

**From:** [Minster, Ryan](#)  
**To:** [Sedlazeck, Fritz](#)  
**Cc:** [TOPMed ACC Publications](#); [Albert Vernon Smith](#); [Weeks, Daniel E](#); [Carlson, Jenna Colavincenzo](#); [Maria Demarco](#); [Patrick Mitchell](#); [Metcalf, Ginger A.](#); [McGarvey, Stephen](#)  
**Subject:** Re: TOPMed Manuscript Study-Specific Approval for Samoan  
**Date:** Sunday, November 27, 2022 11:18:46 AM

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**CAUTION: External Email \***

Good morning Fritz,

If you haven't got them:

Muagututi'a Sefuiva Reupena · [smuagututia51@gmail.com](mailto:smuagututia51@gmail.com)

Take Naseri · [malonaseri@gmail.com](mailto:malonaseri@gmail.com)

Sincerely,

Ryan

On 11/17/22, 9:09 AM, "Sedlazeck, Fritz" <[Fritz.Sedlazeck@bcm.edu](mailto:Fritz.Sedlazeck@bcm.edu)> wrote:

Dear Stephen,

Thank you and your team for working with us on this. I have included the text changes in the manuscript and we will adjust Figure 1A today.

I have also updated the acknowledgement as you suggested.

Sorry about the misspelling of the one person that was a copy paste error on my side.

Could I ask for the emails from:

Muagututi'a Sefuiva Reupena

Take Naseri

I could find their affiliation, but emails are often tricky.

Thank you

Fritz

> On Nov 16, 2022, at 1:17 PM, McGarvey, Stephen <[stephen\\_mcgarvey@brown.edu](mailto:stephen_mcgarvey@brown.edu)> wrote:

>

> Dear Ms Smith, Fritz, Albert et al.,

>

> Our Samoan research group met today after several of us reviewed the latest draft sent on 11-7-22 to us by Fritz.

>

> We request several small edits to the text to make very clear about the classification of the Samoan data from 1,267 individuals of Samoan ancestry together with the 5,602 East Asian individuals into the EAS population category.

>

> The attached Word document of the 11-7-22 draft contains our suggested edits to improve accuracy and clarity.

>

> If you accept our edit, we are happy to approve of the submission of the manuscript and wish Fritz and colleagues good luck with the manuscript.

>

> About authorship, I edited the last name of one of the Samoan co-authors which had been misspelled. We are happy with the two Samoan coauthors being included. But we also request as stated in our usual letter to other TOPMed collaborators that we want the following study group to be named in any Acknowledgements or Supplements: 'The Samoan Obesity, Lifestyle and Genetic Adaptations Study (OLaGA) Group'. In any supplementary files please list the names in the OLAGA group, as follows: Ranjan Deka, Dept. of Environmental Health, University of Cincinnati; Nicola L. Hawley, Dept. of Chronic Disease Epidemiology, Yale University; Stephen T McGarvey, Dept. of Epidemiology and International Health Institute, and Dept. of Anthropology, Brown University; Ryan L Minster, Dept. of Human Genetics, University of Pittsburgh; Take Naseri, Ministry of Health, Government of Samoa; Muagututi'a Sefuiva Reupena, Lutia I Puava Ae Mapu I Fagalele; Daniel E. Weeks, Depts. of Human Genetics and Biostatistics, University of Pittsburgh.

>

> Finally, we are grateful that you used the Samoan data in your analysis and manuscript, and look forward to more collaboration.

>

> best regards,

>

> Steve

>

> Stephen T. McGarvey, PhD, MPH

> Professor of Epidemiology and of Anthropology

> International Health Institute

> Brown University School of Public Health

> Fellow, American Association for the Advancement of Science (AAAS)

> 121 S. Main St, Room 258

> email: Stephen\_McGarvey@brown.edu

> [https://nam12.safelinks.protection.outlook.com/?](https://nam12.safelinks.protection.outlook.com/?url=https%3A%2F%2Fvivo.brown.edu%2Fdisplay%2Fsmcgarve&data=05%7C01%7Cminster%40pitt.edu%7C2ba72c1709c04496ff3408dac8a55eac%7C9ef9f489e0a04eeb87cc3a526112fd0d%7C1%7C0%7C638042909844591012%7CUnknown%7CTWFpbGZsb3d8eyJWljoimC4wLjAwMDAilCJQljoiv2luMzliLCJBTiI6k1haWwiLCJXVCI6Mn0%3D%7C3000%7C%7C%7C&amp;sdata=nXci3YaCC%2F6IMZ37IN%2B7dju4UJysuseTBea02nbEGEs%3D&amp;reserved=0)

[url=https%3A%2F%2Fvivo.brown.edu%2Fdisplay%2Fsmcgarve&data=05%7C01%7Cminster%40pitt.edu%7C2ba72c1709c04496ff3408dac8a55eac%7C9ef9f489e0a04eeb87cc3a526112fd0d%7C1%7C0%7C638042909844591012%7CUnknown%7CTWFpbGZsb3d8eyJWljoimC4wLjAwMDAilCJQljoiv2luMzliLCJBTiI6k1haWwiLCJXVCI6Mn0%3D%7C3000%7C%7C%7C&amp;sdata=nXci3YaCC%2F6IMZ37IN%2B7dju4UJysuseTBea02nbEGEs%3D&amp;reserved=0](https://nam12.safelinks.protection.outlook.com/?url=https%3A%2F%2Fvivo.brown.edu%2Fdisplay%2Fsmcgarve&data=05%7C01%7Cminster%40pitt.edu%7C2ba72c1709c04496ff3408dac8a55eac%7C9ef9f489e0a04eeb87cc3a526112fd0d%7C1%7C0%7C638042909844591012%7CUnknown%7CTWFpbGZsb3d8eyJWljoimC4wLjAwMDAilCJQljoiv2luMzliLCJBTiI6k1haWwiLCJXVCI6Mn0%3D%7C3000%7C%7C%7C&amp;sdata=nXci3YaCC%2F6IMZ37IN%2B7dju4UJysuseTBea02nbEGEs%3D&amp;reserved=0)

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> On Tue, Nov 15, 2022 at 5:34 PM TOPMed ACC Publications <topmed-pubs@westat.com> wrote:

> Dear Dr. McGarvey,

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>

> I wanted to follow up on this to see if there has been any resolution. I understand that the publishing authors would like to make a journal submission deadline in December. So your response would be greatly appreciated.

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> All relevant parties are attached to this email should you have more questions.

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> Best,

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> Ashley Smith on behalf of the TOPMed ACC Publications Committee

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> Ashley S. Smith, MPH, MLT(ASCP)

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> Westat | Public Health & Epidemiology Practice

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> o: 240-314-2344

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> c: 678-596-6467

>

> AshleySmith@westat.com

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> From: Sedlazeck, Fritz <Fritz.Sedlazeck@bcm.edu>

> Sent: Monday, November 7, 2022 1:59 PM

> To: McGarvey, Stephen <stephen\_mcgarvey@brown.edu>

> Cc: Albert Vernon Smith <albertvs@umich.edu>; TOPMed ACC Publications <topmed-pubs@westat.com>; Sedlazeck, Fritz <Fritz.Sedlazeck@bcm.edu>; Dan Weeks <weeks@pitt.edu>; Ryan L <rminster@pitt.edu>; Jenna Colavincenzo <jnc35@pitt.edu>; Maria Demarco <MariaDemarco@westat.com>

> Subject: Re: TOPMed Manuscript Study-Specific Approval for Samoan

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>  
> CAUTION: External Email \*  
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>  
> Dear Steve,  
>  
> Sorry for the delays because of travels and conferences etc.  
>  
> I am working on this list of yours and I think I got it now incorporated.  
>  
> Here is the link to the manuscript: [https://nam12.safelinks.protection.outlook.com/?url=https%3A%2F%2Fdocs.google.com%2Fdocument%2Fd%2F1C5tgVlqiv6fyywEcQR7ODPaU800k52qNY-BU\\_uxWw8A%2Fedit%3Fusp%3Dsharing&data=05%7C01%7Crminster%40pitt.edu%7C2ba72c1709c04496ff3408dac8a55eac%7C9ef9f489e0a04eeb87cc3a526112fd0d%7C1%7C0%7C638042909844591012%7CUnknown%7CTWFpbGZsb3d8eyJWljoIMC4wLjAwMDAilCJQljoIjoiV2luMzliLCJBTiil6lk1haWwiLCJXVCI6Mn0%3D%7C3000%7C%7C%7C&data=EXS0e1jfkVddcZA3hGzx0%2FNTCgmHZmaKqcRBJTPEE8%3D&reserved=0](https://nam12.safelinks.protection.outlook.com/?url=https%3A%2F%2Fdocs.google.com%2Fdocument%2Fd%2F1C5tgVlqiv6fyywEcQR7ODPaU800k52qNY-BU_uxWw8A%2Fedit%3Fusp%3Dsharing&data=05%7C01%7Crminster%40pitt.edu%7C2ba72c1709c04496ff3408dac8a55eac%7C9ef9f489e0a04eeb87cc3a526112fd0d%7C1%7C0%7C638042909844591012%7CUnknown%7CTWFpbGZsb3d8eyJWljoIMC4wLjAwMDAilCJQljoIjoiV2luMzliLCJBTiil6lk1haWwiLCJXVCI6Mn0%3D%7C3000%7C%7C%7C&data=EXS0e1jfkVddcZA3hGzx0%2FNTCgmHZmaKqcRBJTPEE8%3D&reserved=0)  
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> Note I incorporated the two suggested authors, but I would need more information such as email etc. here: [https://nam12.safelinks.protection.outlook.com/?url=https%3A%2F%2Fdocs.google.com%2Fspreadsheets%2Fd%2F1DcLd\\_1K\\_2704-Zzpl9wfbwkXuSw8NVHq7\\_PojlDnkYw%2Fedit%3Fusp%3Dsharing&data=05%7C01%7Crminster%40pitt.edu%7C2ba72c1709c04496ff3408dac8a55eac%7C9ef9f489e0a04eeb87cc3a526112fd0d%7C1%7C0%7C638042909844747248%7CUnknown%7CTWFpbGZsb3d8eyJWljoIMC4wLjAwMDAilCJQljoIjoiV2luMzliLCJBTiil6lk1haWwiLCJXVCI6Mn0%3D%7C3000%7C%7C%7C&data=Zg3dbkGVnpZXjY949t9jtm8F2YfKQlZfy2JeLzEAJb8%3D&reserved=0](https://nam12.safelinks.protection.outlook.com/?url=https%3A%2F%2Fdocs.google.com%2Fspreadsheets%2Fd%2F1DcLd_1K_2704-Zzpl9wfbwkXuSw8NVHq7_PojlDnkYw%2Fedit%3Fusp%3Dsharing&data=05%7C01%7Crminster%40pitt.edu%7C2ba72c1709c04496ff3408dac8a55eac%7C9ef9f489e0a04eeb87cc3a526112fd0d%7C1%7C0%7C638042909844747248%7CUnknown%7CTWFpbGZsb3d8eyJWljoIMC4wLjAwMDAilCJQljoIjoiV2luMzliLCJBTiil6lk1haWwiLCJXVCI6Mn0%3D%7C3000%7C%7C%7C&data=Zg3dbkGVnpZXjY949t9jtm8F2YfKQlZfy2JeLzEAJb8%3D&reserved=0) (first sheet, line 52 and 53).  
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>  
> We fixed Figure 1A and B to highlight the samoans.  
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> I think the questions where we obtained our ancestries from have been answered by Albert and others right? We are working on mentioning this as you requested. Right now : " We note the use of ancestral groupings in this analysis may be limiting due to the inclusion of Samoans in the East Asian population group and population-specific analysis might reveal more differences for isolated populations such as Samoans. "  
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> I have included the acknowledgement statement and special shout out to the samoan research group.

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> About the author list question: We have included 2 authors for each study and included them. We have a longer list of authors in the banner authorship. Please review this here:

>  
> [https://nam12.safelinks.protection.outlook.com/?url=https%3A%2F%2Fdocs.google.com%2Fspreadsheets%2Fd%2F1Dcld\\_1K\\_2704-Zzpl9wfbwkXuSw8NVHq7\\_PojlDnkYw%2Fedit%3Fusp%3Dsharing&data=05%7C01%7Cminster%40pitt.edu%7C2ba72c1709c04496ff3408dac8a55eac%7C9ef9f489e0a04eeb87cc3a526112fd0d%7C1%7C0%7C638042909844747248%7CUnknown%7CTWFpbGZsb3d8eyJWljoiMC4wLjAwMDAiLCJQIjoiV2luMzliLCJBTiI6IjEhaWwiLCJXVCi6Mn0%3D%7C3000%7C%7C7C&sdata=Zg3dbkGVnpZXjY949t9jtm8F2YfKQlZfy2JeLzEAlb8%3D&reserved=0](https://nam12.safelinks.protection.outlook.com/?url=https%3A%2F%2Fdocs.google.com%2Fspreadsheets%2Fd%2F1Dcld_1K_2704-Zzpl9wfbwkXuSw8NVHq7_PojlDnkYw%2Fedit%3Fusp%3Dsharing&data=05%7C01%7Cminster%40pitt.edu%7C2ba72c1709c04496ff3408dac8a55eac%7C9ef9f489e0a04eeb87cc3a526112fd0d%7C1%7C0%7C638042909844747248%7CUnknown%7CTWFpbGZsb3d8eyJWljoiMC4wLjAwMDAiLCJQIjoiV2luMzliLCJBTiI6IjEhaWwiLCJXVCi6Mn0%3D%7C3000%7C%7C7C&sdata=Zg3dbkGVnpZXjY949t9jtm8F2YfKQlZfy2JeLzEAlb8%3D&reserved=0) This study is across many studies and solar everyone agreed to nominate only 2 authors for the main authors.

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> Thank you

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> Fritz

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> On Oct 5, 2022, at 12:39 PM, McGarvey, Stephen <stephen\_mcgarvey@brown.edu> wrote:

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>  
> Dear Ms Smith, Dr Sedlazeck and Albert,

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>  
> Our Samoan study group discussed today the issue of the inclusion and use Samoan data in the 'Structural Variation ... in TOPMed' manuscript. We appreciate that Dr Albert Vernon Smith recognized the importance of not lumping the Samoan data into an East Asian category. But the larger issue is the status of the manuscript, which we do not want to

unreasonably slow down from moving toward completion and submission. I have a version from June 8, 2022 about which I make comments.

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> 1. I see the last two sentences at the end of the first paragraph in Results " .The majority of the samples are of European descent followed by African and Asian based on general inferred categories and we note that these general categories may include individuals from diverse backgrounds. For example, there is a subset of individuals (n=1,267) that are identified as Samoan25 of which the majority appear in the EAS category."

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>

> We appreciate the details contained but would like to ask that the ancestry category named here and shown in Figure 1A reflect the Samoan inclusion in with other 'East Asian' ancestries. Can you change the name to 'East Asians and Samoan'?

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> 2. It is not clear how the ancestral groups in Fig 1A are then deployed in the analyses. Were they used, or is Fig 1A just informational about the overall ancestral diversity in the TOPMed study sample?

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> 3. if ancestral groups were used in the analyses, can you include a brief discussion in the limitations section about this and specifically how the clumping of Samoans with )East Asians might affect the findings?

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> 4. We have questions about acknowledgements and authorship (as written in the June 8, 2022 version).

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>

> Acknowledgements: If you use the Samoan data we ask that you acknowledge the fundings sources relevant to TOPMed participation. These are (following the format in other TOPMed publications) as follows:

>

> " NHLBI TOPMed: Samoan Adiposity Study (Samoan) Data collection was funded by NIH grant R01-HL093093 and R01-HL133040. We thank the Samoan participants of the study, local village authorities, and research assistants over the

>

> years. We acknowledge the support of the Samoan Ministry of Health; the Samoa Bureau

of Statistics; and the Samoa Ministry of Women, Community and Social Development and for our research collaboration."

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> Authorship: In our standard letters of collaboration approving access to the Samoan dbGaP data, including intra-TOPMed collaborations, we require two things, and have some interrelated questions about co-authorship.

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> 1. All manuscripts that use and include Samoan data must have both Dr. Take Naseri and Mr. Muagututi'a Sefuiva Reupena as named authors. They are both from Samoa, and their inclusion is now a condition of our collaboration with the Samoa leadership. This was agreed to by the TOPMed P&P committee.

>

>

>

> 2. We ask that our study group be named in any Acknowledgements or in Supplementary Materials : 'The Samoan Obesity, Lifestyle and Genetic Adaptations Study (OLaGA) Group'. In any supplementary files please list the names in the OLAGA group, as follows: Ranjan Deka, Dept. of Environmental Health, University of Cincinnati; Nicola L. Hawley, Dept. of Chronic Disease Epidemiology, Yale University; Stephen T McGarvey, Dept. of Epidemiology and International Health Institute, and Dept. of Anthropology, Brown University; Ryan L Minster, Dept. of Human Genetics, University of Pittsburgh; Take Naseri, Ministry of Health, Government of Samoa; Muagututi'a Sefuiva Reupena, Lutia I Puava Ae Mapu I Fagalele; Daniel E. Weeks, Depts. of Human Genetics and Biostatistics, University of Pittsburgh.

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> 3. Our question about authorship is this: are all named authors as of the 6/8/22 draft limited to those who directly contributed to the design, analysis, interpretation and writing? How do those who provided the data for the study (data collection, management, etc.) get attribution? Are some people named authors based on having provided the data to TOPMed? In prior TOPMed papers I or someone from our group (in addition to Dr Naseri and Mr Reupena from Samoa) is offered co-authorship based on our leading the Samoan study and providing the data to TOPMed. Will you be offering that to us?

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> We look forward to your replies to my comments and the issues of acknowledgements and authorship.

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> best regards,

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> Steve McGarvey

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> Stephen T. McGarvey, PhD, MPH

> Professor of Epidemiology and of Anthropology

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> International Health Institute

> Brown University School of Public Health

> Fellow, American Association for the Advancement of Science (AAAS)

> 121 S. Main St, Room 258

> email: Stephen\_McGarvey@brown.edu

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> <https://nam12.safelinks.protection.outlook.com/?url=https%3A%2F%2Fvivo.brown.edu%2Fdisplay%2Fsmcgarve&data=05%7C01%7Cminster%40pitt.edu%7C2ba72c1709c04496ff3408dac8a55eac%7C9ef9f489e0a04eeb87cc3a526112fd0d%7C1%7C0%7C638042909844747248%7CUnknown%7CTWFpbGZsb3d8eyJWljoimC4wLjAwMDAilCjQljoiv2luMzliLCJBTiI6k1haWwiLCJXVCI6Mn0%3D%7C3000%7C%7C%7C&mp;sdata=2VMgwZTMJmB95Mz3Udcrxhvt%2BtHabse5YitDcoxq4zl%3D&reserved=0>

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> On Wed, Sep 28, 2022 at 1:05 PM Albert Vernon Smith <albertvs@umich.edu> wrote:

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> Steve-

>

> I didn't realize you were expecting comment directly from myself. I had provide our Fritz and Goo with details on IRC calculated ancestry, and I had thought they were discussion a solution with you. I agree that lumping Samoans with East Asians is inappropriate. In IRC presentations of ancestry, we had only emphasized populations with larger sample size. In other words, we have not given direct comment on Somoans and also East Asians (at times).

>

> Please let me know how I might comment and help resolve this.

>

> Best,

> -albert

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>> On 28 Sep 2022, at 12:51, McGarvey, Stephen <stephen\_mcgarvey@brown.edu> wrote:

>>

>> Dear Ms Smith,

>>

>> Thank you for the additional information about the proposed research Structural Variation across the TOPMed consortium which will use the Samoan data.

>>

>> To my knowledge we have not received a reply from Albert Smith nor anyone else about our concerns regarding lumping the Samoan data with East Asians, which we consider inappropriate (as written earlier). Nor did we get a reply about Dan Week's methods suggestion to derive three PCs which would show Samoans as a separate group. Lacking that response we think nothing much has changed. We don't want to obstruct the paper, but do feel we need some reply about how to properly treat the Samoan data in the analyses. We look forward to some such response.

>>

>> best regards,

>>

>> Steve

>>

>> Stephen T. McGarvey, PhD, MPH

>> Professor of Epidemiology and of Anthropology

>> International Health Institute

>> Brown University School of Public Health

>> Fellow, American Association for the Advancement of Science (AAAS)

>> 121 S. Main St, Room 258

>> email: Stephen\_McGarvey@brown.edu

>> <https://nam12.safelinks.protection.outlook.com/?url=https%3A%2F%2Fvivo.brown.edu%2Fmanager%2Fdisplay%2Fsmcgarve%2F&data=05%7C01%7Crminster%40pitt.edu%7C2ba72c1709c04496ff3408dac8a55eac%7C9ef9f489e0a04eeb87cc3a526112fd0d%7C1%7C0%7C638042909844747248%7CUnknown%7CTWFpbGZsb3d8eyJWljiMC4wLjAwMDAiLCJQIjoiV2luMzliLCJBTiI6IjEhaWwiLCJXVCi6Mn0%3D%7C3000%7C%7C%7C&sdata=554nk7lwcMF2IHRoRGQO8CC0acVo%2BFOfJR65xWuOkSc%3D&reserved=0>

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>> On Tue, Sep 27, 2022 at 11:04 AM TOPMed ACC Publications <topmed-pubs@westat.com> wrote:

>> Good Morning, Dr. McGarvey.

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>> I am reaching out on behalf of the TOPMed ACC Publications Committee, after consulting with Dr. Weiniu Gan, regarding TOPMed Manuscript #14349. We wanted to provide some clarifying language about the purpose, scope, and collaborative nature of this IRC/TOPMed-Wide project. Dr. Sedlazeck and his co-investigators are working as an extension of the IRC

for the purposes of this research. And, therefore, fall under the IRC's umbrella with regards to data access and any required letters of collaboration. Part of the IRC's mission is to publish structure variance without phenotype. This is the agreement when studies gave permission for the IRC to handle their data (variant code is included, not phenotype data). The data access agreement that is in place includes structure variance.

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>>

>> We would like you to consider this information, along with Dr. Weiniu Gan's endorsement of this TOPMed-wide manuscript, which is similar in uniqueness to the TOPMed flagship papers. This is a collaborative effort and Dr. Sedlezeck and his co-investigators would like your acknowledgement so that they can proceed with steps towards publication (co-authorships will be included).

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>> Best,

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>> Ashley Smith on behalf of the TOPMed ACC Publications Committee

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>> Ashley S. Smith, MPH, MLT(ASCP)

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>> Westat | Public Health & Epidemiology Practice

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>> o: 240-314-2344

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>> c: 678-596-6467

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>> AshleySmith@westat.com

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>> From: Metcalf, Ginger A.

>> Sent: Thursday, August 11, 2022 6:21 PM

>> To: McGarvey, Stephen <stephen\_mcgarvey@brown.edu>; TOPMed ACC Publications <topmed-pubs@westat.com>; Albert Vernon Smith <albertvs@umich.edu>

>> Cc: Sedlazeck, Fritz <Fritz.Sedlazeck@bcm.edu>; Dan Weeks <weeks@pitt.edu>; Minster, Ryan L <rminster@pitt.edu>; Carlson, Jenna Colavincenzo <jnc35@pitt.edu>; Maria Demarco <MariaDemarco@westat.com>

>> Subject: RE: TOPMed Manuscript Study-Specific Approval for Samoan

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>> Dear Dr. McGarvey,

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>>

>> Please accept my apologies for this delayed response. I work with Fritz at Baylor College of Medicine and hope to address some of your questions related to the SV manuscript:

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>>

>>

>> 1.) Regarding data access: We do not require data access through dbGap. The SV calling was conducted in collaboration with the TOPMed IRC (we have a subcontract with the University of Michigan) to serve as a resource to TOPMed investigators very similar to the SNV callsets so we received access through the IRC. Since this is the first TOPMed SV release, and the largest joint WGS callset to our knowledge, TOPMed program leadership encouraged a manuscript describing the methods and the resource

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>> 2.) I have copied Albert Smith to comment on the ancestry question from Dan Week's (copied below in green) as his team provided the inferred ancestry. Albert please see below. I hope we can come up with a satisfactory solution that doesn't involve significant reanalysis.

>>

>>

>>

>> "The inference of genetically inferred ancestry is not described in enough detail for me to understand what they did. Their paper reads, "PCA Ancestries were assigned by identifying the genetic ancestry across individuals<sup>24</sup>. Filtering was performed to exclude variants with AC=1. A randomized PCA was performed using scikit-allel v1.3.5 with n\_components=10 and scaler='patterson'."

>>

>> Figure 1A is a pie chart, in which they identified even a small group of people of "Mestizo (MES)" as a separate group. I'm sure if they revisit the PC's in 3 dimensions instead of 2 dimensions, they will find that the Samoans belong in their own separate 'genetic ancestry' group. If so, then the simple fix would be to add another slice for Samoans to the Figure 1A pie chart.

>>

>> In two-dimensional PC plots, we've previously seen that Samoans can appear to overlap other groups, which is why we put three-D PC plots (and a movie) in the Supplement of our 2016 CREBRF Nature Genetics paper.

>>

>> Thank you,

>>

>> Ginger Metcalf

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>>  
>>  
>> From: McGarvey, Stephen <stephen\_mcgarvey@brown.edu>  
>> Sent: Monday, June 20, 2022 9:31 AM  
>> To: TOPMed ACC Publications <topmed-pubs@westat.com>  
>> Cc: Sedlazeck, Fritz <Fritz.Sedlazeck@bcm.edu>; Metcalf, Ginger A. <metcalf@bcm.edu>;  
Dan Weeks <weeks@pitt.edu>; Minster, Ryan L <rminster@pitt.edu>; Carlson, Jenna  
Colavincenzo <jnc35@pitt.edu>; Maria Demarco <MariaDemarco@westat.com>  
>> Subject: Re: TOPMed Manuscript Study-Specific Approval for Samoan  
>>  
>>  
>>  
>> \*\*\*CAUTION:\*\*\* This email is not from a BCM Source. Only click links or open  
attachments you know are safe.  
>>  
>> Dear Ashley,  
>>  
>>  
>>  
>> Thank you for sending me the evidence that the Samoan dataset was passively approved.  
Please advise me if there is a further step of approval needed to actually access the Samoan  
dbGaP data. TOPMed investigators have in the past had to have their local IRB approval for  
their work on the Samoan datas under the terms of our conditions for use of Samoan dbGaP  
data. The specific TOPMed manuscript leader(s) for a project then write me to request a  
letter.  
>>  
>>  
>>  
>> It is this type of letter from me to Dr. Sedlazeck's that I do not find in my records.  
Perhaps I failed to keep a record.  
>>  
>>  
>>  
>> I also recognize that I may not fully understand the TOPMed procedure about data  
access. We certainly do not want to limit access to anybody willing to abide by the dbGaP  
conditions of use, especially TOPMed investigators!  
>>  
>>  
>>  
>> I look forward to your reply about the rules and procedures,  
>>  
>>  
>>  
>> best regards,

>>

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>> Steve

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>>

>> Stephen T. McGarvey, PhD, MPH

>> Professor of Epidemiology and of Anthropology

>>

>> International Health Institute

>> Brown University School of Public Health

>> Fellow, American Association for the Advancement of Science (AAAS)

>> 121 S. Main St, Room 258

>> email: Stephen\_McGarvey@brown.edu

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>> On Mon, Jun 20, 2022 at 10:11 AM TOPMed ACC Publications <topmed-pubs@westat.com> wrote:

>>

>> Good Morning, Dr. McGarvey.

>>

>>

>>

>> The TOPMed ACC has this record of the Samoan dataset being approved for Dr.

Sedlazeck's proposal: <https://nam12.safelinks.protection.outlook.com/?url=https%3A%2F%2Ftopmed.nhlbi.nih.gov%2Frequested-samoangru-irb-pub-col-npu-gso-paperstructural-variation-across-topmed-consortium-id12856&data=05%7C01%7Cminster%40pitt.edu%7C2ba72c1709c04496ff3408dac8a55eac%7C9ef9f489e0a04eeb87cc3a526112fd0d%7C1%7C0%7C638042909844747248%7CUnknown%7CTWFpbGZsb3d8eyJWljojMC4wLjAwMDAiLCJQIjoiV2luMzliLCJBTiI6IjEhaWwiLCJXVCi6Mn0%3D%7C3000%7C%7C%7C&sdata=kMbt2P6JzX%2BrE%2BIB9B5z6kjdRi8Vu5RLRqUWBnD9IEY%3D&reserved=0>

<https://nam12.safelinks.protection.outlook.com/?url=https%3A%2F%2Ftopmed.nhlbi.nih.gov%2Frequested-samoangru-irb-pub-col-npu-gso-paperstructural-variation-across-topmed-consortium-id12856&data=05%7C01%7Cminster%40pitt.edu%7C2ba72c1709c04496ff3408dac8a55eac%7C9ef9f489e0a04eeb87cc3a526112fd0d%7C1%7C0%7C638042909844747248%7CUnknown%7CTWFpbGZsb3d8eyJWljojMC4wLjAwMDAiLCJQIjoiV2luMzliLCJBTiI6IjEhaWwiLCJXVCi6Mn0%3D%7C3000%7C%7C%7C&sdata=kMbt2P6JzX%2BrE%2BIB9B5z6kjdRi8Vu5RLRqUWBnD9IEY%3D&reserved=0>

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>> It was originally requested on 09/17/2021 and automatically approved after two weeks review time.

>>

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>> Dr. Sedlazeck may answer your other items listed below.

>>  
>>  
>>  
>> Best,  
>>  
>> Ashley Smith on behalf of the TOPMed ACC Publications Team  
>>  
>>  
>>  
>> Ashley S. Smith, MPH, MLT(ASCP)  
>>  
>> Westat | Public Health & Epidemiology Practice  
>>  
>> o: 240-314-2344  
>>  
>> c: 678-596-6467  
>>  
>> AshleySmith@westat.com  
>>  
>>  
>>  
>> From: McGarvey, Stephen <stephen\_mcgarvey@brown.edu>  
>> Sent: Friday, June 17, 2022 12:11 PM  
>> To: TOPMed ACC Publications <topmed-pubs@westat.com>; Sedlazeck, Fritz  
<Fritz.Sedlazeck@bcm.edu>  
>> Cc: metcalf@bcm.edu; Dan Weeks <weeks@pitt.edu>; Minster, Ryan L  
<rminster@pitt.edu>; Carlson, Jenna Colavincenzo <jnc35@pitt.edu>  
>> Subject: Re: TOPMed Manuscript Study-Specific Approval for Samoan  
>>  
>>  
>>  
>> CAUTION: External Email \*  
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>>  
>> Dear Fritz et al,  
>>  
>>  
>>  
>> I apologize for the delay in sending a more definitive response about our response  
regarding the Samoan data being classified with East Asians. I also write about our concern  
regarding how detailed the reporting of the SV data would be for Samoans.  
>>  
>>  
>>

>> 1. Dan Weeks made a comment which I paste here, which elaborates on my earlier email about the inappropriateness of classifying Samoans into a East asian category. .

>>

>> I take the liberty of quoting Dan without my editing.

>>

>> \*\*\*\*Start of Dan Weeks comment\*\*\*\*

>>

>> "The inference of genetically inferred ancestry is not described in enough detail for me to understand what they did. Their paper reads, "PCA Ancestries were assigned by identifying the genetic ancestry across individuals<sup>24</sup>. Filtering was performed to exclude variants with AC=1. A randomized PCA was performed using scikit-allel v1.3.5 with n\_components=10 and scaler='patterson'."

>>

>>

>>

>> Figure 1A is a pie chart, in which they identified even a small group of people of "Mestizo (MES)" as a separate group. I'm sure if they revisit the PC's in 3 dimensions instead of 2 dimensions, they will find that the Samoans belong in their own separate 'genetic ancestry' group. If so, then the simple fix would be to add another slice for Samoans to the Figure 1A pie chart.

>>

>>

>>

>> In two-dimensional PC plots, we've previously seen that Samoans can appear to overlap other groups, which is why we put three-D PC plots (and a movie) in the Supplement of our 2016 CREBRF Nature Genetics paper.

>>

>> \*\*\*\*end of Dan Weeks comment\*\*\*\*

>>

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>>

>> Thus, we ask that you not lump the Samoan data into any other genetic ancestry group. We are happy to discuss this.

>>

>>

>>

>> 2. Data release and identification of Samoans

>>

>> When Dan and I re-visited our e-mail chain, you assured us that the data would be shared in a way that would not be traceable at the individual-level or the Samoan-level. If we understand correctly, we agree with that plan.

>>

>>

>>

>> Finally, I hope you understood my email about the need for a letter from me to approve

your access to the Samoan dbGap data. If I did send such a letter, could you please send a copy to me? As I wrote I do not have a copy in my folders.

>>

>> This is very important as we must report to the Samoan Health Ministry government what is happening with the Samoan data, and we want to include your interesting work in that collection.

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>> best regards,

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>> Steve

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>> Stephen T. McGarvey, PhD, MPH

>> Professor of Epidemiology and of Anthropology

>>

>> International Health Institute

>> Brown University School of Public Health

>> Fellow, American Association for the Advancement of Science (AAAS)

>> 121 S. Main St, Room 258

>> email: [Stephen\\_McGarvey@brown.edu](mailto:Stephen_McGarvey@brown.edu)

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>> On Wed, Jun 8, 2022 at 2:25 PM McGarvey, Stephen <[stephen\\_mcgarvey@brown.edu](mailto:stephen_mcgarvey@brown.edu)> wrote:

>>

>> Dear Fritz and Ashley Smith (TOPMed ACC Publications Team),

>>

>>

>>

>> Thank you for the email about the manuscript 'Structural variation across 138,134 samples in the TOPMed consortium'. As Fritz knows, there were emails in February about using and describing the Samoan data, but at no time did we agree to include the Samoan data into any type of Asian or East Asian classification! The second version that we just we



received, succeeds the first version we accessed on Feb 20, 2022. We notice in this new version that the Samoan data are described as included in the EAS group. Unfortunately we cannot now approve this manuscript with the Samoan data as categorized with Asians (nor in East Asians), and analyzed as such.

>>

>>

>>

>> My colleagues will review the present version and we will send a summary review with more specific comments, but for now it is not acceptable to us. Revisions will be needed about how the Samoan data are analyzed and the SV data potentially disseminated.

>>

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>> Here are several quick concerns we have.

>>

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>> 1. We had assumed we would get an opportunity to review the manuscript, which we now will do with this recent version, '2\_0' on the TOPMed website. We did not receive an earlier version after Feb 20.

>>

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>>

>> 2. We did not name any co-authors in Feb 2022 since we didn't see any revised version until now which explicitly included the Samoan data. There will be three authors, including two from Samoa, if the Samoan data are analyzed as we require (see below for preliminary comments, more to be sent).

>>

>>

>>

>> A quick search of the main text for 'Samoa' finds this:

>>

>> 3. "Figure 1A shows the composition of the samples with respect to genetically inferred ancestry<sup>24</sup>. The majority of the samples are of European descent followed by African and Asian based on general inferred categories and we note that these general categories may include individuals from diverse backgrounds. For example, there is a subset of individuals (n=1,267) that are identified as Samoan<sup>25</sup> of which the majority appear in the EAS category."

>>

>> It is incorrect to claim that Samoans fall into the Asian category. This is an issue we dealt with in early TOPMed trans-ancestry manuscripts and is not acceptable. Perhaps the authors did that because they projected into a 2-D PC space, whereas Samoans will be in their own cluster in 3-D PC space. This must be adjusted.

>>

>>

>>

>> 4. What are the plans for sharing the resulting SV information? Will it be disaggregated such that users can look up Samoan-specific SVs and their frequencies? This is crucial since we are not permitted by the Samoa IRB or our verbal agreements with the Samoan collaborators to share Samoan allele frequency information via gnomAD, or any other publicly available source.

>>

>>

>>

>> We are grateful for the inclusion of the Samoan data in this analysis, but it comes with stipulations. I/we will send additional detailed comments soon.

>>

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>> We are happy to discuss by phone or Zoom if you ask.

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>> Best regards,

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>> Steve McGarvey

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>> Stephen T. McGarvey, PhD, MPH

>> Professor of Epidemiology and of Anthropology

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>> International Health Institute

>> Brown University School of Public Health

>> Fellow, American Association for the Advancement of Science (AAAS)

>> 121 S. Main St, Room 258

>> email: Stephen\_McGarvey@brown.edu

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>> On Tue, Jun 7, 2022 at 4:36 PM TOPMed ACC Publications <topmed-pubs@westat.com> wrote:

>>  
>> Good Afternoon, Dr. McGarvey.  
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>>  
>> I am reaching out to you on behalf of the TOPMed ACC Publications Team to confirm study-specific approval for Dr. Fritz Sedlazeck's manuscript "Structural variation across 138,134 samples in the TOPMed consortium" using the Samoan data. This manuscript has TOPMed Structural Variation Working Group Approval (see attached) and formal approval to use Samoan data (proposal #12856).  
>>  
>>  
>>  
>> I will attach this email to Dr. Sedlazeck's TOPMed manuscript submission. He is cc'd on this email should you have any follow-up questions.  
>>  
>>  
>>  
>> Best,  
>>  
>> Ashley Smith on behalf of the TOPMed ACC Publications Team  
>>  
>>  
>>  
>>  
>>  
>> Ashley S. Smith, MPH, MLT(ASCP)  
>>  
>> Westat | Public Health & Epidemiology Practice  
>>  
>> o: 240-314-2344  
>>  
>> c: 678-596-6467  
>>  
>> AshleySmith@westat.com  
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>>  
>>  
>> \* Please use caution when responding and/or clicking on links as this email originated from outside of Westat.  
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><2021\_topmedSVPaper\_version w Samoan additions 11-16-22 STMcG.docx>

