How to read a scientific paper?

Aims

- Learn the basic structure of papers
- Develop an approach to reading papers
- Learn how to interpret an article
- Learn how to write a manuscript…..and getting published!

Papers are one of the most important ways that researchers use to communicate each other.

The main purpose of a scientific paper is to report new results, usually experimental, and to relate these results to previous knowledge in the field.

In understanding how to read a paper, we need to start at the beginning with a few preliminaries.

We then address the main questions that will enable you to understand and evaluate the paper.

1. How are papers organized?
2. How do I prepare to read a paper, particularly in an area not so familiar to me?
3. What difficulties can I expect?
4. How do I understand and evaluate the content of the paper?

The IMRAD structure

Introduction	answers “why?”
Materials and Methods and	answers “when,where, how, how much?”
Results	answers “what?”
Discussion	answers “so what?”

The typical anatomy of a paper:

- Title and Authors [Affiliation]
- Abstract/ Summary
- Introduction/ Background
- Materials and Methods
- Results
- Discussion
- Acknowledgements
- References/Bibliography
- Figures/Tables

Title and authors

- Title should be concise but informative.
- Title is very descriptive (often states the main finding) and is not about being creative and “catchy”!

Cancer Discov. 2015 Sep 25. pii: CD-15-0892. [Epub ahead of print]

Infection exposure is a causal factor in B-precursor acute lymphoblastic leukemia as a result of Pax5 inherited susceptibility.

Martin-Lorenzo A[1], Hauer J[2], Vicente-Duenas C[1], Auer F[2], Gonzalez-Herrero I[3], Garcia-Ramirez I[1], Ginzel S[2], Thiele R[4], Constantinescu SN Prof[5], Bartenhagen C[6], Dugas M[6], Gombert M[2], Schafer D[2], Blanco O[7], Mayado A[8], Orfao A[8], Alonso-Lopez D[9], De Las Rivas J[9], Cobaleda C[10], Garcia-Cenador MB[11], Garcia-Criado FJ[11], Sanchez-Garcia I[1], Borkhardt A[12].

- Order of authors is important. What can you tell from it?

The first author is who did most of the work. The last author is often the coordinator of the research group. Other authors are approximately listed in a decreasing order in relation to their contribution.

Title

Authors

Affiliation

Corresponding author

Bone Marrow Transplantation (2010) 45, 261–267

www.nature.com/bmt

ORIGINAL ARTICLE

Influence of GST gene polymorphisms on busulfan pharmacokinetics in children

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Busulfan (BU) is a key compound in conditioning myeloablative regimens for children undergoing hematopoietic stem cell transplantation (HSCT). There are wide interindividual differences in BU pharmacokinetics, which increase the risk of veno-occlusive disease, graft rejection and disease relapse. As BU is mainly metabolized by glutathione *S*-transferase (GST), it is hypothesized that functional polymorphisms in GST genes may explain in part the variability in BU pharmacokinetics. We analyzed polymorphisms in *GSTA1* (C-69T, A-513G, G-631T, C-1142G), *GSTM1* (deletion) and *GSTP1* (A1578G, C2293T) genes in 28 children undergoing HSCT. All patients had individualized dosing based on pharmacokinetics after the first dose of intravenous BU. *GSTM1*-null individuals had higher drug exposure ($P_{Cmax} = 0.008$; $P_{AUC} = 0.003$; $P_{Css} = 0.02$) and lower clearance ($P_{CL} = 0.001$). Multivariate regression models showed that, other than the drug dose and age, the *GSTM1* genotype was the best predictor of first-dose pharmacokinetic variability. *GSTM1*-null patients also received lower cumulative BU doses ($P = 0.02$). No association was found between BU exposure and major *GSTA1* or *GSTP1* gene variants. In children, *GSTM1* polymorphism seems to modify BU pharmacokinetics after intravenous drug administration.

Bone Marrow Transplantation (2010) **45,** 261–267; doi:10.1038/bmt.2009.143; published online 6 July 2009

Keywords: busulfan; hematopoietic stem cell transplantation; glutathione *S*-transferase; polymorphisms; pharmacogenetics; pharmacokinetics

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Introduction

Busulfan (BU) is an alkylating agent used in a wide variety of myeloablative conditioning regimens for hematopoietic stem cell transplantation (HSCT). BU has a narrow therapeutic index. High drug exposure leads to increased risk of veno-occlusive disease (VOD), whereas low drug exposure has been associated with a higher risk of disease recurrence and graft failure.[1–4] Accordingly, steady-state BU plasma concentration and area under the concentration–time curve (AUC) correlate with the incidence of these clinical events.[1–4] Intravenous (IV) administration has consequently gained popularity, especially in children, as IV pharmacokinetics can be more predictive than pharmacokinetics after oral administration.[5–7] Nevertheless, important interindividual variability still persists[8] and several additional factors contribute to such observations. Metabolism by glutathione S-transferase (GST) is the main route of BU biotransformation. GSTA1 is the predominant GST isoform catalyzing BU conjugation with glutathione, whereas GSTM1 and GSTP1 have 46 and 18%, respectively, of the activity of GSTA1.[9] Interindividual variation may be explained, at least in part, by *GST* polymorphisms. Two *GSTP1* variations leading to Ile105Val and Ala114Val amino-acid replacements result in different catalytic activities.[10] A significant number of individuals lack GSTM1 activity (~50%) because of the homozygous deletion of the *GSTM1* gene.[11] Several polymorphisms, shown in some studies to be functional, have been identified in the *GSTA1* gene.[12–14] Genotyping patients for relevant polymorphisms, even before drug administration, could further individualize BU treatment.

Materials and methods

Patients

The study comprised 28 children who underwent HSCT at the CHU Sainte-Justine in Montreal between May 2003 and January 2006. The CHU Sainte-Justine Institutional Review Board approved the study and all of the patients and/or their parents provided informed consent.

Summary/Abstract

The abstract serves as a summary of the paper, presenting purpose and major findings.

- **Short: journals indicate maximum number of words (150-200 words)**
- **It gives a brief background to the topic**
- **It describes concisely the major findings of the paper and relates this findings to the field of study**
- **Same logical order used in the paper as a whole (same organization)**
- **The language is concise and easy-to-read**

Summary/Abstract

- An abstract is a synopsis, not an introduction to the article.
- It should answer the question: “What should readers know after reading this article?”
- Most journals require that the abstract is divided into four paragraphs with the following headings:
  - Objective
  - Materials and Methods
  - Results
  - Conclusions

The title & abstract are often all that people will read, using this information to decide whether they want to continue.

Keywords

- Below the abstract, authors should provide 3 to 10 keywords or short phrases that will assist indexeres in cross-indexing and may be published with the abstract.
- The terms used should be from the Medical Subject Headings list of the Index Medicus.

Main text

The text of observational and experimental articles is usually (but not necessarily) divided into sections with the headings

- Introduction
- Methods
- Results and
- Discussion

Long articles may need subheadings within some sections (especially the Results and Discussion sections). Other types of articles, such as Case Reports, Reviews and Editorials are likely to need other formats.

Introduction

- The text should begin with an Introduction that conveys the nature and the purpose of the work, and quotes the relevant literature.
- It presents the background information for a fellow scientist (possibly in another field) to understand why the findings of the paper are significant.

Give only strictly pertinent background information necessary for understanding why the topic is important and references that inform the reader as to why the study was undertaken.

Do not review the literature extensively.

Introduction

Structure is usually:

- **Accepted state of knowledge in the field: contest; what is known; supporting literature with citations**
- **Focus on a particular aspect of the field, often the set(s) of data that led directly to the work of this paper**
- **The research question: hypothesis being tested**
- **Conclusions: newness; relevance to field**

Introduction

Introductions usually follow a funnel style, starting broadly and then narrowing. They funnel from something known, to something unknown, to the question the paper is asking.

The final paragraph should clearly state the hypothesis or purpose of the study. Brevity and focus are important.

Materials and Methods

It provides instructions on exactly how to repeat the experiment.

- Steps taken to:
  - gather data
  - analyze data
- Statistical methods
- Should be detailed enough for another scientist to replicate the work (volumes, times, company material was purchased from etc.)
- Not a “cookbook”
- In reality, often compressed and you may need to look up another paper that is referenced for more detail.

Materials and Methods

Should give a full description of:

- **Patients:** Demographic characteristics
  All relevant information
- **Methods:** Surgical technique
  Radiological technique
  Drug (preparation, dose, timing…etc)
- **Type of study:** Design (Type of control)
  Randomization
- **Statistical methods:** Common (List)
  Uncommon (List + References)

Materials and Methods

Describe the selection of the observational or experimental subjects (patients or laboratory animals, including controls) clearly.

Identify the age, sex, and other important characteristics of the subjects (explicitly justify them when included e.g. authors should explain why only subjects of certain ages were included or why women were excluded).

- *Our study population was selected from …*
- N *patients underwent …*
- N *consecutive patients …*
- N *patients with proven …*
- *Patients were followed clinically …*
- N *patients with … were examined before and during…*
- N *patients with known or suspected … were prospectively enrolled in this study.*
- *More than* N *patients presenting with … were examined with … over a period of* N *months.*
- N *patients were prospectively enrolled between … (date), and … (date).*
- N *patients (*N *men,* N *women: age range,* N–N *years; mean,* N ± N *years).*

Materials and Methods

The methods section should be a clear & briefly stated, chronological description of what you did & how you did it.

- **In principle, the description should be detailed enough to allow other researchers to replicate the work.**

Identify the methods, instrumentation (trade names and manufacturer's and location in parentheses) and procedures in sufficient detail to allow other workers to reproduce the study.

> Varicella antibodies were quantified using an immunoenzyme micro-method (Enzygnost anti-VZV-virus/IgG, Dade Behring GmbH), which has a high sensitivity and specificity (respectively, 99.3% and 100%).

Materials and Methods

Identify precisely all drugs and chemicals used, including generic names, doses and route of administration.

The ECX regimen consisted of epirubicin 50 mg/m^2 (15-minute intravenous [IV] infusion) plus cisplatin 60 mg/m^2 (1-hour IV infusion) on day 1 followed by oral capecitabine 1 g/m^2 twice per day from day 2 to day 15 every 3 weeks[18]; the maximum cumulative dose of epirubicin authorized was 900 mg/m^2.

The FOLFIRI regimen consisted of irinotecan 180 mg/m^2 (90-minute IV infusion) and leucovorin 400 mg/m^2 (2-hour IV infusion) followed by a fluorouracil 400 mg/m^2 IV bolus and then fluorouracil 2,400 mg/m^2 as a 46-hour continuous infusion every 2 weeks. Dose modifications, appropriate hydration, and premedication were predefined in the study protocol.

- *Entry/inclusion criteria included …*
- *These criteria had to be met: …*
- *Patients with … were not included.*
- *Further investigations, including … and …, were also performed.*
- *We prospectively studied* N *patients with …*
- *The reviews were not blinded to the presence of …*

Materials and Methods

- Give references to established methods, including statistical methods that have been published but are not well known.
- Describe new or substantially modified methods and give reasons for using these techniques and evaluate their limitations.
- In practice, information are highly compressed and they often refer back to previous paper by the same authors (self-citation).
- In some journals this section is the last one.

Statistics

- **Describe statistical methods with enough detail to enable a knowledgeable reader with access to original data to verify the reported results.**
- **When data are summarized in the Results section, specify the statistical method used to analyze them.**

- *To test for statistical significance, …*
- *Statistical analyses were performed with … and … tests.*
- *The levels of significance are indicated by P values.*
- *Interobserver agreement was quantified by using k statistics.*
- *All P values of less than 0.05 were considered to indicate statistical significance.*
- *Univariate and multivariate Cox proportional hazards regression models were used.*
- *The χ^2-test was used for group comparison. Descriptive values of variables are expressed as means and percentages.*

Statistics

- **Give details about randomization.**

> - *They were selected consecutively by one physician between February 1999 and June 2000.*
> - *This study was conducted prospectively during a period of 30 months from March 1998 to August 2000. We enrolled 29 consecutive patients who had …*

- **Specify any software used.**

> - *All statistical analyses were performed with SAS software (SAS Institute, Cary, N.C.).*
> - *The statistical analyses were performed by using a software package (SPSS for Windows, release 8.0; SPSS, Chicago, Ill.).*

Should you read the materials and methods?

- Often you can skim over them.
- However, when you get to the results, you will need to flip back to them to clarify how experiment was done.
  - **Who?** How many study participants were selected? What criteria were used to choose them?
  - ***Where?***
  - ***When?***
  - **How?** *Did they do the measurement more than once? Am I looking at a reduced or non-reduced protein gel? Which method was used to measure Ab titers?*

Results

- The results section is meant to highlight trends in the data (most often presented in figures and/or tables). Text should complement the tables/figures, NOT repeat the information presented therein.
- While the introduction poses the questions being asked, the results describes the outcome of the experiments that were done to answer the questions→ statistical results.
- Results are often simply stated with interpretation of them coming later in the discussion.

Results

The Results section DESCRIBES but DOES NOT INTERPRET the major findings.

1.Objective presentation of experiment

Present the results as text, tables or graphs, but do not repeat the same data in more than one.

2. Interpretation

Associate your data with each others to obtain an objective proof of your hypothesis.

Results

- Figures, graphs and tables allow the reader to see the outcomes of the experiments for themselves!
- Read the text straight through, but as a figure is referred to, examine the figure.
- Present your results in logical sequence in the text, along with tables and illustrations.
- Emphasize or summarize only important observations.
- Give numbers of observations and report losses (such as drop-outs from clinical trial).

Figures and Tables

- They contain data described in the text.
- Figures and Tables are enumerated and also have a legend, whose purpose is to give details of experiments or information shown.
- Take care that each table/figure is cited in numerical sequence in the text.
- Explain in foot-notes all non-standard abbreviations used.
- In the text or at the end of paper as:
  - Additional files
  - Supplementary material

Discussion

- Data are interpreted → Answer to research question
- Data are analyzed to show what the authors believe the data show → Facts should clearly be separated from speculation (You don't have to agree with their interpretations!)
- Findings are related to other findings in the field (contribute to knowledge, correct errors, future direction, etc.).
- How is this work significant?

Discussion

- Emphasize the new and important aspects of the study and the conclusions that follow from them.
- Do not repeat in detail data given in the Introduction or Results sections.
- Include implications of the findings and their limitations, including implications for future research.
- Relate the observations to other relevant studies.
- Avoid unqualified statements and conclusions not completely supported by the data.

- *In conclusion, …*
- *In summary, …*
- *This study demonstrates that …*
- *This study found that …*
- *This study highlights …*
- *Another finding of our study is …*
- *One limitation of our study was …*
- *Other methodological limitations of this study …*
- *Our results support …*
- *Further research is needed to understand …*

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- Contribution of other workers are recognized.
- Financial and material support should also be acknowledged.
- List all contributors who do not meet the criteria for authorship, such as person who provided purely technical help, writing assistance or general support.

- *The authors express their gratitude to … for their excellent technical support.*
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Author's contribution

- Contribution of different authors are explicated

Competing interest

- Sources of funding

Received/Published

- Time taken for publication

SURVEILLANCE AND OUTBREAK REPORT

Hospital-based *Clostridium difficile* infection surveillance reveals high proportions of PCR ribotypes 027 and 176 in different areas of Poland, 2011 to 2013

H Pituch [1], P Obuch-Woszczatyński [1], D Lachowicz [1], D Wultańska [1], P Karpiński [1], G Młynarczyk [1], SM van Dorp [2], EJ Kuijper [2], the Polish Clostridium difficile Study Group [3]

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Pituch H, Obuch-Woszczatyński P, Lachowicz D, Wultańska D, Karpiński P, Młynarczyk G, van Dorp SM, Kuijper EJ, the Polish Clostridium difficile Study Group. Hospital-based Clostridium difficile infection surveillance reveals high proportions of PCR ribotypes 027 and 176 in different areas of Poland, 2011 to 2013. Euro Surveill. 2015;20(38):pii=30025. DOI: http://dx.doi.org/10.2807/1560-7917.ES.2015.20.38.30025

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Conflict of interest

None declared

Authors' contribution

Hanna Pituch designed and conducted the survey. Piotr Obuch- Woszczatyński, Dominika Lachowicz, Dorota Wultańska and Paweł Karpiński performed the laboratory investigations and data analyses Hanna Pituch and Grażyna Młynarczyk performed data analyses. Sofie van Dorp supported data analyses and interpretation of the data. Hanna Pituch and Ed Kuijper interpreted the data and wrote the manuscript. The Polish C. difficile Study Group, coordinated the study in the hospitals, enrolled patients, and collected epidemiological data.

Eurosurveillance

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Safety, tolerability, and immunogenicity of zoster vaccine in subjects on chronic/maintenance corticosteroids☆

Amy F. Russell[a,*], Janie Parrino[a,1], Chester L. Fisher Jr.[b], Wolfgang Spieler[c], Jon E. Stek[a], Kathleen E. Coll[a,2], Shu-Chih Su[a], Jin Xu[a], Xiaoming Li[a,3], Katia Schlienger[a,4], Jeffrey L. Silber[a,5]

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This study was supported by Merck & Co., Inc. (sponsor). Although the sponsor formally reviewed a penultimate draft, the opinions expressed are those of the authorship and may not reflect those of the sponsor. All authors approved the final version of the manuscript.

Financial disclosure

Other than employees of Merck & Co., Inc. (as indicated on the title page), all authors have been investigators for the sponsor. Employees may hold stock and/or stock options in the company.

Author contributions

Fisher, Spieler: subject enrollment, data collection, data interpretation, and manuscript preparation.

Li, Schlienger, Silber: study concept/design, data analysis/interpretation, and manuscript preparation.

Parrino, Stek, Russell, Coll, Su, Xu: data analysis/interpretation, and manuscript preparation.

Study identification: V211-017

CLINICALTRIALS.GOV identifier: NCT00546819

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References

- List of sources cited
- Usually other journal articles
- Previous studies in same field
- References should be numbered consecutively in the order in which they are first mentioned in the text.
- Citation styles differ depending on
  - field of study
  - journal
- EndNote and RefWorks

Understanding Journal Article References

Authors (et al.)→ Title→ Journal → Volume Number → Issue Number → Page (doi)

doi: Digital Object Identifier è uno standard che consente l'identificazione duratura, all'interno di una rete digitale, di qualsiasi entità che sia oggetto di proprietà intellettuale e di associarvi i relativi dati di riferimento; si distingue dai comuni indicatori internet, come gli URL, in quanto identifica un oggetto direttamente e non semplicemente attraverso qualche suo attributo, come il luogo in cui l'oggetto è collocato.

Weiss PA. Does smoking marijuana contribute to the risk of developing lung cancer? *Clinical Journal of Oncology Nursing* 2008; 12(3): 517-519. doi: 10.1188/08.CJON.517-519

Babayan A et al. Heterogeneity of estrogen receptor expression in circulating tumor cells from metastatic breast cancer patients. *PLoS One* 2013;8(9):e75038. doi: 10.1371/journal.pone.0075038.

nature International weekly journal of science

Science AAAS

I.F. 41,456
Ranking 1/55
Multidisciplinary Sciences

I.F. 33,611
Ranking 2/55
Multidisciplinary Sciences

The formats differ markedly from the above outline.

The space limitations of the journals are severe:

Prose is highly compressed

There are no discrete section, except for a short abstract and a reference list.

Lightowlers RN et al. Mutations causing mitochondrial disease: What is new and what challenges remain? Science. 2015 Sep 25;349(6255):1494-9. doi: 10.1126/science.aac7516

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Wei K. et al., Epicardial FSTL1 reconstitution regenerates the adult mammalian heart. Nature 525 (September 2015) doi:10.1038/nature15372

Online Content Methods, along with any additional Extended Data display items and Source Data, are available in the online version of the paper; references unique to these sections appear only in the online paper.

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Supplementary Information is available in the online version of the paper.

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Author Contributions K.We. and W.C. performed experiments on EMCs and mESCs. K.We. generated mCMs^{ESC}, and performed cardiomyogenic and proliferation assays on mCMs^{ESC}, proliferation assays on NRVC. K.We. and W.Z. performed mass spectrometry experiments. M.D.-C. performed immunostaining of Fstl1. K.We. and A.S. performed calcium transient experiment. V.S. generated cardiac patch. V.S., A.W., and M.J.B. performed biomechanical analysis of cardiac patch biomaterial. M.Z. and V.S. performed mouse MI experiments and echocardiography. Y.M. and P.C.Y. performed MRI analysis. K.We. and W.C. performed immunostaining of α-actinin, pH3 and aurora B. K.We. performed GFP, TUNEL and f4/80 staining. K.We. and P.B. performed analysis of high throughput imaging results. M.Mh. analysed the release of Fstl1 from the patch *in vitro*. V.S. and G.F. performed assays of adult mouse cardiomyocytes. K.Wa., K.N. and S.M. performed experiments with Fstl1-TG mice. B.Z. performed experiments with adult mouse epicardium-conditioned media. X.T., Q.L. and B.Z. performed *Wt1*^{CreERT2} lineage tracing studies and experiments with adult mouse epicardium conditioned medium. K.Wa. and S.M. provided data on systemic delivery of FSTL1. M.N. and M.D.S. provided data on myocyte progenitors. M.J.B. supervised AFM studies. D.B. supervised and coordinated *in vivo* mouse physiology experiments. V.S., Y.M., and P.C.Y. conducted the preclinical swine study. C.H. performed FSTL1 overexpression and western blot experiments. K.We., V.S., M.Me. and P.R.-L. designed experiments and prepared the manuscript. M.J.B.v.d.H. provided materials.

Author Information Reprints and permissions information is available at www.nature.com/reprints. The authors declare no competing financial interests. Readers are welcome to comment on the online version of the paper. Correspondence and requests for materials should be addressed to P.R.-L. (prlozano@stanford.edu).

Variations on organization of a paper

- In most scientific journals the above format is followed.
- Occasionally Results and Discussion are combined → Data need extensive discussion to allow the reader to follow the logic developed in the course of the research.
- Materials and Methods follows Discussion.
- Summary is given at the end of the paper.

In many papers, not all experimental data are shown, but they are referred to as:

- **"data not shown"→ the practice is accepted when the authors have documented their competence to do the experiments properly in previous paper**
- **"unpublished data"→ data are not of publishable quality or work is part of a larger one that will be published in the future**
- **"preliminary data"→ the experiment was done only once**
- **papers accepted but not yet published should be designated as "in press" or "forthcoming"**

How to read a paper

Generally, you first read the Abstract in order to understand the major points of the work.

One extremely useful habit in reading a paper is to read the Title and the Abstract and, before going on, review in your mind what you know about the topic.

The logical flow of most papers goes straight from the Introduction to Results → the paper should be read in that way as well, skipping Materials and Methods and referring back to this section as needed to clarify what was actually done.

A reader familiar with the field who is interested in a particular point given in the Abstract often skips directly to the relevant section of the Results, and from there to the Discussion for interpretation of the findings.

Evaluation of the paper

- What are the main conclusion of the paper?
- What evidence supports those conclusions?
- Do the data actually support the conclusions? → The logical connection between the data and the interpretation is not sound.

  There might be other interpretation that might be consistent with the data.

  What is the quality of that evidence?
- Do authors cite their own publications needlessly?
- Do authors use recent references (within the last 2 or 3 years) so that their analysis is up to date?

When trashing an article

1.The study does not address issues scientifically relevant
2. The study is not original (it has already been extensively carried out using the same methods and follows them on similar samples of subjects)
3. The study does not work on the assumptions listed by the authors
4. The authors used important methodological compromises in order to compensate technical difficulties
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- Once you believe everything is correct, give the draft to a native English speaker reviewer.

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The following is an example of a covering letter to accompany an article submitted to a journal:

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Please find enclosed a copy of our manuscript entitled "……..", which we hereby submit for publication in [name of the journal].

The paper considered……

The manuscript has not been previously published, it has not been accepted for publication elsewhere and is not under consideration (as whole or partly) elsewhere.

I look forward to hearing from you.

Yours sincerely

……..

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We hope this revised version will now be judged ready for publication in [name of the journal].

Yours sincerely

……..