



May 06, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: ESPS Manuscript N 10364-edited.doc).

**Title:** An update on pythiosis immunobiology and immunotherapy

**Author:** Érico S. Loreto, Juliana S. M. Tondolo, Régis A. Zanette, Sydney H. Alves, Janio M. Santurio

**Name of Journal:** *World Journal of Immunology*

**ESPS Manuscript NO:** 10364

The manuscript has been improved according to the suggestions of reviewers:

**Reviewed by 02909950**

(1) -some journals in reference are not necessary to show doi:...../..... because it published ( not in on line ) -reference no.18 You write "DOI" but other "doi" was written

*Thank you. Reference n° 18 was updated. DOI and PMID were added to the reference list according to the guide to authors of the World Journal of Immunology.*

**Reviewed by 02851161**

Comments to the suggestions from the attached file (ESPS10364.pdf and MAN\_ESPS\_10364.pdf)

*We agree with all the suggestions. The changes were highlighted in the text. Thank you very much.*

**Reviewed by 02446789**

(1) The manuscript entitled " An update on pythiosis immunobiology and immunotherapy" is an interesting manuscript. This is well written and concise with updates on recent studies in an area of the diagnosis and treatment of pythiosis. I recommend that this manuscript should be accepted for the publication in the World Journal of Immunology.

*Thank you for your review and considerations.*

**Reviewed by 02903408**

1. The author used almost 1/4 of paper to explain the epidemiology and immunobiology of pythiosis. It's good for readers understand the background of origin, infection and pathogenesis of *P. insidiosum*, however, there are only collected a lot of information from amount of papers without reprocessing.

2. There are some new cases which should but not included in this review, like pythiosis in two dogs from Wisconsin, USA by Oldenhoff W, et al. Which is not match the word update in the title.

3. This paper mean to provide an update about the immunotherapy, however, only 1/4 of manuscript involved in immunotherapy. All the clinical treatment cases are animals with very less clinical index. The paper now is not too much value used for example of clinical treatment of human, less information of Immunological indicators and treatment cycle and therapeutic methods for human.

*Thank you for your considerations.*

*We removed the reference Oldenhoff, W et al. Vet Dermatol., Vol. 25, e21-52, 2014 from the review because the dog was lost to follow-up. Thus, there is no way to know the efficacy of treatment (chemotherapy and immunotherapy) performed.*

*The sections of the work have been organized to provide a better understanding of the immunobiology and*

*immunotherapy of pythiosis, through our experience. Importantly, immunotherapy is not an approved or available treatment for human pythiosis cases. When this occurs, it is used with the consent of the patient and as an alternative therapy after failure of surgery and/or chemotherapy treatments. Thus, it is understandable the lack of data on immunotherapy against pythiosis in humans.*

Thank you again for publishing our manuscript in the *World Journal of Immunology*.

Sincerely yours,

Janio M. Santurio, Dr.

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