

# How to Write a Manuscript for Submission to a Biomedical (Clinical) Journal



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## How to Write a Manuscript for Submission to a Biomedical (Clinical) Journal

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*Note: This manual was prepared for Department of Pediatrics House Staff, Medical College of Georgia, using the New England Journal of Medicine as a prototype. I have broken down "the manuscript" into its component elements and have described how to write each of these sections. At the end are some general tips on writing.*

Many journal editors have agreed to use a set of uniform guidelines for manuscripts submitted to their journals. These guidelines are frequently updated and are known as the Uniform Requirements for Manuscripts Submitted to Biomedical Journals (<http://www.icmje.org>). The Uniform Requirements are particularly helpful with respect to policies on authorship and styles for citing references.

### **Before you start to write:**

Keep in mind the following mantras:

- LOGIC, LOGIC, LOGIC
- Your paper should represent a critical argument.
- Clear writing results from clear thinking.
- Clear thinking results from clear writing.
- Write with vigor.

### **Sections (Elements) of the Manuscript:**

#### **Title page:**

- Title: should be concise and descriptive, not a declarative sentence (journals may vary on this criteria), e.g., "Bone Marrow Failure Associated with Human Herpesvirus 8 Infection after Transplantation" (from Luppi, et al, (2000) NEJM, 343:1378); not "Two Patients Expressed DNA Sequences from the K1 Gene of Human Herpesvirus 8 after They Each Received a Kidney from the Same Cadaver Donor"
- At bottom of page, include a "running head" version of the title (fewer than 40 characters), e.g., HHV-8 infection after transplantation
- Names of authors, with first name, graduate degrees (no more than two degrees!), name of department and institution where work was done (not where author currently is), institutional affiliation of each author (either indicated with asterisk or other marking, or done as a footnote). Note that for non-clinical journals, graduate degrees are not listed.
- Name and address of corresponding author, including phone and FAX numbers and e-mail address.
- Acknowledgment of grant support (funding agency, grant number)
- Any disclaimers, if necessary

#### **Authorship:**

- Who should and should not be an author on a paper is a major topic of concern. The Uniform Requirements and most journals address this issue. MCG has recently posted its own guidelines on authorship (see

<http://www.mcg.edu/research/policy/guidelines.htm>), which are summarized here.

- To be an author, the investigator should
  - Have contributed significant ideas and experimental design to the project,
  - Have taken part in significant aspects of the experimentation, data analysis, or interpretation, AND
  - Be familiar enough with the project to be able to defend or present it.
- Each author should see the final version of the manuscript and give consent to co-authorship.

### **Abstract page:**

- Abstract should be less than 250 words, so make every word count.
  - Consists of 4 paragraphs:
    - Background (describe problem being addressed)
    - Methods (how the study was done)
    - Results (what are the data)
    - Conclusions (what did the authors learn from the results)
  - Note: non-clinical biomedical journals do not use a breakdown in the abstract; the abstract is all in one paragraph.
- List 3 to 10 key words at bottom of page. The choice of these words is important because they will be used for indexing the article, not only for the journal, but on the web. Use Medical Subject Headings (MeSH) from Index Medicus.
- It is helpful to make a (very) rough draft of your abstract as you begin writing. This can serve to help organize your thoughts. However, often new ideas or interpretations emerge as you are writing, so the abstract always needs a lot of fine-tuning at the end.

### **Introduction:**

- States the purpose of the paper. What problem are you addressing? Why should people care about this problem?
- Gives background information of the problem. Why is this problem important? What other experiments have been done to address the problem? How will you expand (or challenge) the findings of others? You need to summarize other relevant papers, but do it in an orderly fashion. A common problem for beginning, and even experienced writers, is to **randomly** summarize all papers on the subject, without focusing on the specific problem. Your presentation of the background should flow in a **logical** manner. Remember, **logic** is a key word in writing any scientific manuscript.

### **Materials & Methods:**

- Description of experimental subjects. Include:
  - age
  - sex
  - ethnicity if important (do not use the term “race,” however, since it is imprecise)
  - other important characteristics, e.g., clinical symptoms, diagnoses
  - exclusionary criteria
  - descriptions of controls
- Describe how each experiment was done in enough detail so that another investigator can repeat the experiment without having to e-mail (or phone) the authors. When using an established method, give the reference, but include

any modifications that you might have made. For methods that have been published but are not widely known, include a brief description. Identify chemicals and pharmaceuticals precisely, and give name of manufacturer and city and state in parentheses, e.g., “rofecoxib (Vioxx, Merck & Co., Whitehouse Station, NJ).” For specific instruments and equipment, also give precise name and manufacturer information, e.g., “analyzed on a FACScan (Becton Dickinson, Mountain View, CA).” However, for common, generic instruments, e.g., blood pressure cuff, stethoscope, you need not provide this information unless the brand has a bearing on your results. For drugs, give dose and route of administration. For chemicals, give concentration in conventional units (molarity, mg/ml). For biochemical assays or experiments, give final concentration of the solution, not how much you added.

- Be careful that your protocols do not sound like a lab manual. Do not say, “Add 3 ml of X to 15 ml tube. Then add 6.3 ml of solution Y.” Rather, say, “Solution Y was added to 3 ml X to a final concentration of 0.3M.” Include tube size or volume added only if it is vital to the assay (sometimes it is).
- Provide details of statistical methods used. Give numbers of observations and report subject losses. Specify computer programs used.
- For clinical trials, provide details on methods of randomization and blinding.
- When human subjects are involved, indicate whether the procedures followed were in accordance with the Institutional Review Board (at MCG, Human Assurance Committee) and Declaration of Helsinki. Indicate if informed consent was obtained. Do not use patient names, initials, or hospital numbers in the manuscript. Rather, use unique identifiers that allow only the investigator to link the data to the patient.
- When animal studies are involved, indicate whether procedures were in accordance with the institutional guide or Animal Care and Use Committee. At MCG, this is the Committee on Animal Use in Research and Education (CAURE).
- Organize the Materials & Methods section in chronological order. Start with materials, continue with protocols as they were used, and end with data analysis. Do not just randomly throw in the components of this section as you remember them.

### Results:

- The Results section should flow in a linear fashion. Once again, **logic** is very important.
- Each set of experiments should be presented as follows:
  - why you did the experiment
  - how you did it
  - presentation of data
  - conclusions from data
  - but not the interpretation (leave that for the Discussion section).
- Topic or introductory sentences are very important in the Results section. You must tell the reader why you did the experiment, and what your thinking (rationale) was. Thus, common ways to start new paragraphs are: “In order to determine whether.....,” or “Results from the previous experiment suggest that protein X is elevated in serum from patients with EFG disease. This may be due to excess synthesis of protein X or defects in its degradation. To determine which mechanism is responsible, we did the following experiment.....”
- In describing the experiment, refer to the Materials & Methods section, e.g., “Western analysis was performed as described in Materials and Methods, using antibody RM 203 as a probe.” The details here should not be too

specific, unless necessary. Often, some of the specific details about the individual experiment can be included in the figure legend, e.g., “Wild-type and mutant cells (as indicated) were grown to log phase at 25° C. Half of each culture was shifted to 37° C for 45 min. Whole cell lysates were incubated with anti-GFP beads as described in Materials and Methods. Precipitated complexes were resolved by SDS-PAGE, transferred to nitrocellulose filter, and probed with anti-GFP antibody (upper panel) and anti-.....”

- Briefly state what the data tell you, e.g., “As can be seen in Fig. 3B, sera from patients receiving drug QR show a linear decrease over time in levels of protein N...” It may be helpful at times to add in the text, “...(compare lanes 1 and 2 to lanes 5 and 6, Fig. 4A).”

### **Discussion:**

- State your conclusions and explain why they are novel and important. Do not reiterate the actual data (numbers, for example) presented in the Results section.
- Discuss the implications of your work in reference to studies by others. Do not repeat what is in the Introduction, but relate your work to what you presented earlier. If your experiments are in conflict with other reports, discuss possible reasons for this (e.g., different experimental system, different dosages of drugs).
- You can make speculations based on your observations, but be sure that the reader knows that you are speculating and not stating another observation.
- It is acceptable to suggest new experiments, which would be a continuation of the work reported, or to refer to new experiments in progress. However, keep in mind that competitors may also jump on the band wagon and complete those suggested experiments before you do.
- Make every word count in your Discussion. Do not be verbose.

### **Acknowledgments:**

- Be sure to acknowledge and thank colleagues who contributed to the work but do not meet the criteria for authorship (see above). This includes individuals who provided reagents (e.g., cell lines, antibodies), referred patients to you, provided technical help, suggested an experiment, discussed your results with you, or critically read the manuscript. Also acknowledge financial support: where the money came from (e.g., NIH, Bristol-Meyers), specific grant number, and which investigator received the financial support (indicate the initials of the investigator; if the recipient of the award is not an author of your paper [rare, but occasionally possible], give the recipient's full name).
- Some journals may require written permission from individuals to be acknowledged, although this is rare.

### **References:**

- Every time you read or refer to a reference, type it into your reference list or library.
- Consult the Uniform Requirements or the journal's Instructions to Authors for proper style of references. Be consistent with the style, and be complete with the information. (It is common for a reviewer to want to refer to one of the references. Finding the information incomplete and inaccurate is sure to tick him/her off and could make the reviewer wonder about other sloppy details in the paper.)

**Figure legends:**

- Many novice writers underestimate the importance of figure legends. The reader should be able to look at the figure and its legend and be able to understand how the experiment was done as well as see the results.
- The first statement in the legend should be the title of the figure. This does not have to be a complete sentence, although it often is. There are two ways to approach the title for the figure. Some investigators (and journals) prefer to state what the figure represents, e.g., “Levels of p53 protein in human lymphomas,” or “Northern blot analysis of *myc* oncogene in colon carcinomas.” Others give the conclusion of the figure in the title, e.g., “p53 protein expression is absent in most human lymphomas,” or “Expression of *myc* oncogene is increased in colon carcinomas.” One danger with stating the conclusion is that it biases the reader; on the other hand, it tells the reader what you want him/her to look for, which may be helpful especially if the figure is complicated.
- The legend should state how the experiment was done, but give only the necessary specifics. For example, “Tumors were excised from brains of mice and DNA isolated as described in Materials and Methods. Equivalent amounts of DNA were digested with *Eco RI* as described and loaded onto agarose gels. Southern blotting was performed using *c-myc* probe 468. Lanes 1-4, DNA isolated from malignant glial tumors from four different mice; lanes 5-8, DNA isolated from normal glial cells from syngeneic control mice; lane 9, size markers as indicated. Arrow indicates 683 bp band, as expected for.....” Note here that no conclusion of the experiment is presented. The legend states the facts, and gives enough information to understand what was done, but it does not overwhelm the reader with details that are presented in Materials and Methods.
- Many journals like figure legends to be written in a brief, clipped style. This means that you can delete “a/an/the” as well as other extra words.
- Check several times to be sure that lane numbers, graph symbols, and other notations in the figure correspond to the legend and to the text. This is one of the biggest problems with which journal editors (and reviewers) have to contend.

**Submission to the Journal:**

- Many, if not most, journals now require electronic submission. Consequently, this requires certain dramatic changes in how you prepare your manuscript.
- Graphics must be in electronic form, so avoid hand-drawn figures and graphs. Common formats used are TIFF or EPS.
- The requirements for individual journals vary considerably, so be sure to consult the journal’s Instructions to Authors.
- In all cases, whether submission is electronic or hard-copy, a cover letter should be sent explaining the important points of your paper and why it should be published in that particular journal.

**Writing Style:**

- Make every word count!
- Sentences
  - Every sentence should make a single point.
  - The new information (“stress point”) that each sentence provides should be at the end of the sentence.
  - Old information, which links the reader to the previous sentence, should be at the beginning of the sentence.

- Word order should be subject—verb—object. Keep your subject and verb as close together as possible.
- Use the active voice, e.g., “We measured.” Passive voice is useful when there are two or more actions in a sentence (because it can help to indicate the order of the actions) and when the doer of the action doesn't matter (or you don't really know who did it), e.g., “cells were washed”).
- Sentences should contain no more than 20-22 words.
- Paragraphs
  - Every paragraph should have a topic sentence that says what you are going to tell the reader about in that paragraph. [Analogy: Don't jump into the lake without telling bystanders why you are doing it. Are you going swimming? Are you going to rescue someone? Are you just fooling around, and perhaps endangering yourself?]
  - Use transition sentences to link paragraphs and sections. Why are you jumping from one experiment to another?
- As you write each sentence or paragraph, ask yourself: What am I trying to say? What is my question and why did I ask it?
- Always keep in mind who your reader is. How you write depends on the audience. Will the reader understand your jargon? Usually the reader does not know as much about the topic as you do (otherwise, you wouldn't be writing this), so keep in mind that you need to explain things as you go along.

#### **Points of grammar to keep in mind:**

- subject/verb agreement: singular subject takes singular verb; plural subject takes plural verb. Remember that the noun closest to the verb might not be the subject. Common mistake: data is plural and takes a plural verb; the singular form is datum.
- a/an/the: a common problem for non-native English speakers
- which/that:
  - Use “that” without commas for essential (restrictive) material that cannot be omitted without changing the meaning of the sentence.
  - Use “which,” with commas setting off the clause, for nonrestrictive, extra information.
- and vs. or: use them correctly. “and/or” should never be used, except in legal matters.
- dangling modifiers
- present/past/perfect tense:
  - use present tense for established, general knowledge
  - use past tense for particular results and for what you are reporting in this manuscript
  - use present tense when referring to your figures and graphs
  - use present perfect (have/has been) for observations that have been repeated or are ongoing
- use parallel construction in clauses and verb forms

#### **Other tips:**

- Write for an extended period of time, e.g., all afternoon, or even all day. Don't try to write for just an hour at a time—it doesn't work!
- Once you finish your first draft, let it lie dormant for a while. Reread your key references. When you return to your manuscript, look for the following:
  - Flaws in logic
  - Misquoted or misremembered facts
  - Excess verbiage

- When you do your rewrite, polish up your prose and style.
  - Check meaning of every word.
  - Check relationships between words.
  - Make every word count.
  - Check requirements of your journal. Are there word, page, or figure limits?

**One final piece of advice: Don't get discouraged. No book, journal article, or masterpiece was ever written in a day!**