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Writing a scientific paper—A brief guide for new investigators

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ABSTRACT

When applying for funding, researchers must demonstrate their productivity. For most funding organizations, a key measure of productivity is the number of papers published. The road to publication is rarely straightforward; few journals provide practical guidance to researchers who are struggling to publish their data. Here, we outline the sections of a research paper and describe practical steps in each part of the publication process as an aid to newer authors.

1. Introduction

A research paper communicates scientific work to a wide audience. Without publishing results, the important data collected, analyzed, and interpreted is inaccessible to the scientific community and hence of little or no value. In order to advance the science, researchers must share their results. Publishing data and results provides an opportunity to explain why the work is important and how it might be applied. To get to the point of publication, authors first must have a firm understanding of what should be included in the paper. This is not always clear, especially to new investigators. Many journals provide general guidelines that explain how a paper should be organized, but these guidelines rarely specify exactly what should appear in each section of the paper. This article is meant to fill those gaps of missing information and provide a checklist and template for newer scientific writers.

2. The title page

Choose a title for the paper that succinctly explains the message or "takeaway" point you hope to convey. This assists other investigators in rapidly identifying articles of interest to them. The title should be short (~150 characters)–most journals enforce a limit on the number of characters that can be included in the title. Information regarding title format, length, and style (e.g., some journals prohibit titles that are in the form of a question or state a conclusion) can be found on each journal's "Instructions for Authors" page. The title is often used in information-retrieval systems, such as search engines. The goal is to make it easier for other researchers to find—and cite—your work. The Letchford et al. study regarding the advantages of having a short paper title [1] suggests that papers with shorter titles are more frequently cited. The logic behind this is that shorter titles receive more "hits" during a literature search, which leads to more visibility for the paper.

Unless otherwise instructed by the journal, include author names and affiliations on the title page. Most journals require listing the corresponding author's contact information (i.e., name, email address, mailing address) on the title page.

Keywords, typically provided on the title page, also make your work searchable. These keywords, or Medical Subject Headings (MeSH), can be found using the MeSH browser (http://www.nlm.nih.gov/mesh/MBrowser.html). MeSH terms are common in scientific research; using MeSH terms for keywords ensures that you are using the most relevant search terms available. The browser is updated weekly by the U.S. National Library of Medicine in Bethesda, MD. Another option is to use the MeSH On Demand tool, which is available online (http://www.nlm.nih.gov/mesh/MeSHonDemand.html). Copy and paste the text of the paper into the text box, and MeSH On Demand returns a list of MeSH terms relevant to the text.

Most journals require an abstract word count, along with the main-text word count (i.e., text from the introduction to the discussion, inclusive), on the title page.

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2.1. Authorship

On its website, the International Committee of Medical Journal Editors (ICMJE; http://www.icmje.org/) outlines the four authorship criteria that should be met when listing authors on a paper. Authorship should be based on whether the individual (1) made "substantial contributions to the conception or design of the work, or the acquisition, analysis or interpretation of data for the work; *and* (2) drafted the work or revised it critically for intellectual content; *and* (3) gave final approval of the version to be published; *and* (4) agreed to be accountable for all aspects of the work, ensuring that any questions relating to the integrity of any part of the work are appropriately investigated and resolved" [2]. Many journals require authorship information to be available upon article submission, and some journals will not process the manuscript until the contribution of each author is explicitly listed. It is essential to ensure that each author listed meets each of the four ICMJE criteria before the paper is submitted. So-called gratuitous and honorary authorship is inappropriate and should not be used.

3. The abstract

While the abstract word limit varies by journal (typically 150–300 words), all journals require one. Some journals require a structured abstract, which is typically organized with these headings: Background, Methods, Results, and Conclusions. An unstructured abstract includes the same information as that of a structured abstract, but does not need to include headings. If your paper includes work performed as part of a clinical trial, you must register the clinical trial and include the registry's URL and the trial's registration number (https://clinicaltrials.gov/). This information should be included in the abstract:

- *Introduction/background:* Give a basic idea of what the scientific issue(s) are and what question(s) you are trying to answer
- *Methods:* Provide a very brief high-level sketch of what subjects or methods you used to investigate the research question
- *Results:* Give KEY results only; What is the "newspaper headline" or main finding(s) of the study?
- *Conclusion:* Describe the significance of your key findings, what they mean, and what their implication is on the field.

4. The introduction

The first section of the paper is the Introduction. Here is where you summarize what questions or hypotheses you are pursuing and why. What are the missing gaps in the scientific database that this work fills? This section also gives readers an opportunity to understand the major points of content background in the field.

Typically, the introduction can be organized in the following way:

- Paragraph 1**:** Context—Explain why this research is important to public health, science, or technology; Tell the readers why this topic is an important one to study
- Paragraph 2: Gaps—Describe what gaps exist in the knowledge base that this research was designed to address; Explain the scientific "hole" in knowledge or controversy that this research is attempting to fill or solve
- Paragraph 3: Hypothesis being tested—Explain what you set out to do and why (what is the hypothesis to be tested?).

The journal you choose for your paper may set limits regarding allowable word count. While this ultimately influences the length of the introduction and the sections that follow, it's best to include a brief one-page introduction.

5. Methods

This section includes a summary of how the research was conducted; here is where you explicitly state the study design and describe the cohort of subjects or animals used for the research (including age, race sex, number of subjects) [3]. It is important to include a statement regarding informed consent, and whether your institutional review board reviewed and approved the research. You should provide information about the research setting and what laboratory or other techniques were used. The statistical methods and analysis information should appear in this section. If you have previously published the statistical—or other—methods that were used during this research, include a statement declaring that similar (or identical, depending on the research) methods were previously used, and provide references pointing to that work. This avoids the issue of self-plagiarism [4]. The methods should be clear and concise and at a level of detail to allow readers to understand what was done, how it was done, and under what conditions. While it is important to be concise, some journals require very detailed methods to ensure reproducibility; however, many journals that require detailed methods also have limitations on article length. To address this, some of these journals allow these detailed methods sections to be included as supplementary material. *Nature Genetics*, for example, introduced an "Online Methods" section for letters, articles, and technical reports. This section, which includes material previously labeled as methods and supplementary methods, includes hyperlinks and can be downloaded in PDF format from the journal's website.

5.1. Report the details

Our group previously reported that important factors in analyzing vaccine-related studies are often inadequately reported in publications [3]. As the study suggested, many important details, which may affect the interpretation of vaccine immunogenicity and efficacy data, are frequently left out of research papers [3]. These details should be included so the study results can be replicated and, if appropriate, the results generalized to patients. Needle length and anatomic site of injection, for example, are details that may seem trivial, but proved to be critical in interpreting immunogenicity studies of hepatitis B vaccine. As discovered during hepatitis B vaccine studies, comparing the vaccine's antibody response rate in subjects who were immunized in the deltoid muscle to the response rates in subjects who were immunized in the buttocks resulted in significantly skewed results. The subjects immunized in the deltoid demonstrated significantly higher antibody response rates in early studies [5], but these studies did not report data on vaccination site, injection technique, or needle length; this led to subsequent studies being unable to replicate the results because subjects were immunized in the buttocks [6,7].

Additional factors known to affect vaccine response, such as storage and handling of temperature-sensitive live viral vaccines, should be acknowledged and documented in all research. As noted in Poirier et al., this documentation is necessary to interpret the results of the study [3]. Subject characteristics (i.e., age, race, sex, and ethnicity), along with any concomitant biologic/drug use in subjects, may also influence vaccine response. These important details about study subjects should be well documented and reported. Table 1 includes a list of primary and secondary considerations that should be reported.

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Table 1
Primary and secondary considerations for vaccine studies: a checklist.

Dose
Route of administration
Number of doses
True interval between doses
Vaccine antigen
Use of vaccine adjuvants
Injection technique and anatomic site of vaccine injection
Cold-chain maintenance
Concomitantly administered drugs
Race, gender, age, obesity status, smoking status
Vaccine lot number and manufacturer information

Table adapted from information in Poirier et al. [3].

Information about the vaccine itself (e.g., manufacturer name and lot number of licensed vaccines) should be reported. Such information is critical to compare vaccine immunogenicity or efficacy between different vaccines or vaccine lots for the same pathogen.

5.2. CONSORT and ARRIVE guidelines

The issue of inadequate reporting of randomized controlled trials is not new. CONSORT, or Consolidated Standards of Reporting Trials, is led by a group of clinical trial methodologists, guideline developers, journal editors, and knowledge-translation specialists. The CONSORT Group offers guidelines and a detailed checklist—known as the CONSORT Statement—designed to help authors report on their studies [8,9]. The CONSORT checklist includes 25 items that focus on reporting trial design, as well as analytical methods and interpretation [10]. The CONSORT flow diagram illustrates the progress through the phases of a parallel randomized trial of two groups [11]. Researchers are strongly encouraged to use and cite CONSORT material for all of their published clinical trial work.

Researchers reporting on animal studies should use the ARRIVE (Animals in Research: Reporting *In Vivo* Experiments) guidelines, which, like the CONSORT guidelines, are intended to improve the reporting of research that uses animals [12,13]. These guidelines are intended for researchers doing studies where two or more groups of experimental animals are being compared, as well as studies that compare different drug doses in an animal that is used as its own control [13]. ARRIVE guidelines consist of a 20-item checklist that outlines the minimum information required in each section (i.e., title, abstract, introduction, methods, results, discussion) for publication (see https://www.elsevier.com/__data/promis_misc/622936arrive_guidelines.pdf).

5.3. STROBE guidelines

Observational studies must also be conducted with full transparency. With this in mind, an international group of epidemiologists, methodologists, statisticians, researchers, and journal editors crafted the STROBE guidelines and checklists, which are available online (http://strobe-statement.org/index.php?id=available-checklists) [14]. STROBE is an acronym that stands for "Strengthening the Reporting of Observational studies in Epidemiology." The STROBE Initiative covers three main study design types: cohort, case-control, and cross-sectional studies. Similar to the CONSORT and ARRIVE checklists, the STROBE checklists outline guidelines regarding a paper's title and its abstract, introduction, methods, results, and discussion sections.

Other guidelines exist for review studies [15,16], meta-analyses [17–19], and other study types.

5.4. Statistical methods

Reporting the details regarding the collection of data is crucial, as is reporting the details of data analysis. In 1988, the ICMJE provided guidelines to assist researchers reporting the statistical methods used in their research [20]. The first point from the ICMJE instructs the investigator to provide enough detail when describing statistical methods so a reader with access to the original data could validate the published results. Now, nearly 30 years later, the goal of reproducibility is becoming paramount (see Section 7.2). In a recent editorial in *Vaccine*, the journal's Editor-in-Chief (Poland) and Associate Editor (Oberg) outlined statistical and analytical guidelines each article must meet in order to be considered for publication [21]. Poland and Oberg stress that, while each study is different, there are several general points that must be followed to ensure that statistical reporting is complete (e.g., clearly state the sample size and include a description of how the sample was chosen for primary and secondary hypotheses; provide enough detail regarding hypothesis testing so the analyses could be repeated by an informed reader; provide an explanation regarding why a complex analyses method was used; and provide all information regarding any analytical software that was used for analyses). *Vaccine* provides a checklist for statistical and analytical guidelines, which is available online (https://www.elsevier.com/journals/vaccine/0264-410X/guide-for-authors) (Supplemental Table 1).

Altman et al. stress that all statistical methods used in the paper should be identified and techniques should be clearly explained [22]. This group advises authors to include their rationale for using a particular method of analysis, which is essential when non-standard or novel methods are utilized. Lang and Altman published the "Statistical Analyses and Methods in the Published Literature" (SAMPL) guidelines in 2013 [23]. These guidelines instruct authors, journal editors, and reviewers how to report statistical methods and results. The intent of the guidelines is to focus attention on the key points of analyses, which should prevent many of the deficiencies (e.g., lack of details on distributional assumptions/considerations, or missing information regarding the level of significance) that exist in scientific articles.

5.5. Study reproducibility

Collins and Tabak report that one of the major concerns in research is what *is not* published [24]. Crucial experimental design elements are frequently missing from research articles—information regarding blinding, randomization, replication, sample-size calculation and the effect of sex differences are under-reported. Without this information, it is impossible for scientists to recreate and replicate scientific findings, which cripples any significant advancement of the science. The importance of this is illustrated by the fact that the NIH has launched a "Big Data" initiative, which calls for the development of a Data Discovery Index (DDI) to hold unpublished primary data. Investigators can access this data and use it for new research, while citing the data's owner in the publication [24].

To encourage authors to be as detailed as possible in their work, several journals are relaxing the restrictions on the length of methods sections in papers. Authors are also encouraged to submit their raw data to accompany the online publication; however, it is imperative that they receive permission from the appropriate institutional review boards before sharing any data. During the submission process for Nature Publishing Group journals, the author completes a checklist that is designed to assist editors and reviewers in verifying that critical experimental design features have been included in the paper (http://www.nature.com/authors/

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policies/checklist.pdf). Collins and Tabak speculate that this will be the trend other publishing groups use going forward [24].

In a commentary regarding the importance of validating and reproducing cancer-specific research findings, Begley and Ellis described an exercise that the biotechnology firm Amgen (Thousand Oaks, CA) uses to confirm research findings prior to embarking on similar research. The results were surprising: scientific findings were confirmed in only 11% of the 53 studies they chose to review [25]. The studies that could be reproduced provided adequate information regarding controls, reagents, investigator bias, and all described the complete dataset. In the case of preclinical cancer research, the ability to reproduce research findings can have significant effects on patient health: patients with various cancers have been placed into trials based on one non-reproducible study and completed treatment regimens (with the resulting risk or toxicity) with insufficient data for benefit [25]. Going forward, Begley and Ellis comment that researchers must pay close attention to reporting positive and negative controls and they (or, ideally, different investigators in the same lab) should repeat any critical experimental findings before publishing the results. Perhaps most importantly, the entire dataset must be represented in the final publication [25].

6. Results

Provide information about study subject demographics in this section. Do not explain or duplicate in the text what can be easily included in tables, graphs, or figures. Most journals would rather include eye-catching figures to illustrate data (see Section 10 below for more information). Describe the assay and statistical results in this section, along with the quality assurance, quality control, and coefficient of variation of the assays, to ensure accurate interpretation of the data.

6.1. Statistical results

It is helpful to use graphics to illustrate the data variables utilized in analyses. Graphical methods can provide an adequate description of the data along with the formal statistical analysis. Report any deviations from the proposed/intended study design, and describe why the change was necessary. Altman et al. outline all of the major topics of a proper statistical analysis section of a paper: significance tests, confidence intervals, paired observations, repeated measurements, data transformation, outliers, correlation, regression, and complex analyses [22]. According to Altman et al., "the purpose of statistical methods is to provide a straight-forward factual account of the scientific evidence derived from a piece of research" [22].

7. Discussion

The discussion is a critical aspect of your paper. Summarize the key findings in the first paragraph, but take care not to repeat what was already included in the previous sections of the paper. Relate these key findings to the *a priori* hypothesis that was stated in the Introduction section.

After you summarize your key findings, use the second paragraph to state your case: explain your interpretation of the results and how it relates to what is already known or—more importantly—not known in the literature. Use this section to refer to other reviews and published papers, but sparingly cite your own work in this field when relevant to avoid excessive self-referencing. Clarify what your study adds to the knowledge base, or to effects on patient care, technology development, or new diagnostics. Use paragraphs three and four to discuss the possible mechanisms that explain the results—these are key paragraphs of the paper. Paragraph five should clearly describe the strengths and limitations of the study, which can include issues relating to the study question or design, the methods, analysis, or interpretation of results. In the sixth paragraph, describe the potential controversies (if any) raised by this study.

In the final paragraph, describe the implications of the study results and future research directions for your lab—or labs worldwide—as a result of this study. Explain what the findings mean to science in the bigger, long-term picture. Address what effects your results may have on future translational or clinical research or care.

8. The acknowledgements section

This section should include a statement acknowledging the subjects, technicians, nurses, and/or data personnel who were substantially involved and helpful during the study. You must have written approval to acknowledge specific people in this section. If your study was funded by any outside agencies and grants, use this section to include the grant names and numbers. This will ensure that your published work is correctly linked to funding, which is particularly important for publicly funded grants. Include a statement similar to this one: "Research reported in this publication was supported by the National Institute of Allergy And Infectious Diseases of the National Institutes of Health under award Number XXXXXXX. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health."

9. Conflict of interests/competing interests

It is essential to practice full disclosure. In this section, include each author's relationships (e.g., consulting activities, board memberships) that could be *perceived* as a conflict of interest. If this research was presented in full or in part at any meetings or conferences, it is important to disclose that information in this section. Most journals have explicitly written policies specifying information that must be reported and in what detail.

10. Tables and figures/legends

Tables and figures are an important way to illustrate a large amount of information concisely in one place. As O'Connor and Holmquist point out, crafting the figures and tables is a "critical first step" in the outline-writing process [26]. By designing each figure to be based on a single piece of data for the manuscript, the writer can then construct a helpful working outline and, eventually, a detailed first draft by viewing the figures in the order they would appear in a paper [26].

The graphical display of data is both art form and scientific in intent and purpose. Decide what analyses and data will be needed to answer the question(s) you pose in the paper. Provide a short name for each figure and legend, and ensure each table and figure has a legend that clearly explains the information being illustrated. The legend should include a brief description of the materials and methods used to generate the data conveyed in the figure, as well as a brief summary of the displayed results. The figure legend should be able to stand alone, without requiring any effort on the reader's part to interpret the illustration. Some journals only print in color if the author pays color charges—if you are unwilling to pay for color, consider this when you design the figures. Important findings should not be conveyed by a color in a figure; consider using different patterns or lines to illustrate the information.

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11. References

Each journal has a style for including references in the paper text and for listing the bibliography at the end of the paper. Most journals include this information online in the "Instructions for Authors" page. Reference databases such as ReferenceManager and EndNote are extremely helpful in terms of organizing and formatting references. EndNote, which includes output styles for nearly every journal, is the most widely used reference database. If the output style is not in the database, it can easily be added by searching for it on the EndNote website [27]. Authors can also use EndNote to create output styles that can be tailored to include the exact information the journal requires in the bibliography. Ensure that the references are formatted correctly and are complete. Most journals will return a submission if it does not meet their requirements for references.

12. Plagiarism

Unfortunately, it has become increasingly common to see nearly identical papers, or sections, published by different research groups. Some authors make the mistake of "self-plagiarizing" by including identical sections of their previously published papers without properly citing the work. This typically occurs within the methods sections of papers where there is essentially only one way to describe the methods used and the assays performed. As previously mentioned in the "Methods" section above, include a statement that acknowledges the work has been previously published, and include the proper references for that work. Many journals use software to check submissions for plagiarism. We recommend using an online software program, such as TurnitIn [28], to check each manuscript draft against several databases of published papers. This software scours databases, such as ScienceDirect, and generates a report that indicates which text in the manuscript may be similar or identical to previously published papers. It is essential to identify any potential instances of inadvertent plagiarism before submitting your work to the journal. Become familiar with how journals identify and address plagiarism issues—we and others have written about the emerging issue of plagiarism and self-plagiarism [4,29–32]. Photographs, graphs, and data-output figures should never be enhanced or manipulated without indicating specifically what has been done, and should include information justifying the reason for any changes.

13. Choosing a journal

Consider the journals that you and your colleagues subscribe to—those are the journals most likely to publish topics that are of the most interest to scientists in your field. It is also helpful to make note of the journals that publish your colleagues' work. Next, consider the impact factor of each potential journal. This factor is a widely used indicator of journal quality, but it is not the only quality measurement available. Also review other journal metrics including Eigenfactor [33], h-index [34], and SCImago Journal Rank (SJR) [35], which all provide helpful metrics regarding citation rate and frequency of downloads.

Some journals may take longer than others to complete the peer-review process. The typical timeframe for review is four to eight weeks, approximately three weeks for a revision cycle, and another four to six weeks before a final decision. Open Access journals have publication fees to support a faster review/decision process. Several published articles offer valuable guidance and insights regarding factors to consider in choosing a journal [36–38]. Table 2 lists some key factors that should be considered when choosing a journal.

14. Manuscript submission

Each journal has its own manuscript submission system and process. Before you begin the submission process, be sure you have contact information for your co-authors. Some journals require an affiliation and email address for each co-author, and contact information for the corresponding author. Take the time to review the journal's submission instructions, as most of the information you need is outlined there. One tip—if you cannot find specific information in the submission instructions (e.g., whether the journal requires suggested reviewer names), start the submission process within the journal's editorial system. Each element required for submission is clearly marked, and the system will issue an error prior to submission if you missed any of the required elements. When in doubt, check in the system.

It is also important to include a list of potential reviewers with your paper submission. Many journals require a list of three to six reviewer names. Do not list friends, colleagues with whom you have collaborated, or others for whom the appearance of a conflict of interest exists. Conduct a literature search on your paper topic and review the authors who have published in your field—those authors are potential reviewers for your paper.

Including a cover letter during the submission process may not be mandatory, but it is encouraged. In the cover letter, you can provide details about your manuscript, such as information regarding data availability, or a statement outlining how your study will advance the science in your field of research. If your submission describes similar or identical methods to your previously published papers, it is beneficial to disclose this in the cover letter by providing bibliographic information for those publications. In addition, a cover letter provides an opportunity for you to list potential reviewers with whom you have a conflict of interest

Table 2
Choosing a journal: some considerations.

Audience	Is this a journal you and your colleagues read on a regular basis? Determine who your target audience is and a find a journal that reaches that readership
Aims and scope	Read about the journal to determine its aims and scope. Consider the type of research covered in the journal
Impact factor	While not the sole indication of journal quality, the impact factor is an important factor to consider when choosing a journal
Speed of review/ publication	The journal may indicate the typical timeframe from article submission to publication. If you strive for quick publication, such information is an important factor
Open access	Many journals offer an Open Access option for publishing; this requires a page fee (sometimes as much as $3000), but this means your article will be quickly available widely accessible
Article restrictions	Many journals have strict limits on word counts and the number of allowable references, tables and figures. If your article is more than 3000 words, you may need to consider a journal that offers flexibility for article length
Journal reputation	Consider only well-established journals; make sure the journal is indexed in Web of Science, Scopus and MEDLINE/PubMed. An increasing and disturbing trend is so-called "predatory journals" that take advantage of the open-access publication model by promising rapid acceptance and publication, but fail to provide the editorial and publishing services that legitimate journals provide [39]

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and request that they do not review your paper. While this information may not be required by the journal, editors may find it useful to have it in a single document.

15. The decision

Once your manuscript is under review, you should expect to hear a decision from the journal within six to eight weeks. If you receive a revise decision with reviewer comments, be sure you address each comment in detail in a "Response to Reviewers' Comments" document. Every journal requires a document that explicitly outlines how the authors addressed reviewer concerns. On its website, Elsevier offers guidance on the review process (https://www.elsevier.com/authors-update/story/publishing-tips/3-top-tips-for-responding-to-reviewer-comments-on-your-manuscript). While many reviewer comments provide insight that will make your revised paper stronger, it is not unusual to disagree with some reviewer comments. In fact, this disagreement often leads to helpful scientific discussion among authors and reviewers. When you respond, clearly explain your point of view, and back up your explanation with facts. Be polite—but firm—in your rebuttal.

Organize the reviewer comments by copying and pasting them into a Word document, and provide your responses under each comment. It is helpful to assign each comment to a specific co-author to address, and develop timelines in order to ensure timely resubmission. Many journals require authors to indicate edits within the revised manuscript. This can be done using the "Track Changes" feature in Word, or by highlighting the changes with a different background or font color. Each co-author must review and approve the revised manuscript before it is resubmitted. Journals typically allow approximately two to four weeks for authors to submit a revised manuscript.

Once this part of the process is complete, you should receive a decision within a few weeks. If your manuscript is accepted—congratulations! If the journal rejects your paper, do not abandon your work. Your manuscript will undergo several iterations before it is published. Even the most seasoned and prolific writers have had their work rejected several times. This process ensures that the finished product (i.e., your published paper) will help advance the science. That is, after all, the main purpose for publishing your work.

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Competing interest statement

Dr. Poland is the chair of a Safety Evaluation Committee for novel investigational vaccine trials being conducted by Merck Research Laboratories. Dr. Poland offers consultative advice on vaccine development to Merck & Co. Inc., CSL Biotherapies, Avianax, Dynavax, Novartis Vaccines and Therapeutics, Emergent Biosolutions, Adjuvance, Microdermis, Seqirus, NewLink, Protein Sciences, GSK Vaccines, and Sanofi Pasteur. Dr. Poland holds two patents related to vaccinia and measles peptide research. These activities have been reviewed by the Mayo Clinic Conflict of Interest Review Board and are conducted in compliance with Mayo Clinic Conflict of Interest policies.

Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.vaccine.2016.11.091.

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