manuscript followed by one bullet point for each major subsection or point that you want to make. This is a good way to get past a blank screen. As you can see in the example in Figure 1, the bullet points in the concept outline are mostly place-fillers to help organise thoughts.

Step 3: Build a detailed outline

The detailed outline goes into extensive detail and contains essentially all the information to be included in the final manuscript. Providing the detailed outline to collaborators saves substantial time because it is easier to make major changes in content or organisation than at the first draft stage because little time has been put into crafting and perfecting the prose.

Building a detailed outline is simple with a good concept outline. For each bullet point in the concept outline, simply fill in all the details from whatever source materials are available, which can

- **Introduction**
 - Background of SLE
 - Current treatment of SLE and the need for improvements
 - Compound X in SLE and what information is needed/missing
 - This study
 - Objective
 - This study: dose-escalation study of safety, immunogenicity, and efficacy of compound x in adults 18 to 50 years of age with SLE
- **Methods**
 - Study design
 - Subject population
 - Treatments
 - Assessments
 - Safety
 - Immunogenicity
 - Efficacy
 - Statistical analysis
- **Results**
 - Disposition & demographics
 - Safety
 - Immunogenicity
 - Efficacy
- **Discussion**
 - Major points
 - Discuss safety findings in comparison to literature
 - Discuss immunogenicity findings
 - Limitations and strengths
 - Conclusions/recommendations

Figure 1: Example of a concept outline.

include clinical documents (clinical study report, protocol, statistical analysis plan, statistical output, or investigator's brochure), presentations, posters, and abstracts. Writing the detailed outline can be done in any order, although a logical method is to start with the results and then continue with the methods, followed by the introduction and, finally, the discussion.

The results section of a detailed outline should include the detailed findings that directly address the problem statement and the principal objective, question, aim, or hypothesis. This section can be populated by extracting the data (i.e. cutting and pasting) from the clinical study report, statistical output, poster, or presentation (Figure 2). Figures and tables are included directly in the sections or at the end of the detailed outline.

Once the results section is complete, what to include in the methods section should be obvious; each result must have a method. In addition, the methods should conform to the CONSORT or other relevant guidelines.³ Keep in mind that problems with the methods or methods section are the main reason that manuscripts are rejected.⁴ By populating this section now, it will become clear what information is missing, allowing it to be requested from collaborators early in the writing process. For this section, wherever possible, cut

and paste from the protocol, clinical study report, or other texts containing methodological details.

The introduction section is the next logical part of the detailed outline to complete. Include detailed information for each point in the concept outline, for example specific definitions, descriptions, epidemiological data, and clinical data. Refer to your problem statement and, if you have them, the study objectives to make sure that you are addressing them. This section can be populated by copying and pasting text from the introduction of a study protocol or clinical study report or with background information from a slide presentation, monograph, or other printed information, but be aware that data or references in these documents are often out of date or inaccurate, so consider any such information preliminary and do your own literature search to find valid, up-to-date information and ideas. Including references in the introduction section of the detailed outline will avoid having to later track down sources and will allow the co-authors to determine whether you are using the references they prefer. Listing the references by author rather than as numbered citations will simplify this for you and the co-authors.

The discussion section is the most difficult part of a detailed outline to complete because it is difficult to know what the co-authors want to say and because

Introduction

- Background:
 - SLE general background (Johnson et al., 2002; Smith et al. 2011):
 - Chronic autoimmune disease
 - Affects virtually all organs, but more frequently the skin and mucosa, muscles and joints, the kidneys, the hematopoietic system and the central nervous system.
 - Autoantibodies
 - Clinical course
 - Prognosis
 - Epidemiology (Weber et al. 2012):
 - Primarily affects young women
 - Global prevalence (Thompson et al. 2013)
- Treatment:
 - Current treatment (Smith et al. 2011):
 - Current therapies

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Methods

- Study design:
 - Design: double-blind, randomized, placebo-controlled, staggered dose, multicenter, phase I/II
 - Dates: May 6, 2010 to August 3, 2011
 - Sites: Belgium, Israel, Switzerland, Austria
 - Ethical considerations:
 - Performed in accordance with the available EMEA guidelines on clinical evaluation of new vaccines, EMEA guidelines on evaluation of medicinal products of subjects suffering from SLE.
 - Performed in accordance with ICH efficacy and safety guidelines (e-guidelines, particularly E6 concerning good clinical practice (GCP).
 - Conducted according to cGCPs, cGMPs, and cGLPs.
 - Subjects gave written informed consent before being included in the trial.
- Subject population for phase I/II study:
 - Inclusion criteria:
 - 18- 50 years

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Results

- Disposition:
 - 28 subjects were included in the study
 - 3 discontinuations, none for AEs
- Demographic Characteristics

	30 MCG	60 MCG	120 MCG	240 MCG	PLACEBO
N	3	6	6	6	7
Female (%)	100	100	100	100	100
Age (Mean, Years)	36	39.3	34.2	34.8	40.1
Race					
White-Caucasian (%)	100	100	100	100	85.7
Asian (%)	0	0	0	0	14.3
Duration SLE disease (Mean Years)	10	8.9	7.3	11.9	6.5
Concomitant Medications					
Corticosteroids (%)	100	66.7	83.3	66.7	100
Anti-Malarial (%)	0	66.7	50	66.7	71.4
Methotrexate (%)	0	16.7	16.7	16.7	14.3
Azathioprine (%)	0	16.7	16.7	16.7	0

- Immunogenicity:
 - Time course:
 - Peak after 15 weeks at lowest 3 doses, after 25 weeks at highest dose.

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Discussion

- Major points:
 - This was a first-in-human study of compound X.
 - Compound X is well tolerated with no major safety issues in this phase I/II study.
 - Compound X is immunogenic in 100% of patients.
 - Immunization with Compound X down-regulates IFN-related genes.
- Discuss safety findings in comparison to

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Figure 2: Example of a detailed outline.

the messages may change up until the last draft of the manuscript. Therefore, this part of the detailed outline is often much less detailed than the other parts, but include at least the main points that you think should be part of the discussion so that the co-authors have a framework to begin considering what should be in this part of the manuscript.

As a final step in preparing a detailed outline, include a cover page containing a proposed title, the names and affiliations of the co-authors, the target journal (or proposed target journals), and key information about the target journal, such as limits for the number of words and figures or tables.

Step 4: Convert the detailed outline into a first draft

To generate the first draft of the manuscript, simply connect the individual points in the detailed outline to a text. Be sure to avoid plagiarising any information that you copied from another document or reference and, of course, make sure that the manuscript is formatted according to the instructions to authors for the target journal.

Conclusion

Writing a manuscript is simplified by starting with a clear problem statement and then developing it first into a concept outline and then a detailed outline.

With a detailed outline – and hopefully comments on it from the co-authors – writing the text is easy.

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