APPENDIX 6. Guide for External Researchers Requesting Sample 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 samples generated during the study.

In this case, the external researcher is only requesting samples to perform certain types of analyses, incurring no additional costs for the PREDIMED PLUS study, but with a commitment from PREDIMED PLUS researchers, who will later establish the link between the results from the samples analysed and the corresponding data from the PREDIMED PLUS study. The internal researcher will in turn have to request authorisation to formalise the collaboration from the centres that recruited the patients whose data and samples would be analysed.

Special value will be given to collaborations 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 will not be considered appropriate.

Because the numerous groups that are part of the PREDIMED PLUS study already produce a high level of internal demand for sample analysis, and given the finite nature of the samples, proposals submitted by external researchers must be clearly justified, and must not overlap with similar proposals already in progress and being performed by internal researchers, or those that appear as objectives of the various research projects defined.

1. Submission of a collaboration proposal

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

1.1. Production of a collaboration request letter:

This letter is addressed to the Steering Committee for the PREDIMED PLUS study (predimed_plus_scommittee@googlegroups.com), and in it the external 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 from APPENDIX 5. Collaboration Request Form for External researchers for Access to Samples).

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

This form is used to provide further details about the study: hypothesis, objectives, methodology to be used, PREDIMED PLUS researcher who will perform the data study, variables to be analysed, sample size, duration of the study, type of samples being requested, quantity, concentration, conditions for transport, shipping location, determinations to be performed, etc.

2. Submission and evaluation of the proposal

The proposal must be submitted electronically to the Steering Committee for the study (predimed_plus_scommittee@googlegroups.com) 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 availability of samples
- 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 quality of the group that will be performing determinations using the samples
- The suitability of the PREDIMED PLUS researcher(s) supporting the sample sharing proposal, and their commitment to performing data analyses and/or collaborating with other internal PREDIMED researchers
- The type and availability of other data that would be combined with the results from the sample analysis
- The proposed study's compliance with the contents of the informed consent form signed by the patients whose data is being requested

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

If the proposal is accepted, a **Collaboration Agreement for Access to Samples** (*Appendix 9*) will first need to be signed. This document contains details on the terms and conditions under which samples are being transferred to the external researcher, and these terms and conditions must be accepted by the collaborating researcher. An agreement must also be established with the internal PREDIMED PLUS researchers, and their permission must be requested to use the data that the analyses performed on the samples will require.

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 in this case the internal PREDIMED PLUS researchers are the ones who will perform the data analysis, the data file for the variables does not need to be given to the external researcher. This means that the internal researchers from PREDIMED will be responsible for ensuring compliance with the principles of security, confidentiality,

privacy, data integrity, and non-distribution to third parties, and they will fill in the data access commitment form.

The data requested may be either from the General Project or from Sub-Projects, and the internal researchers must be the ones to request those data. This will therefore require the collaboration of the researchers who generated those data (general and/or specific). Access to the data will be provided by means of transfer of the corresponding data file, after these agreements have been established.

External researchers gaining access to samples (which will be sent to them at the address specified) are committed to:

- maintaining the security and integrity of the samples, ensuring that transport takes place under appropriate conditions of freezing/refrigeration and storage;
- using the samples exclusively for the determinations approved by the PREDIMED PLUS study, with no permission to perform additional determinations or to transfer samples to other researchers;
- returning any remaining samples under optimal conditions of preservation following the determinations;
- submitting a copy of the results from the determinations performed to the central database for the PREDIMED PLUS study, or to the federated database that will be designated for this purpose if there are technical restrictions on the formats, in order to allow those data to be incorporated after the processing period has ended, which is established as 2 years after reception. *In exceptional cases it will be possible to request an extension.*
- providing each node with a copy of the data corresponding to the samples it provided whenever a paper is produced using determinations performed on samples from multiple nodes;
- establishing the pertinent collaboration agreements with internal PREDIMED PLUS researchers, who will carry out data analyses using the determinations produced;
- adhering to the publication policy and data management plan and sharing policy for the PREDIMED PLUS study.

4. Data analysis and publications

External researchers must ensure the quality of the determinations performed on the samples. Each node that has provided samples used for the determinations must be provided with, in addition to the data, details on the methodology used, the type of data generated, the quality control performed, and the metadata corresponding to each variable measured.

It will not be possible to authorise new papers for nodes other than the one performing the determinations until the paper corresponding to that data analysis has published, and unless this takes place in collaboration with those generating the data.

The internal researchers will perform the statistical analyses after establishing linkage with the pertinent PREDIMED PLUS variables.

The internal researchers, along with the external ones, must fill out the publication proposal form, 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, and also considering the contributions made by the external researchers and internal researchers 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 and approved before they are sent out for publication, so that the appropriate quality controls can be performed.

5. Cost

In addition to an economic cost, the procedures that must be carried out in order to locate samples, prepare them, ship them using dry ice, etc. incur a cost in terms of the time investment for the researchers from the PREDIMED PLUS study. Therefore, like other large international groups have done, a fee is being established in relation to data access, which will be collected after the 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"*).