



APPENDIX 4. Guide for External Researchers Requesting Data Sharing Collaboration with the PREDIMED PLUS Study

Those of us associated with the PREDIMED PLUS study are aware that a focus on collaborative research is advantageous to researchers, who can collaborate on several studies and contribute to the generation of joint benefits.

Researchers who are affiliated with research organisations and who are investigating topics related to the objectives of the PREDIMED PLUS study can request collaboration with the PREDIMED PLUS researchers in order to gain access to particular data generated during the study.

Special value will be given to collaboration projects with relevant and novel objectives, and to those in which the collaborating researcher could provide other data for comparative purposes or increase the sample size. Proposals to evaluate highly speculative hypotheses or those with ethical restrictions are not considered appropriate.

Because the numerous groups that make up the PREDIMED PLUS study already produce a high level of internal demand for data analysis, proposals submitted by external researchers must be clearly justified, and must not overlap with similar proposals already in progress and being conducted by internal researchers, or those that appear as objectives of the various research projects.

Collaboration proposals may be submitted for both general data from the PREDIMED PLUS study and for specific projects. In the case of specific projects, the coordinator of the corresponding specific project must be the one maintaining the most direct contact with the external researcher submitting the collaboration request.

1. Submission of a collaboration proposal

The following steps must be followed in order to submit a proposal for collaboration and access to data:

1.1. Production of a collaboration request letter:

This letter is addressed to the Steering Committee for the PREDIMED PLUS study, and in it the researcher must provide a general description of the collaboration request, along with a brief CV summarising his or her research activities. The benefits of the collaboration must also be described (see further details on the form attached as APPENDIX 4. Collaboration Request Form for External researchers).

1.2. Completion of the collaboration request form for external researchers for the PREDIMED PLUS study, in order to access data generated during the PREDIMED PLUS study.

This form is also used to submit further details about the study: hypothesis, objectives, methodology, variables requested, sample size, duration of the study, etc.

In cases involving **meta-analysis of aggregate data**, where the researcher is not requesting access to raw data for the variables but only to coefficients and P-values corresponding to specific models of association, the variables that will be included in the analysis must be indicated in this section, along with the specific analyses to be performed, and including specification of the control variables and the syntaxes corresponding to the models.

2. Submission and evaluation of the proposal

The proposal must be submitted electronically to the Steering Committee for the study, during the first week of each month. Each proposal will be assessed and assigned a status: accepted, corrections needed, or rejected.

The basic criteria used to evaluate the proposals will be the following:

- The scientific excellence of the proposal
- The strategic priority of the proposal, with respect to the PREDIMED PLUS studies in progress, in order to avoid unnecessary duplication of work
- The scientific research background of the person or group submitting the request
- The scientific quality and capacity to administer the project
- The advantages that the collaboration could imply for researchers from the PREDIMED PLUS study (funding, publications, projects, etc.)
- The proposed study's compliance with the contents of the informed consent form signed by the patients whose data are being requested

3. Conditions for accessing data requested from the PREDIMED PLUS study:

If the proposal is accepted, a **Collaboration Agreement** (*Appendix X*) will first need to be signed. This document contains details on the terms and conditions under which access to the requested data is being granted, and these terms and conditions must be accepted by the collaborating researcher. New authorisation from the PREDIMED PLUS study's Ethics Committee may also be required, depending on the type of study proposed (the centralised committee or those from the various recruiting nodes from which data are being requested).

Because the PREDIMED PLUS study does not currently have a data management system based on data enclaves, which would give external researchers the ability to access data for the variables securely but without the ability to modify or copy them, some additional requirements must be specified in order to ensure the security, integrity, and confidentiality of the data.

External researchers will be given a password which is used to access a data file that contains the variables requested. In order to better protect the identities of the participants, this data file will be anonymised, without any variables that could serve as identifiers. The corresponding metadata will also be provided.

The external researcher must commit to:

- Refrain from attempting to identify the individual patients, while maintaining confidentiality.
- Maintain the integrity of the data.

- Maintain secure data storage environments.
- Refrain from distributing any data to unauthorised third parties.
- Use the data provided only in relation to the specific objectives for the collaboration.
- Submit the syntaxes used for the analyses performed so the results can be reproduced.
- Destroy the data provided at the end of the active establishment period for the Collaboration Agreement.

In the case of **collaboration proposals for performing aggregate meta-analysis** the external researcher will not be requesting raw data on the variables, but instead only performance of the statistical analyses and provision of the coefficients.

4. Data analysis and publications

The external researcher must ensure the quality of the statistical analyses performed as well as application of best practices. The software used must be listed and the syntax must be saved and submitted.

In the case of proposals for **meta-analysis**, the statistical analysis will be performed by an internal researcher from the PREDIMED PLUS study, who will be assigned based upon the experience required for the collaboration, and in this case the aggregate results requested will be provided in the form of tables.

The publication proposal form must be completed, including the names of the authors of the publication(s). In the case of original studies, the publication policy will be followed when establishing authorship, taking into account whether the collaboration involves data from the general study and for the total sample, or if specific projects are involved.

In the case of collaborative studies or meta-analyses where a large number of authors from other groups are participating and the number of authors that can be included is limited, the general rule to be followed is to include the maximum number of authors from the PREDIMED PLUS study, also establishing an ongoing rotation system for authorship of the various meta-analyses.

The publication proposal must be approved by the Steering Committee, and the results in the form of tables and the full article must be submitted before they are sent out for publication, so that the appropriate quality controls can be performed.

5. Cost

The procedures carried out by the researchers from the PREDIMED PLUS study incur a cost in terms of their time investment, including their review of the data access request, preparation of the data, provision of access to the data and metadata, statistical analyses in some cases, and review of the publication proposal and results. Therefore, like other large international groups have done, a fee is being established in relation to data access, which will be collected after a data request has been approved.

A bank transfer can be used to deposit this amount into the PREDIMED PLUS account opened for this purpose, or payment can be made using a credit card. Depending on the

type of collaboration involved, this fee would vary from situations with full exemption up to a cost of €12,000 (*see document on "Fees for data and samples"*).