RE: **Resignation in protest, Frontiers in Pharmacology Topic Editors, "Treating COVID-19 With Currently Available Drugs"**

To: Frontiers Chief Executive Editor, Manager | Frederick Fenter
Frontiers in Pharmacology, Respiratory Pharmacology Chief Editor, Prof. Paolo Montuschi
Frontiers Director of Publishing Operations | Judyta Sorokowska-Yammin
Frontiers Head of Research Integrity, London Office | Elena Vicario, PhD
Topic Authors

From: **Guest Editors:**

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Dear Dr. Fenter, Ms. Sorokowska-Yammin, Dr. Vicario, Prof. Montuschi, Topic Authors,

It is with sincere regret that we write at this time to resign from our roles as founding topic editors for the Frontiers in Pharmacology Research Topic "**Treating COVID-19 With Currently Available Drugs**". Since developing this topic and associated justification documents and

applying to and receiving permission to proceed with this special topic volume from “Frontiers in Pharmacology“ for publication under the “Frontiers in Pharmacology (Respiratory Pharmacology)” we have invested many hundreds of volunteer hours in soliciting manuscript submissions, identifying reviewers for submitted manuscripts, and managing the peer review process. We took this action not for any commercial gain, but rather to address an unmet need. This has been done in full and careful compliance with all “Frontiers” criteria, and with approval by “Frontiers”.

The Topic had been created with the aim to contribute to identification of better and more effective pharmacological treatments during the COVID-19 pandemic by suggesting repurposed drugs. Our goal has been to reduce the barriers to publishing earlier stage clinical research regarding repurposed drugs, and in this way help reduce the terrible burden of global death due to COVID-19. While awaiting development of herd immunity (during vaccination), we wanted to contribute in COVID-19 therapy. In proposing the guest topic, we noted that Frontiers purports to provide rapid review, and explicitly allows publication of earlier stage clinical research findings including case series reports. CVs of each guest editor and the Topic proposal were accepted after evaluation and Mr. Nathan Watkins was assigned by the Frontiers organization to support the guest editors.

The recent extraordinary and unprecedented actions by Frontiers in the rejection of the review manuscript “REVIEW OF THE EMERGING EVIDENCE DEMONSTRATING THE EFFICACY OF IVERMECTIN IN THE PROPHYLAXIS AND TREATMENT OF COVID-19” and the original research manuscript “HOSPITALIZED COVID-19 PATIENTS TREATED WITH CELECOXIB AND HIGH DOSE FAMOTIDINE ADJUVANT THERAPY SHOW SIGNIFICANT CLINICAL RESPONSES” after review and acceptance of each manuscript by four/five well qualified peer reviewers (during final validation) is what has prompted our collective resignation.

To place this into context of the Frontiers review process, the papers have been rejected during the final validation phase, having previously passed the evaluation (peer review) phase. In general, the Frontiers review process consists of the following steps: initial validation, editorial assignment, independent review, interactive review, review finalized (acceptance/rejection), final validation (this last step is the final editorial review decision prior to invoicing and finalizing manuscript proofs before actual publication). The **initial validation** step performed by Frontiers is independent of the Guest Editors’ evaluation and is performed prior to **editorial assignment to Guest Editors**. Guest Editors are then asked to look for reviewers for **independent review** and **manage interactive review**. **Review is finalized** by guest Editors but the final validation depends on Frontiers decision.

Since approval of the special topic, Mr. Watkins stopped communicating with the guest editors. After some time and multiple inquiries, we were told that he had left Frontiers, and that no replacement had been assigned. Since Nathan Watkins disappeared, as Guest Editors, we have had to go “on strike” to receive an answer to emails sent or telephone messages left for requests of information. After a couple of weeks we finally had the possibility to interact with

Frontiers Chief Executive Editor (Manager) Dr. Frederick Fenter (and subsequently with Judyta Sorokowska-Yammin).

After Dr. Fenter unilaterally rejected the ivermectin review manuscript after it has completed peer review, all of the pending manuscripts associated with the special topic were placed on hold with executive "quality" review. Most were eventually released and allowed to proceed through the review and publication process. In the case of the celecoxib and high dose famotidine case series (which had also completed peer review), the hold was continued and then the manuscript unilaterally rejected by the specialty editor for the Respiratory section of Frontiers in Pharmacology (Prof. Paolo Montuschi). The authors appealed this unilateral rejection. Since Dr. Fenter perceived an abnormal evaluation process, he agreed with us to reactivate the review of the manuscript (11/03/2021) and tried his best to interact with guest editors to find a final positive conclusion. After different calls, additional review by external reviewers (added to the previous ones), and determination that the rationale for rejection by Prof. Montuschi was without merit, we were informed that the specialty Chief Editor had again insisted that the paper not be published. Frontiers senior management then informed us that to have the paper published we had to submit it in another section of Frontiers Journal (maintaining all the reviewers positive evaluation). Finally, in another Frontiers section, the paper could be accepted. This is inconceivable! We believe in our scientific integrity, and would like to protect scientific integrity of each authors who submitted (or are submitting) their papers. This process described above took nearly 5 months (and was stopped in the "review finalized" stage for nearly 2 months!). At this point, we decided to close the topic if any solution was not found before 16/04/2021 (another ultimatum we had to apply to receive an answer) to have the paper published in the topic. On 15/04/2021 the paper has been formally rejected .
Dr. Fenter formally evidenced that the paper could only be published in another section of the journal indicating that for our topic the different Frontiers' policies are applied and ethical science is not respected. Soon after (16/04/2021), Dr. Fenter informed Prof. Maria Cristina Albertini (part of the Review Editor board in the section "Experimental Pharmacology and Drug Discovery ") that the "term as Review Editor in the section Experimental Pharmacology and Drug Discovery will end on May 16, in accordance with our Terms and Conditions" **since it has become apparent that we do not agree on editorial procedures and need for quality control for published articles, accordingly to Frontiers' policies.** Prof. Maria Cristina Albertini never had problems with editorial procedures in "Experimental Pharmacology and Drug Discovery " section.

Are Frontiers policies applied differently in the different sections? Why could the paper be published in a section different from "Respiratory pharmacology"?

To provide additional detail, in the instance of the second rejection of the original manuscript, after three months in peer review, and again gaining acceptance by four well qualified peer reviewers, the journal elected to Prof. Paolo Montuschi (Specialty Chief Editor, Frontiers). The review of that special reviewer was final; not subject to appeal or response by the authors.

The rationale provided for rejection was stated as follows:

> "The manuscript could not be sufficiently revised by the authors to address the concerns raised by the reviewers or editor during the review process.
> This manuscript deals with very preliminary clinical data, it is essentially a case series report, yet it is presented as original research. The patients in this case series all received vitamin C and zinc which is not the standard of care, therefore we are unable to untangle any effect of famotidine and celecoxib from that of vitamin C and zinc. The paper then goes on to suggest that famotidine and celecoxib are beneficial in COVID-19, given the fact that patients were taking vitamin C and zinc, plus the lack of controls, such generalized statements have no place in this article. Therefore we must proceed to reject this manuscript. We do not exclude that celecoxib or famotidine or both can be efficacious in COVID-19 treatment, but the present study do not provide sufficient evidence for that."

The journal elected to implement an ad-hoc and arbitrary final "super review" by a reviewer with no specialty experience or training relevant to the manuscript scope. In this case, the assertions were demonstrably false or incorrect. 1) Each of the four peer reviewers accepted the manuscript for publication. The independent journal appointed editor Giuseppa Pistritto never corresponded with the authors in any form about any topic. 2) The manuscript was clearly and explicitly described as a case series, and this clinical evaluation (case series) is explicitly allowed for publication both as a general category for this journal and in this special topic volume. 3) Administration of Vitamin C and Zinc are, in fact, standard of care in many US hospitals for treatment of COVID-19, and specifically is standard of care at Beloit Memorial Hospital where this case series arises. 4) Regarding controls, this manuscript describes a retrospective case series. Case series do not include internal controls. Reference laboratory bioassays widely accepted and previously published which correlate with typical outcomes were explicitly provided for all patients in this case series. 5) The principal conclusion was not as the reviewer states, but rather that these data provide justification for initiation of randomized clinical trials to assess this combination of agents – which trials are either currently enrolling or have been funded and are in late stage planning. We note that the language used in the rejection rationale provided by Prof. Paolo Montuschi to Drs. Tomera, Malone and Kiddah mirrors that of the rejection letter provided to Dr. Kory and colleagues, which appears to suggest that Prof. Montuschi was adapting and paraphraising language provided to him by the journal for a pre-planned rejection rationale.

In a final chapter of this unfortunate history, Prof. Albertini and Sestili were able to obtain agreement with Frontiers leadership for a final Zoom meeting to discuss what has taken place and seek some sort of mutually agreeable accommodation which might salvage the situation. This final Zoom meeting took place on April 19 between Prof. Albertini, Dr. Fenter, Dr. Johnson Prof. Sestili and Dr. Sorokowska in which we unsuccessfully tried to find a solution. Prof. Sestili wrote to Prof. Montuschi (after he had been invited many times by us to discuss the above problems) communicating that the Guest Editors were nearly to resign and again - but this time as a simple colleague - asked for an explanation of the entire story. As Italian citizens, both Prof. Albertini and Sestili are embarrassed by the enduring silence and avoidance of confrontation of Prof. Montuschi. The Guest Editors suggest that this repeated very unpolite behavior calls into

question the scientific authoritativeness, impartiality and credibility of Dr. Montuschi as the lead editor for the respiratory branch of Frontiers in Pharmacology, and consequently that of the Frontiers organization.

Upon reviewing these events, some might conclude that the journal is practicing extraordinary and unprecedented censorship of fully peer reviewed manuscripts. The rationale for doing so is speculative, and the journal has communicated that these actions are justified by the following considerations:

1) "The papers considered for publication in this Research Topic will require more specific oversight, as the subject and aim of the collection has an important involvement with the ongoing public health crisis. Frontiers aims for editorial independence while also being ultimately responsible for all article publications. We need to anticipate potential impact on the population and maintain standards of rigour for our Journals and the scientific record overall."
2) "Moving forward, the Editorial Office will continue to monitor submissions to this topic. Articles will be screened at submission, with the support of our Specialty Chief Editor, to ensure that all articles submitted are valid, and fulfil our acceptance criteria. We ask that, as you continue to act as Handling Editors for articles, you remain vigilant and ensure that any serious recommendations for rejection are addressed swiftly. These steps, combined with increased awareness and participation from all parties involved, will help ensure the recent situation around the ivermectin paper is not repeated. We hope that you understand the rationale behind these additional measures, which are in place in the interest of maintaining scientific integrity, both for your collection, and Frontiers in Pharmacology as a journal."

The Guest editors reject any assertion that scientific integrity was compromised or breached during the review process for either of these submissions, or that this special edition has not been managed with full integrity, except in the case of the unethical breach of the journal itself and its senior management in performing an extraordinary, arbitrary and capricious post-peer review process.

At this point, based on these many actions, we are unable to assure scientific integrity of the peer review process on the part of the journal for this special topic. Our time and that of the peer reviewers has been donated to the journal, and our reputations used without compensation. We ask to be removed from association with this special topic area, that an apology be issued to ourselves and our respective institutions for the actions of the journal in this matter, and that the special topic (which we had developed with full approval by the journal) be discontinued effective immediately. Having communicated to Frontiers that this would be our collective action if corrections were not made to this extraordinary re-review process, Frontiers has elected to expel each of the guest editors from any ongoing or future role as editors, and to close down and wipe all electronic evidence that the special topic had ever even been approved or had manuscripts submitted under the topic approved. This decision was disclosed in email communications with all corresponding authors of published, approved,

or pending manuscripts, but not with the guest editors who had created the topic and solicited and managed review of the manuscripts.

The scientific process requires fair, open, and transparent peer review to proceed effectively and efficiently – particularly at this time and for this topic. The actions of "Frontiers" in this matter clearly violate well established norms and processes for peer review and publication of scientific works and intellectual contributions, and instead have substituted a unilateral, arbitrary, and capricious process. On behalf of our peers, our institutions, and our scientific and medical colleagues we cannot allow this precedent to remain unchallenged. In our opinion, these unfortunate events constitute gross editorial misconduct by "Frontiers".

Best regards,

Prof. Maria Cristina Albertini

Prof. Piero Sestili

Dr. Robert Malone, MD, MS

Dr. Howard Haimes, PhD.