

Jury Member Report – Doctor of Philosophy thesis.

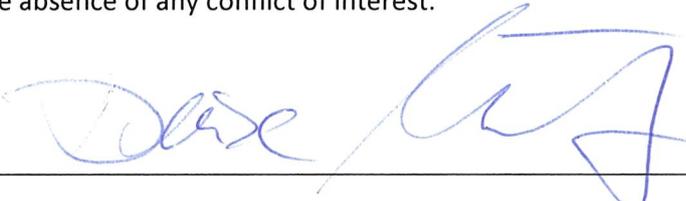
Name of Candidate: Kseniia Safina

PhD Program: Life Sciences

Title of Thesis: Molecular epidemiology of socially important infectious diseases

Supervisor: Professor Georgii Bazykin

Name of the Reviewer: Denise Kühnert

<p>I confirm the absence of any conflict of interest.</p> 	<p>Date: 12-11-2021</p>
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The purpose of this report is to obtain an independent review from the members of PhD defense Jury before the thesis defense. The members of PhD defense Jury are asked to submit signed copy of the report at least 30 days prior the thesis defense. The Reviewers are asked to bring a copy of the completed report to the thesis defense and to discuss the contents of each report with each other before the thesis defense.

If the reviewers have any queries about the thesis which they wish to raise in advance, please contact the Chair of the Jury.

Reviewer's Report

Kseniia Safina is presenting her PhD thesis containing of 2 research projects. The thesis is of high quality, well-written and well-structured. It contains a thorough introduction (chapter 1) and literature review (chapter 2). The thesis content is very relevant to the topic of dissertation. The research was performed using state-of-the-art scientific methodology yielding results of clear scientific significance.

One of the research projects (chapter 4) has resulted in a high-quality publication published in Nature Communications, on which the candidate is shared first-author.

Chapter 3 presents the molecular epidemiology of HIV-1 in Oryol Oblast, Russia. I would expect this study to be published in a high-profile scientific journal and have high impact due to its epidemiological relevance. Particularly, the finding that the recombinant CRF63 cluster is growing much more rapidly than than the previously dominant subtype has important epidemiological implications.

Summary of issues to be addressed before/during the thesis defense:

- A major issue to be addressed before the thesis defense is in chapter 3 (p.57) is a “re-use” of the data set. The BEAST analyses should not be run using a prior distribution on the evolutionary rate that was obtained from the same data set. Please re-run all affected analyses with a prior obtained from a different data set (from the literature). Fortunately, this is unlikely to cause major qualitative differences to the results, as all analyses were performed with the same prior. However, quantitative differences are expected and the results should be updated accordingly.

Minor comments:

- I am somewhat surprised that publications 2 and 3 as listed on page 5 are not mentioned anywhere else in the thesis. I would find it useful to relate them to the rest of the work, if only in the abstract.
- Pages 57/58: multitree is not the first method to allow for this kind of analysis, although it may be more convenient than previous approaches (Novitsky et al 2015, *Epidemics*, Kühnert et al 2018, *PLoS Path.*). Please rephrase.
- Please explain why the sampling proportion inferred from data set I is suited for data set II (p.58).
- Why was R_e assumed to be constant? A 3-4 interval approach may have captured interesting transmission dynamics through time (p.67). Please justify.
- Supp. Fig A-9 ranges until year 2030, which may be due to a mistake in the plotting script.
- Please note that there is an option to not assume sampling to lead to becoming non-infectious using the sampled ancestors approach (Gavryushkina et al 2014, *PLoS Comp. Biol.*). Please remove this statement or rewrite accordingly (p.81).
- For SARS-CoV-2, page 91, why were problematic sites not masked (see e.g. de Maio et al 2020, *Virological.org*).
- Why were time-varying R_e estimates obtained from EpiEstim instead of bdsky? Please justify and discuss.

Provisional Recommendation

I recommend that the candidate should defend the thesis by means of a formal thesis defense

I recommend that the candidate should defend the thesis by means of a formal thesis defense only after appropriate changes would be introduced in candidate's thesis according to the recommendations of the present report

The thesis is not acceptable and I recommend that the candidate be exempt from the formal thesis defense