

## Reviewer Template: IDM 2025: MPH Journal Club

### 1) Overview: what kind of article is this?

a. Research article – Longitudinal study, it measured infertility in infected male mice over time.

b. What were the major findings?

There was recorded male infertility that was determined to be caused by zika virus infection in seven of 20 total infected males. No infertility was shown in males that were in the mock group, or were vaccinated for zika.

### 2) Abstract

a. Does the abstract accurately summarize the article?

Yes, I believe the abstract accurately summarized the article to a degree. I actually prefer a sectioned abstract like presented in this article compared to a paragraph style abstract.

### 3) Introduction

a. Is the review of relevant literature prepared adequately and is it properly sourced? Yes, I believe the introduction adequately introduced relevant literature. Although some may believe the few sentences about vaccines was not needed, I believe having this bit of information will allow readers to not have to do background research of their own to understand the vaccine, and why it was used in this study.

b. Is the research question clear and does it respond to a gap in the literature? Although there is no clearly defined research question, this sentence seems to show what the authors were trying to understand with their research “In the current study, we sought to investigate ZIKV-induced fertility loss in male IFNAR  $-/-$  mice that developed viremia without clinical signs of disease”. Also, this article does seem to attempt to fill a gap in literature.

### 4) Methods

a. Is the sampling strategy reasonable and sound? Assumingly random mice were purchased from the model provider that fit the researchers needed criteria. Sampling seems reasonable if this assumption was met.

b. Is the statistical analytic plan rigorous and sound?

To me the data seems to have been tested rigorously enough to draw conclusions. It seems to me that the researchers performed two independent tests for fertility because of possible concern in sample size. This could have been corrected because of previous reviewer comments.

**Do the “authors” have a differing opinion why there were two tests performed? I personally think it was because of sample size of the first test. Also, the methods section does mention confirming the data by performing two tests.**

I have never heard of the Tukey's multiple comparison posttest, also, I have never used the Grubb's test for outliers. However, upon doing some background research it seems to my knowledge that these tests were sufficient. However, someone who has a stronger understanding of these tests could disagree.

## 5) Results

- a. Are the results presented clearly and comprehensively?

For the most part, yes, they were presented clearly. The tables and figures do well conveying the messages that the typed results section provides. It could get slightly confusing when trying to separate different groups, and on which days post infection there was a confirmed pregnancy. However, table 2 helped greatly with understanding all the needed information on the mating tests.

I also like that the authors chose to use unique colors AND shapes for each group, especially for marked line plots. Clear figures definitely go a long way in helping the reader understand the results.

- b. Do the results cohere to the research question?

Yes, the results do attempt to draw conclusions about zika infected INFAR +/- male mice and how it affects infertility. The tests performed and the data recorded is logical for what the research question is addressing.

- c. Do the results presented cohere to the Tables and Figures?

Yes, the results section and the tables and figures agreed with one another from what I see. I do wish that the second experiment reproduction table was published in the article, however I can understand that there may have been a lack of space for the table and supplementary figures would be sufficient. I do like that the authors still chose to write about the second experiment and reported results, then referred the reader to the supplementary figures if the table was absolutely needed.

- d. Are the Tables and Figures clear and precise? Do they respond to the research question?

I believe the tables and figures were clearly defined and easy to understand, and also responded to the research question.

**My biggest issue with the results that goes hand in hand with the methods pertains to the second experiment. The authors state that the second experiment was only performed to confirm fertility loss in the males. Why was the second experiment not extended to 75 days after infection to possibly confirm partial recovery of fertility in the infected males? This is a minor issue, and the authors did state that this data ONLY confirmed fertility loss, but I find it helpful to also confirm recovery and strengthen the first experiment's results.**

6) Discussion/conclusion

- a. Does this article add to the existing literature?

Yes, this article does add to existing literature on immunodeficient male mice with zika virus infections. Although the usefulness of this article for public health can be debated because of the highly specific non-human model, it still adds to existing literature.

- b. Do the discussion points appropriately contextualize the findings (do they speak to the data presented in the results)?

Yes, the authors were concerned with nonlethal zika infections and how it affected male infertility. The discussion sufficiently tied in previously discussed points in the introduction and then applied their results.

- c. Are the implications for public health presented beyond “future research is needed”?

No, this article does state that future research is needed to understand zika infection mechanisms and how it affects male infertility. However, I believe that this is acceptable because this article specifically only studies mouse infertility, not human. Not drawing conclusions to the possible effect on humans, and accepting that their article does not provide answers for humans infected with zika, is an intelligent move by the authors.

- d. What is the overall recommendation for this manuscript?

- i. Accept as is

**The biggest issue I found in the discussion was the disclosure that the authors cannot exclude the possibility that there was no mating. Although, it is unlikely that only the males in the Zika infected group did not mate. Is there a solution to this problem that can be fixed before “publishing” or do the authors believe that making that statement should be sufficient? (I personally believe that making that statement is sufficient, and that future research can be done if it becomes cause for concern with the science community)**

7) Class discussion/“authors” response

- a. What did the reviewers miss?  
b. Are the reviewers’ points valid?  
c. Do the reviewers’ overall recommendations cohere with their review comments?  
d. How would you respond to the reviewers’ points?