Clinical Therapeutics provides peer-reviewed, rapid publication of recent developments in drug and other therapies as well as in diagnostics, pharmacoeconomics, health policy, treatment outcomes, and innovations in drug and biologics research. In addition, Clinical Therapeutics features updates on specific topics collated by expert Topic Editors. Clinical Therapeutics is read by a large international audience of scientists and clinicians in a variety of research, academic, and clinical practice settings. Articles are indexed by all major biomedical abstracting databases.

Published articles range from pivotal studies exploring new chemical entities in large, multicenter trials to those exploring repurposing of marketed agents. Additionally, pilot studies; reports that assess drug safety and tolerability in all phases of development; new routes of administration and new formulations; pharmacokinetic, bio-availability, and biosimilarity; and changes in practice guidelines and standards, are all of interest for publication. Clinical Therapeutics also understands the importance of strengthening the body of evidence surrounding particular agents through the publication of replication studies, negative trials, and failed trials.

Beyond the clinic, we seek reports that examine the real-world implications of therapeutics such as comparative effectiveness and pharmacoeconomics studies as well as work that has implications for health policy. Commentaries, which include perspectives and contemporary issues, are sought to offer a balance of viewpoints and scholarly opinion on a broad array of drug-related topics. Case reports, which remain a vital part of our mission, offer clinically valuable lessons. All manuscripts are peer reviewed by independent clinicians or scientists for clinical relevance, technical accuracy, methodological rigor, clarity, and objectivity using a blind review process.

In addition to feature articles published monthly, each issue of Clinical Therapeutics features a specific theme section dedicated to an annual update of a specific topic area. A special guest editor will comprise each update with reviews, commentaries, and original research highlighting what's new or controversial in the topical specialty. Authors are invited to submit manuscripts for consideration in the topic updates, identifying submissions as such in their cover letters. Submissions not selected for the updates will be considered for general publication. Submit your manuscript at https://www.editorialmanager.com/clinther.
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Introduction

Clinical Therapeutics provides peer-reviewed, rapid publication of recent developments in drug and other therapies as well as in diagnostics, pharmacoconomics, health policy, treatment outcomes, and innovations in drug and biologics research. In addition Clinical Therapeutics features updates on specific topics collated by expert Topic Editors. Clinical Therapeutics is read by a large international audience of scientists and clinicians in a variety of research, academic, and clinical practice settings. Articles are indexed by all major biomedical abstracting databases.

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Submissions categorized as Original Research describe substantive, well-controlled clinical research projects including clinical trials, pharmacokinetic/pharmacodynamic studies, meta-analyses, observational studies, health economic evaluations, and epidemiologic studies. Manuscripts should be prepared as described (See PREPARATION AND FORMATTTING) and must provide enough detail about the study design, population, interventions, data collection and analysis methods, and outcomes to permit study replication. Data must be original and presented in accordance with journal policies (See EDITORIAL POLICIES) and EQUATOR Reporting Guidelines for the applicable study design (eg, CONSORT for randomized trials, STROBE for observational studies, CHEERS for economic evaluations, PRISMA for meta-analyses).

Abstract: ≤400 words, structured (See Abstract)
**Keywords**: 4-6 terms  
**Main Text**: ≤6000 words, structured as follows: Introduction, Participants and Methods, Results, Discussion, Conclusions  
**Tables/Figures**: ≤8  
**References**: Required, unlimited  
**Supplemental Material**: Allowed, unlimited length (See Supplemental Material)

**Reviews**

Comprehensive, evidence-based narrative and systematic reviews are welcome. Systematic reviews without meta-analyses are considered and published as Reviews, while systematic reviews with meta-analyses should be submitted as Original Research. For the Pharmacoeconomics, Outcomes, and Health Policy section, only systematic reviews will be considered. Authors should contact the editorial office to discuss the topic area to avoid duplication with previously submitted or accepted manuscripts.

**Systematic reviews** should critically assess available data on a specific topic relevant to clinical practice, disease prevention, diagnostics, therapeutics, or health policy. Systematic reviews should follow PRISMA guidelines (http://www.prismastatement.org/index.htm) and include a PRISMA-style flow diagram (as a Figure or Supplemental Material) and checklist for review. The Methods section should identify the databases that were searched, search terms used, and inclusion/exclusion criteria for identified articles; an assessment of the validity of reviewed studies; and a summary that includes future directions for studies in this area. Each study mentioned in the review should include the study design, a description of the study population (age range, disease/severity), the dose and duration of each treatment administered, and the data and P values to accompany any valid comparisons. While not required, prospective registration of systematic review protocols is strongly encouraged. If available, the protocol registration number, registry name, and URL should be indicated in the Methods. Systematic reviews should be identified as such in the title or subtitle.

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**Keywords**: 4-6 terms  
**Main Text**: ≤6000 words, structured as follows: Introduction, Methods, Results. Discussion, Conclusions  
**Tables/Figures**: ≤6  
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**Narrative reviews** should provide up-to-date information relevant to clinical practice, public health, or clinical-stage development of therapeutics and/or diagnostics. Narrative reviews should not focus solely on the authors' own work. Narrative reviews should include an Introduction that describes the background, purpose, and perspective of the article; a Methods section that describes the approach and literature search criteria (if any). A separate Results section is not required. Each study mentioned in the review should include the study design, a description of the study population (age range, disease/severity), the dose and duration of each treatment administered, and the data and P values to accompany any valid comparisons. Discussion of pre-clinical data is permitted to complement discussion of therapeutic/diagnostic strategies and their development. Narrative reviews must be identified as such in the Abstract and Methods.

**Abstract**: ≤400 words, structured (See Abstract)  
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**Main Text**: ≤6000 words, structured as follows: Introduction, Methods, Results (optional), Discussion, Conclusions  
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**References**: Required, unlimited  
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Abstract: ≤250 words, structured (See Abstract)
Keywords: 4-6 terms
Main Text: 2000-3000 words, structured as follows: Introduction, Methods, Discussion, Conclusions
Tables/Figures: ≤3
References: ≤30, required
Supplemental Material: Allowed, unlimited (See Supplemental Material)

**Pilot Studies**
A pilot study is a preliminary, exploratory, preparatory, small-sample effort undertaken to decide whether a larger study is warranted. The sample size is too small to permit generalizability, but it should provide a window into what a larger trial would look like. The submission should include a descriptive and succinct title, a structured Abstract, an Introduction that specifies the importance of the study, a Methods section, Results, a Discussion, a Conclusion, and references. Pilot Studies must adhere to the journal's ethical requirements and data reporting policies (See EDITORIAL POLICIES).

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Tables/Figures: ≤3
References: ≤30, required
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These letters are focused on previously published studies from which new findings have been generated. Since methods and other informative material are contained in the original paper, they can be referenced rather than repeated. Alternatively, research letters can describe novel or hypothesis-generating research that may stimulate further investigation or alert readers to clinically relevant but preliminary findings. These submissions should include a descriptive and succinct title; an Introduction that specifies the rationale for the report, beginning with a statement similar to "This communication provides..."; a description of any new methods and results; a Discussion/Conclusion section; and selected references. Please note that Research Letters may be chosen, at the editor's discretion, to be published online only. In such instances, authors will be informed of this decision at acceptance and are free to withdraw their submission. Online only articles are indexed and are available in full text or PDF formats identical to that of print articles.

Abstract: None
Keywords: 4-6
Main Text: 1000-2000 words, structured as follows: Introduction, Methods, Discussion, Conclusions
Tables/Figures: ≤2
References: ≤30, required
Supplemental Material: Not permitted

**Case Reports**
Case reports are retrospective analyses of one, two, or three clinical cases. Case reports are an important part of post-marketing surveillance. They serve an alerting function by informing about new, unusual, or unexpected events. These events may be adverse drug reactions, drug-drug interactions, or drug-disease interactions. Before submitting a case report, the author(s) must conduct a thorough literature search as well as a review of product labeling when a drug is involved. This will reduce the reporting of what may already be well known.
Reports of suspected adverse drug reactions should provide a description of the event, details regarding the implicated medication (e.g., purpose, when initiated), effects of discontinuation or re-challenge, treatment for the reaction, and duration of patient follow-up, if any. Evidence for causality must be strong. In the case of adverse drug events, use of the Naranjo Adverse Drug Reaction probability scale to determine the likelihood that the events were drug-related (Naranjo CA, et al. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther 1981;30:239-245) is recommended. The manufacturer of the drug in question should be notified regarding any event before publication.

Importantly, authors should clearly indicate in the cover letter whether the case was part of a larger study or meta-analysis, and whether the case was reported in aggregate elsewhere.

The report should include a descriptive, succinct title; an introduction; a well-documented case description; discussion; conclusions; and references. The Introduction should announce the subject and purpose of the report, including statements of why the case is important and how the literature search was performed. The Case Description should include a narrative account of the case with brief, pertinent clinical, laboratory, and medication information. The Discussion should comment on evidence that the case is new or unusual and consider possible alternative explanations for case features. The Conclusions should provide a summary of the adverse drug reaction-medication relationship, how to treat it, and how to avoid it. (For more information about what constitutes a good case report, see Vandenbroucke JP. In defense of case reports and case series. Ann Intern Med. 2001;134:330-334 and DeBakey L, DeBakey S. The case report. I. Guidelines for preparation. Int J Cardiol. 1983;4:357-364.)

To be considered, authors must provide documentation of patient informed consent to publish, which can be attached to the cover letter. All identifying information must be masked per HIPAA guidelines prior to submission. (See Ethical Considerations for Case Reports).

Please note that Case Reports may be selected, at the editor's discretion, to be published online only. Additionally, authors may be asked to reduce the length of the report substantially if similar cases were reported previously. In such cases, authors will be informed of the decision to forgo print at acceptance. Online only articles will be indexed and available as full text or PDF, identical to that of print articles.

Abstract: None
Keywords: 4-6
Main Text: 1500-3500 words, structured as follows: Introduction, Case Description, Discussion, Conclusions
Tables/Figures: ≤2
References: ≤15, required
Supplemental Material: Not permitted

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These are objective, constructive, or educational critiques of papers published in Clinical Therapeutics. Accepted letters will be sent to the author of the original paper for a response. Each letter and response is published together. Alternatively, letters may focus on topical issues that are of interest to readers of

Abstract: None
Keywords: None
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Supplemental Material: Not permitted

Video Articles
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Although a graphical abstract is optional, its use is encouraged as it draws more attention to the online article. The graphical abstract should summarize the contents of the article in a concise, pictorial form designed to capture the attention of a wide readership. Graphical abstracts should be submitted as a separate file in the online submission system. Image size: Please provide an image with a minimum of 531 × 1328 pixels (h × w) or proportionally more. The image should be readable at a size of 5 × 13 cm using a regular screen resolution of 96 dpi. Preferred file types: TIFF, EPS, PDF or MS Office files. You can view **Example Graphical Abstracts** on our information site.

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**Title**

The title should be concise, informative, and focused on the study objective. Statements about the conclusion(s) of the work should be avoided. Randomized controlled trials, meta-analyses, and systematic reviews should be identified as such in the title. Subtitles can be used to provide supplementary information (eg, study design); however, titles should be able to stand alone. Use nonproprietary drug names (See Names of Drugs and Devices); avoid abbreviations and formulae where possible.
Abstract
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Structured abstracts are required for Original Research (≤400 words), Reviews (≤400 words), Brief Reports (≤250 words), and Pilot Studies (≤250 words). Structured abstracts should contain sufficient detail as directed by the extension to the CONSORT statement for abstracts, and should be formatted as follows:

**Purpose:** Briefly provides the frame of reference for the reader and identifies the knowledge gap that the article seeks to address; clearly states the purpose of the research; and identifies the scientific hypotheses and questions being asked.

**Methods:** Succinctly describes study methodology, including study design, study dates, setting/data sources, inclusion and exclusion criteria, interventions, outcomes, statistical approaches, and adverse event assessment methodology.

**Findings:** Provides demographics of the study population, including sex, age range, and numbers of participants in each group; reports principle data and outcomes in a quantitative fashion, including effect sizes and confidence intervals or P values; includes adverse events.

**Implications:** Covers any limitations or problems in interpretation or generalization from the study findings as well as implication and future directions; must be strictly limited to what can be supported directly by the Findings, and what was identified in the Purpose section.

For manuscripts that require clinical trial registration (See Reporting and Registration of Clinical Trials), the name of the trial registry, trial registration number, and URL of the registry should be included immediately following the Implications section of the abstract.

Unstructured abstracts are required for Commentaries (?300 words). Unstructured abstracts should briefly describe the importance and clinical relevance of the topic, the objective, approach, and a summary of key points. Abstracts are not required for Research Letters, Case Reports, and Letters to the Editor.

Keywords
Immediately after the abstract, provide 4-6 keywords, using American spelling and avoiding general and plural terms and multiple concepts (avoid, for example, 'and', 'of'). Be sparing with abbreviations: only abbreviations firmly established in the field may be eligible. These keywords will be used for indexing purposes.

Body of Manuscript
The main text should adhere to word limits and structure according to article type as detailed above. All submissions should adhere to journal policies (See EDITORIAL POLICIES) and EQUATOR Reporting Guidelines for the applicable study design (e.g., CONSORT for randomized trials, STROBE for observational studies, CHEERS for economic evaluations, PRISMA for systematic reviews and meta-analyses).

Introduction: State the objectives/hypotheses of the work and provide an adequate background; avoid a detailed literature survey or a summary of the results. Required for all article types except Letters to the Editor.

Methods: Provide sufficient detail to allow the work to be replicated by others. Methods already published should be indicated by a reference: only relevant modifications should be described. For work involving human subjects, describe the (1) study design and randomization procedures; (2) study dates and setting; (3) institutional review board (RB) approval or waiver, including name of the IRB/ethics committee; (4) details of patient consent or assent of youth and children; (5) participants and conditions/factors studied, including full inclusion and exclusion criteria; (6) interventions, if any, with full description of placebo, sham, or control conditions [See Placebos in Clinical Trials]; (7) primary and secondary outcome measures, including whether secondary analyses were pre-specified; (8) detailed statistical analyses, with a priori significance thresholds, methods for handling missing data or outliers if applicable, and any relevant citations. Rationale for inclusion of only one sex or age group should be provided and scientifically justified [See Inclusion of Sex and Gender]. Systematic
reviews and meta-analyses should follow PRISMA guidelines. Subheadings (up to two additional levels) are encouraged. A Participants and Methods section is required for Original Research, Brief Reports, Pilot Studies, and Research Letters. A Methods section is required for Reviews.

**Results:** The Results should be clear, concise, and relevant to the stated objectives/hypotheses. Describe the study population first, including sex, age, and other relevant demographic characteristics of subjects. All numeric data should be reported with descriptive and/or inferential statistical test results (including exact p-values, if available). For each outcome, report results for each group, the effect size, and its precision (ie, 95% confidence interval). Do not discuss implications or limitations in this section. Tables, figures, and subheadings (up to two additional levels) are encouraged. Results are required for Original Research (including meta-analyses), systematic Reviews, Brief Reports, and Pilot Studies; optional for narrative Reviews.

**Discussion:** The Discussion should explore the importance and relevance of the results of the work, not repeat them. Authors should critically examine the work, describe unexpected and/or contradictory findings, and address any limitations of the study design or statistically indeterminate results here. All inferences must be supported by evidence presented in the Results section. Authors should also discuss generalizability and clinical implications of findings, as well as any future studies needed. Avoid extensive citations and discussion of published literature. Subheadings (up to one additional level) are permitted. A Discussion is required for all article types except Letters to the Editor; a combined Results and Discussion section is often appropriate for narrative reviews.

**Conclusions:** The main conclusions of the study should be present

**Acknowledgments**

Collate acknowledgments in a separate section at the end of the article before the references and do not, therefore, include them on the title page, as a footnote to the title or otherwise. List here those individuals who provided materials or assistance during the research (eg, language help, writing assistance, or proofreading the article, etc). Do NOT list the names of authors or funder(s) in this paragraph.

**Disclosure of Funding Support**

All financial support for the submitted work must be reported in a separate section below the Acknowledgements. Authors should declare the role of study sponsors, if any, in the study design; in the collection, analysis and interpretation of data; in the writing of the manuscript; and in the decision to submit the manuscript for publication.

List funding sources in this standard way to facilitate compliance to funder's requirements:

Funding: This work was supported by the National Institutes of Health [grant numbers xxxx, yyyy]; the Bill & Melinda Gates Foundation, Seattle, WA [grant number zzzz]; and the United States Institutes of Peace [grant number aaaa].

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References should include only published works or articles in press. Citation of a reference as 'in press' implies that the item has been accepted for publication and a DOI number must be included. Abstracts, unpublished data, and personal communications are not permitted in the reference list. Unpublished results and data published in abstract form may be mentioned in the text only if the methodological details and data are made available in supplemental digital content. Research datasets that have been assigned a global persistent identifier number are permitted.

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Number tables consecutively in accordance with their appearance in the text. Each table should have a concise and descriptive caption. Place footnotes to tables below the table body and indicate them with superscript lowercase letters. Avoid vertical rules. Be sparing in the use of tables and ensure that the data presented in tables do not duplicate results described elsewhere in the article. Submit each table as a separate file in its original file format.

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Figures should be numbered consecutively in accordance with their appearance in the text and uploaded as individual high-resolution files. Brief Figure Captions are required and should be supplied separately above the References section in the manuscript file (See Figure Captions). Authors are urged to consult the detailed guide on electronic artwork and adhere to the following:

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STYLE
Manuscripts submitted to Clinical Therapeutics should be prepared in accordance with AMA Style unless otherwise noted. See American Medical Association Manual of Style: A Guide for Authors and Editors, 10th Edition.

Abbreviations
Define abbreviations that are not standard in this field in a footnote to be placed on the first page of the article. Such abbreviations that are unavoidable in the abstract must be defined at their first mention there, as well as in the footnote. Ensure consistency of abbreviations throughout the article.

Names of Drugs and Devices
Drugs should be referred to by their universally accepted generic names, not by proprietary names, unless the specific trade name is essential to the methods or discussion. In such cases, use the proprietary name once and the generic or descriptive name thereafter. US adopted names (USANs)
are acceptable. If unnamed compounds are referred to, as much information as possible (eg, class of compound) should be included and published references to the compound should be provided. If this is not possible because of intellectual property reasons, then this should be stated.

For drug-device combinations, capitalize the first letter of each term. At first mention in the abstract and in the main text, include the active ingredient and dose in parentheses following the product name.

Where proprietary names of drugs and drug-device combinations are used as permitted above, capitalize only the initial letter of the trademarked word (unless the trademarked name is an abbreviation) and do not include trademark symbols.

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Follow internationally accepted rules and conventions: use the international system of units (SI). If other units are mentioned, please give their equivalent in SI.

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Clinical Therapeutics endeavors to make all manuscripts readily understandable by using universally accepted chemical names, structures, spelling, abbreviations, and formatting. For Pharmacoeconomics submissions, results are sometimes reported in the currency of the author(s)'s country. The relative value of currencies from some countries may not be obvious to some readers. Therefore, we now require that equivalencies in US dollars (USD) and European Union euros (EUR) be added in parentheses after other currencies. For example, 68 Indian rupees or INRs would be followed by ($1.00 USD/0.85 EUR). We recognize that currency values fluctuate. Therefore, equivalencies should reflect values at the time of submission.

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Please write your text in standard, grammatically correct English. If English is not your first language, authors are encouraged to consult with a colleague or professional whose native language is English to improve grammar and syntax prior to submission. Alternatively, authors may wish to visit Elsevier's language editing and copyediting services which are available both pre- and post-submission at: http://webshop.elsevier.com/languagediting or our customer support site at https://service.elsevier.com for more information. Articles that are not cogent and clearly written will be returned to the author.

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Inclusive language acknowledges diversity, conveys respect to all people, is sensitive to differences, and promotes equal opportunities. Articles should make no assumptions about the beliefs or commitments of any reader, should contain nothing which might imply that one individual is superior to another on the grounds of race, sex, culture or any other characteristic, and should use inclusive language throughout. Authors should ensure that writing is free from bias, for instance by using 'he or she', 'his/her' instead of 'he' or 'his', and by making use of job titles that are free of stereotyping (e.g. 'chairperson' instead of 'chairman' and 'flight attendant' instead of 'stewardess').

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The term sex should be used when describing biological factors and the term gender should be used when referring to sociocultural factors.

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Footnotes should be used sparingly. Number them consecutively throughout the article. Many word processors can build footnotes into the text, and this feature may be used. Otherwise, please indicate the position of footnotes in the text and list the footnotes themselves separately at the end of the article. Do not include footnotes in the Reference list.

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For information on Ethics in publishing and Ethical guidelines for journal publication see https://www.elsevier.com/publishingethics and https://www.elsevier.com/journal-authors/ethics.

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summarizes tips and "best practices" to increase awareness of editorial requirements, journal selection, submission processes, publication ethics, peer review, and effective communication with editors.

**Authorship**
All authors should have made substantial contributions to all of the following: (1) the conception and design of the study, or acquisition of data, or analysis and interpretation of data, (2) drafting the article or revising it critically for important intellectual content, (3) final approval of the version to be submitted.

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All authors must disclose any financial and personal relationships with other people or organizations that could inappropriately influence (bias) their work. Examples of potential competing interests include employment, consultancies, stock ownership, honoraria, paid expert testimony, patent applications/registrations, and grants or other funding. Authors must disclose any interests in two places: 1. A summary declaration of interest statement in the title page file (if double-blind) or the manuscript file (if single-blind). If there are no interests to declare then please state this: 'Declarations of interest: none'. This summary statement will be ultimately published if the article is accepted. 2. Detailed disclosures as part of a separate Declaration of Interest form, which forms part of the journal's official records. It is important for potential interests to be declared in both places and that the information matches. More information.

Authors should declare the role of study sponsors, if any, in the study design; in the collection, analysis and interpretation of data; in the writing of the manuscript; and in the decision to submit the manuscript for publication.

**Submission Declaration and Verification**
Submission of an article implies that the work described has not been published previously (except in the form of an abstract, a published lecture or academic thesis, see 'Multiple, redundant or concurrent publication' for more information), that it is not under consideration for publication elsewhere, that its publication is approved by all authors and tacitly or explicitly by the responsible authorities where the work was carried out, and that, if accepted, it will not be published elsewhere in the same form, in
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The work described in your article must have been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans [https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/](https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/); EC Directive 86/609/EEC for animal experiments [http://ec.europa.eu/environment/chemicals/lab_animals/legislation_en.htm](http://ec.europa.eu/environment/chemicals/lab_animals/legislation_en.htm); Uniform Requirements for manuscripts submitted to Biomedical journals [http://www.icmje.org](http://www.icmje.org). This must be stated at an appropriate point in the article.

**Ethics Review of Studies Involving Human Subjects**

Pre- or post-marketing studies must undergo review by an institutional review board (IRB) or ethics committee. Patients must give written informed consent unless a waiver of consent is allowed by the IRB. Patients must be informed of any real or potential conflicts of interest, including compensation of the investigator and potential costs to the patient that may result from their participation in the study. The amount of the remuneration of the investigators for their participation in pre- or post-marketing studies must be approved by the IRB/ethics committee. If the design of a prospective pre- or post-marketing study calls for a treatment intervention such as a switch or withdrawal, then criteria must be established a priori for patient selection, the implementation of the intervention, and assessment of success/failure of such intervention. Such criteria must be scientifically justified, documented, uniformly applied and enforced, and clearly reported in the study report. Additionally, the patient or his/her insurance provider will not be required to pay for costs related to prospective interventions, such as those that may result from a drug switch or withdrawal.

All other studies that involve identifiable human subjects, including retrospective studies, chart reviews, post-marketing surveillance studies, or government mandated phase IV trials require IRB or ethics committee approval or waiver. In each case, detailed IRB or ethics committee information should be clearly stated in the Methods section.

Studies that only utilize pre-existing, de-identified (according to HIPAA standards) patient data are not required to seek IRB approval.

**Informed Consent and Patient Details**

Studies on patients or volunteers require ethics committee approval and informed consent, which should be documented in the paper. Appropriate consents, permissions and releases must be obtained where an author wishes to include case details or other personal information or images of patients and any other individuals in an Elsevier publication. Written consents must be retained by the author but copies should not be provided to the journal. Only if specifically requested by the journal in exceptional circumstances (for example if a legal issue arises) the author must provide copies of the consents or evidence that such consents have been obtained. For more information, please review the Elsevier Policy on the Use of Images or Personal Information of Patients or other Individuals. Unless you have written permission from the patient (or, where applicable, the next of kin), the personal details of any patient included in any part of the article and in any supplementary materials (including all illustrations and videos) must be removed before submission.

**Reporting and registration of clinical trials**

All randomized controlled trials submitted for publication should include a completed Consolidated Standards of Reporting Trials (CONSORT) flow diagram (as a Figure or Supplemental Material) and a completed CONSORT checklist for review. Please refer to the CONSORT statement website at [http://www.consort-statement.org](http://www.consort-statement.org) for more information.

This journal has adopted the proposal from the International Committee of Medical Journal Editors (ICMJE) which require, as a condition of consideration for publication of clinical trials, registration in a public trials registry such as [https://clinicaltrials.gov](https://clinicaltrials.gov), which can be used by all countries. In addition to a listing in [https://www.clinicaltrials.gov](https://www.clinicaltrials.gov), submitting authors should also include the identification number received from trials listed in [http://www.controlled-trials.com](http://www.controlled-trials.com), another registry recognized by the World Health Organization and the International Committee of Medical Journal Editors. The controlled-trials site provides listings to trials at various stages -- complete, in process, proposed. Please note that requirements for registration may change so authors should always check that they
are consulting an up-to-date site. Trials must register at or before the onset of patient enrollment. The clinical trial registration number should be included at the end of the abstract of the article. For this purpose, a clinical trial is defined as any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects of health outcomes. Health-related interventions include any intervention used to modify a biomedical or health-related outcome (for example drugs, surgical procedures, devices, behavioral treatments, dietary interventions including vitamin or herbal supplements, and process-of-care changes). Health outcomes include any biomedical or health-related measures obtained in patients or participants, including pharmacokinetic measures and adverse events. Purely observational studies (those in which the assignment of the medical intervention is not at the discretion of the investigator) will not require registration. Further information can be found at http://www.icmje.org.

Studies that were initiated without registration can be registered retrospectively and will be considered for publication on a subjective basis.

**Placebos in Clinical Trials**

A full description of any placebo (PBO) or matched control used in a clinical trial must be given in the Methods section. It will no longer be sufficient to simply indicate that a PBO was used. This means that color; type (capsule or pill or liquid); contents (eg, lactose) including dyes; taste (if there is any); and packaging (eg, double-dummy) must be noted. For solid PBOs, shape must also be described, as well as whether the PBO is active or inactive. In addition, any efforts to study the success of matching should be included. For example, could subjects/patients or evaluating/rating clinicians guess assignments? Sham procedures must also be described in detail. We are instituting this change as part of our ongoing effort to facilitate replication of findings from trials. All too often this valuable information is omitted from published trial results. When appropriate these descriptions may be designated as Supplemental Digital Content. For more information, see Shader RI. Placebos, Active Placebos, and Clinical Trials. Clin Ther. 2017;39(3):451-454.

**Safety and Tolerability**

For submissions to *Clinical Therapeutics*, a statement about safety should explicitly include the time period and only when there is a clear absence of harm as determined by relevant questioning, observation, and testing. It is possible that a drug or biologic may be considered tolerable at the same time that tests show it to be unsafe (e.g., a lengthened QTc interval). Conversely, a drug may be considered safe by all objective assessments, and yet produce side effects that can contribute to high degrees of dose interruption or discontinuation. Furthermore, a drug may also be considered prima facie unsafe when pharmacogenomic information suggests it will yield unwanted metabolites in certain individuals or be highly prone to clinically significant drug interactions with frequently used additional agents or foods. Safety assessments may need to be different for different age groups (e.g., effects on growth and development in children and youth, increased propensity to falls in the elderly, effects on life style for active adults). It is also important to remember that safety concerns may stem from excipients added during the manufacturing process rather than from the drug or biologic per se.) For more information, see Shader RI. Safety Versus Tolerability. Clin Ther. 2018;40(5):672-673.

**Pharmacology, Pharmacokinetics, and Pharmacodynamics**

For submissions to the Pharmacology, Pharmacokinetics, and Pharmacodynamics section of *Clinical Therapeutics*, all manuscripts must include a complete description of the bioanalytic assay(s) and methodology utilized in the generation of the data presented. *It is not acceptable to simply state that a validated method was used.* Although the complete information included in a pure "Methods" paper is not necessary here, required items at minimum should include: type of instrumentation used, method of extraction, HPLC column and mobile phase, internal standard, type of detection used (e.g. ultraviolet), mass spectrometer settings, m/z monitored, and basic quality control information such as within- and between-day variability, and lower limits of sensitivity. Finally, if the assay(s) have been previously published, or are based upon a published method, appropriate citations must be provided.

*Clinical Therapeutics* does not accept articles dealing with bioequivalence between innovator and generic small molecules. *Clinical Therapeutics* will consider studies comparing innovator biologics to follow-on biologics, dose-escalation studies, studies that examine different formulations and/or routes of administration of the same drug, and studies that assess the influence of genetic variation on the ADME (absorption, distribution, metabolism, and excretion) processes. For more information, see Shader RI. Phase I Trials. Clin Ther. 2014;36(4):459 and Shader RI. More Thoughts on Phase I Trials. Clin Ther. 2014;36(8):1127-1128.
**Health Economic Evaluations**

To optimize the quality, consistency, and transparency of health economic and outcomes research reporting and dissemination, *Clinical Therapeutics* endorses the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement. Authors submitting economic evaluations of pharmacotherapies and other treatment interventions for publication should consult with the CHEERS statement and follow its 24-item checklist of recommendations. Please refer to the statement published in *Clinical Therapeutics* (http://dx.doi.org/10.1016/j.clinthera.2013.03.003; Husereau D, Drummond M, Petrout S, Carswell C, Moher D, Greenberg D, Augustovski F, Briggs AH, Mauskopf J, Loder E, CHEERS Task Force. Consolidated Health Economic Evaluation Reporting Standards (CHEERS) Statement. 2013;35:356-363) or the CHEERS statement website for more information. For this purpose, health economic evaluation is defined as the comparative analysis of alternative pharmaceutical and health interventions in terms of their costs and their consequences. All health economic evaluations assess costs, but approaches to measuring consequences of health interventions may differ and can be valued in terms of monetary units; natural units, such as life years gained or disability days avoided; and preference-based health measures, such as quality-adjusted life years or disability-adjusted life years.

**Ethical Considerations for Case Reports**

Because case reports place patient-specific information into the public domain, *Clinical Therapeutics* requires that authors obtain written consent to publish case details. Cases involving patients under 18 require assent by children and/or youth as well as written consent from a parent or guardian. In the United States, case reports must comply with the Health Insurance Portability and Accountability Act of 1996 (HIPPA) regulations. While some institutions exempt case reports that de-identify the patient completely, *Clinical Therapeutics* requires consent to publish even if the case details have been de-identified. Authors must:

- Provide **de-identified documentation** of patient or parental informed consent to publish, which can be attached to the cover letter. Indicate in the manuscript text that written consent has been obtained.

*Clinical Therapeutics* requires that the patient’s age and sex be correctly reported. *Clinical Therapeutics* does not allow inclusion of other information such as the patient’s name, initials, case number, or any other identifying material that could allow the patient to be recognized. Some institutions require potential case report authors to use consent forms developed by the institution.

Case reports cover past experiences and as such most institutions do not require review or approval by ethics committees or institutional review boards (IRBs). However, some institutions do require IRB approval when four or more cases are involved and their data are aggregated and analyzed. *Clinical Therapeutics* concurs with this requirement because when four or more patients are involved and analyzed such findings are best reported as a Brief Report or Pilot Study.

**Inclusion of Sex and Gender**

*Clinical Therapeutics* encourages authors to consider sex and gender as variables in biomedical research. Studies involving human subjects should include both males and females. If only one sex is included in the study design or results, the reason for exclusion of the other sex should be scientifically justified and explained in the Methods, except for investigations of conditions that affect only one sex. To facilitate future studies and meta-analyses, authors are encouraged to make sex-disaggregated data available in the article or supplemental material. Further statistical analysis of disaggregated data is not required and should be conducted only when sample size is sufficient.

**MULTIMEDIA AND ARTICLE ENRICHMENTS**

**Video Article Guidelines**

*Clinical Therapeutics* encourages authors who have presented a talk at a meeting to convert their talk into a video production for online publication. The video article may be submitted in one of two ways:

1. Slide set and scripted narration.
2. A full video presentation of the author discussing his/her manuscript.

**Slide Set Requirements:**

The slide set presentation will consist of:

- PowerPoint slides without audible narration.
- A separate manuscript consisting of the written narrative.

Both the slides and the script will be submitted for peer review. When finalized, each slide will have its own narrative.
At the time of revision, the author will make any required changes to the slides and accompanying written narrative. Once the revised slides and narrative have been found acceptable, the author will provide us with audible narration to accompany the presentation.

**Video Requirements:**

The formats for video will be accepted:
- MP4 (.mp4); QuickTime (.mov); MPEG-1 or MPEG-2 (.mpg).
- Each video must start with a slide listing the authors' conflicts of interest.
- Maximum length of videos is 4.5 minutes.
- Video file may not exceed 100 MB.
- Please ZIP the file and upload the zipped file to hasten the upload time.

**Video Abstract Guidelines**

*Clinical Therapeutics* offers authors a chance to submit a video abstract to accompany the online version of their article.

The following YouTube links explain

- Why Create a Video Abstract
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There are different approaches to presenting the information in your paper, and it is readily possible to impart to viewers the main take home message, the conceptual interest of the findings, and some supporting details in fewer than five minutes.

It is generally effective to use schematics, minimizing the amount of raw data/figure panels, to communicate your findings clearly, especially within the size of the flash player windows in which your video will appear. It is especially important not to have small text that won't be legible in the flash player (see below for more details on font size). While it may be tempting to primarily film slides presenting the figures in your paper with your voice explaining the data, the video is likely to be more engaging if you can mix up the presentation with both. Please see below for more specific information about video and file preparation.

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