CONSTANCES CHARTER

This document sets forth the rights and responsibilities of the research teams associated with the Constances cohort. It reviews the institutional environment of Constances and its governing bodies and then specifies the stages and requirements of research projects associated with the cohort.

- Procedures for project selection
- Conditions for using cohort data
- Procedures for the collection and use of and access to data collected in supplementary investigations
- Funding of research projects associated with the cohort
- Scientific responsibilities
- Data protection
- Dissemination of research results
- Declaration of agreement to comply with the operating rules

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Soutenu par
MINISTÈRE DU TRAVAIL DE LA SANTÉ ET DES SOLIDARITÉS
Liberté
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FOREWORDS

The CONSTANCES project is conducted as a partnership between the National Health Insurance Fund (Caisse nationale d'assurance maladie, CNAM) and its Health Screening Centres (HSC), the National Old-Age Insurance Fund (Caisse nationale d'assurance vieillesse, CNAV), the National Institute of Health and Medical Research (Institut national de la santé et de la recherche médicale, INSERM) and the Université de Paris, Paris Saclay University, University of Saint Quentin en Yvelines (Université de Saint Quentin en Yvelines, UVSQ), and supported by the Ministry of Health (Direction générale de la santé). The cohort is implemented and conducted by the "Population-based Epidemiologic Cohorts Unit-UMS 11". The head of this Unit is the scientific and technical Director of Constances.

The Constances Cohort Study was supported and funded by the Caisse nationale d'assurance maladie (CNAM). The Constances Cohort Study is currently supported by the Investments of the Future governmental program as an « Infrastructure nationale en Biologie et Santé » and benefits from a grant from ANR (ANR-11-INBS-0002). Constances has also established public-private partnerships with companies and start-ups in the health and wellness sector.

PROCEDURES FOR ACCESS BY THE SCIENTIFIC COMMUNITY TO THE CONSTANCES COHORT

1. GOVERNANCE OF THE CONSTANCES COHORT

The governing bodies of the Constances cohort are the International Scientific Committee (ISC) and the Institutional Steering Committee which brings together all of the institutions that supports the Constances cohort.

1 SCOPE OF THE CONSTANCES COHORT

The Constances general-purpose cohort is intended to serve as an epidemiological research infrastructure open to the health research and public health studies. Its use is therefore restricted exclusively to work of interest for health research and / or public health.

The Constances cohort is an observational study, and has received legal and regulatory authorizations for this type of study and research. Interventional studies are thus excluded from the scope of the Constances cohort.

2 PROCEDURES FOR RESEARCH PROJECTS ASSOCIATED WITH THE CONSTANCES COHORT

2.1 ACCESS REQUESTS

The procedures described in this document concern French and foreign research teams as well as organizations in the field of public health who wish to use the Constances cohort. All research teams, French or foreign, that wish to use the Constances cohort must submit an application via an online application (https://www.constances.fr/en/scientific-area/access-to-constances/). It may involve the use of available data as well as the biological materials collected, and/or the collection of supplementary data for a specific objective.

2.2 SELECTION OF RESEARCH PROJECTS BY GOVERNING BODIES OF THE CONSTANCES COHORT

It includes the following steps:

1. Research proposals receipt by the Constances' Scientific Secretariat. It controls that proposals are curate and complete;
2. Technical examination by the Constances cohort team (of feasibility, confidentiality, consistency, etc.). The conclusions of the technical examination of the application are transmitted to the International Scientific Committee. If the project plans for the collection of supplementary data, special attention will be paid to the procedures for its collection, their compliance with existing guidelines and their complementarity with already recorded data and to the procedures for contacting cohort's participants. Where appropriate, the Constances team will provide technical support for setting up the project.
3. Scientific and methodological quality evaluation by the International Scientific Committee. If the project has already been the subject of a scientific evaluation by a public body or a non-profit research foundation, the opinion of the scientific body which examined the project must be attached to the application. The ISC de Constances does not carry out a new scientific evaluation, but it takes into account various criteria such as compatibility with the general objectives of Constances, coherence with possible projects already underway, burden for the participants, etc. In the event of additional data collection, in particular by questionnaire, the ISC examines the final version of the questionnaire.

4. If needed the application may be transmitted to the INSERM Ethics Committee for its advice.
5. The evaluation of the ISC is transmitted to the Institutional Steering Committee and, when appropriate, with the advice of the Ethics Committee.

Important note: CNAM and CNAV may refuse to allow the data coming from their own databases (SNIIRAM and SNGC) to be transmitted for a project; if that happens, they motivate their refusal.

2.3 LEGAL AUTHORIZATIONS

Personal data used in health research: Constances data will only be accessible once the legal and regulatory formalities have been carried out by the person in charge of the project. The Constances team can help the investigators to complete the legal and regulatory procedures.

> **Important note**: it is essential to obtain the consent of the cohort Director prior to any step. In addition, the Constances team will not provide the data requested if the realization of these legal and regulatory formalities has not been made in connection with it.

2.4 DATA PROTECTION

It is the responsibility of the Constances Director and of each research project director to ensure the security of the data and compliance with confidentiality and to enumerate the precautions taken to avoid the direct or indirect identification of participants.

> **Important note**: Constances data resulting from linkage to the *Système National des Données de Santé* (SNDS) are hosted at the CASD, a highly secure infrastructure (https://www.casd.eu/). Researchers wishing to access Constances data linked to the SNDS must therefore establish a contract with CASD.

2.5 MEMORANDUM OF AGREEMENT

A referent of the Constances team is on hand to support accepted projects. In compliance with the GDPR, the specific modalities of the collaboration between the Constances cohort team and the applicant team must be recorded in the form of a memorandum. The Memorandum must specify the following points, in particular:

- definition of the sample concerned;
- list of the variables to be transmitted (made available by the Constances team from a data catalogue);
- duration of the project, frequency and modalities of transfer (name and contact information of recipient);
- procedures for data protection;
- confidentiality clauses;
- exclusivity-of-use clauses (if pertinent);
- clauses concerning the provision of supplementary data collected as part of the proposal, including the format of the associated documentation and the exclusive-use period (if pertinent);
- modalities of project follow-up, including the possibility to stop the project before its planned ending by decision of the investigators, or of the governing bodies of the Constances cohort; a clause may imply compulsory transmission to the Constances Director of already collected data; if applicable, contract with CASD;
- modalities of communication of results;
- rules concerning publication;
- financial clauses;

- appendices: copy of legal and regulatory opinions and authorizations; copy of the decision of the Scientific Committee and, when appropriate, of the Ethics Committee; declaration of agreement to comply with the Constances Charter.

2.6 ACCESS TO DATA: RESEARCH PROJECTS USING DATA ALREADY AVAILABLE IN THE CONSTANCES DATABASE

2.6.1 General case

Subject to the positive advice of the ISC, to regulatory and legal provisions, problems of confidentiality, ethics, professional practices, or property, all data collected by the Constances team and recorded in the cohort database can be transmitted to researchers whose proposal has been accepted. The Constances team will prepare, in collaboration with the requesting team, the data selected and supply them in the most appropriate form, as a function of the technical possibilities at the time.

Analyzes must relate only to what has been described in the proposal for a research project evaluated by the Constances ISC and then by the bodies involved in the legal and regulatory processes. Therefore, only the data described in the application can be requested from the Constances team. In case of a major extension of the initial project, a new application must be filed and new legal and regulatory steps be taken.

In the absence of an explicit prior agreement, only the director of the research project that seeks to use Constances cohort is authorized to request data from the cohort team.

The transfer of data supplied by the Constances team to any person other than those foreseen in the application is forbidden. At the conclusion of the study, the research project director must no longer use the data file supplied by the Constances team and have to destroy these data.

2.6.2 Particular case of genetic data

Because this type of data is governed by specific legal and regulatory provisions, projects intended to use it must comply with the specific conditions applicable at the time of application. The application must enumerate all measures taken to comply with these dispositions.

2.7 ACCESS TO DATA: RESEARCH PROJECTS INVOLVING THE COLLECTION OF SUPPLEMENTARY DATA

2.7.1 Modalities for the collection and safeguarding of the new data

Beyond the data collected by the Constances cohort team during normal cohort operations, supplementary data may be collected by investigators whose research projects are accepted. These data may be collected by questionnaires, dosimeters sent to participants, or by any other method authorized by the competent authorities. If the research project requires direct access (interview, examination, etc.) to cohort members, the operational aspects of this access must be defined in detail in the research project protocol.

Additional data collection is evaluated by the Scientific Committee based on scientific value, financial considerations and assessment by Constances investigators of the burden to the participant and balance to the Constances cohort as a whole.

> **Important note:** It is essential to contact the Constances team before submitting an access request involving the collection of additional data.
> Any additional data collection tool (questionnaire or other) must be approved by the Constances Director before legal and regulatory formalities are carried out.
> A copy of all correspondence sent to participants in the Constances cohort must be approved by the Constances Director prior to dispatch. This correspondence will be co-signed by the Constances Director and the Project PI.

No other information can be requested from cohort members other than that explicitly authorized as part of the accepted research project.

All precautions concerning potential authorizations, confidentiality, ethics, and professional practices must be complied with and described in the application form.

Data collected directly by the investigator belong to him/her, and he/she is responsible for conserving it. Nonetheless, after an appropriate period of exclusive use after the end of collection of data (set by written agreement in the above-mentioned agreement memorandum), the investigator of the research project agrees that the new data will be incorporated into the overall Constances database, in a usable form and accompanied by adequate documentation. The investigator who has collected these new data shall renounces its rights of exclusive use. The Constances Director may decide to not include these data in the cohort database if there is some concern with their quality. Rights on additional data collected directly by the investigator, including intellectual property, are specified in the above cited agreement memorandum.

2.7.2 Access by other researchers to supplementary data collected by investigators of other projects

One of the advantages of the openness of the Constances cohort to the scientific community is the possibility of mutualizing the data from the different research projects associated with the cohort. Access by researchers managing a project within Constances to new data collected by the directors of other associated projects is therefore encouraged.

When a researcher wishes to use complementary data collected for a specific project by another team, an agreement must be sought between the teams concerned. When agreement is reached, a document must be drawn up between the teams, specifying the data transferred, their intended use and publications; a copy of this document must be sent to the Constances Director.

Once decisions have been taken concerning data transfers between project leaders, these must be made through the Constances team, as the assignment of specific study numbers to the subjects included in each study makes it impossible to share individual data directly between projects.

> **Important note**: the transfer of individual data between different projects implies the completion of the usual legal and regulatory formalities.

2.7.3 Use of the new data transferred to the Constances cohort team after the exclusive-use period has expired

On transfer of these new data to the Constances team, the investigator who collected them renounces its rights of exclusive use. These data can then be used by all researchers, according to the same rules as for data collected by the Constances team.

2.7.4 Destruction of additional data transferred to the Constances team after the exclusive exploitation period

In order to avoid the uncontrolled dissemination of data concerning Constances participants, the research PI undertakes to destroy these data after the exclusive exploitation period (by sending a destruction report to the Constances team). If he/she wishes to reuse the data at a later date, he/she must submit a written request to the Constances team, which will archive all extractions.

2.8 FOLLOW-UP OF RESEARCH PROJECTS

For various reasons, the ISC or Ethics Committee may recommend that a project be terminated before completion. In the latter case, the Constances Director may request the transmission of any data already collected by the PI for integration into the Constances database; this data can then be used by all researchers according to the same rules as for data collected by the Constances team.

2.9 FUNDING OF RESEARCH PROJECTS ASSOCIATED WITH THE CONSTANCES COHORT

The implementation of projects using the Constances infrastructure implies a financial participation.

2.9.1 Research projects from academics funded only by public agencies

The costs of the work performed by the Constances cohort team to provide data to the investigator are assessed on a case-by-case basis and enumerated in the mentioned above agreement memorandum.

The specific costs related to the research project (potential collection of additional data, data analysis, etc.) shall be borne by the associated research project PI.

Where appropriate, the Constances cohort team can provide methodological support for obtaining funding from other sources.

> **Important note**: applications by the PI to funding bodies must include the costs of the work performed by the Constances cohort team, and no application can be made without the written agreement of the Constances Director.

2.9.2 Research projects funded by private companies

Any funding from a private for-profit organization, or supported by a private for- profit organization, must be reported. This applies at the time of the initial application and throughout the implementation of the project, whether proposed by an academic or private team.

For research projects funded by private companies, proposed either by an academic or by a private group, specific rules have been established. In these cases, it is necessary to contact the Constances Director before submitting an application.

2.10 SCIENTIFIC RESPONSIBILITIES

2.10.1 Scientific responsibility of the Constances team

The Constances Director is responsible for the quality of the data collected (completeness, validity) and for the verification of its consistency. The quality assurance protocol and the procedures for implementation and management of the database are to be made available to all research teams that so request.

2.10.2 Scientific responsibility of research project teams

The PIs of the research projects hold the intellectual property relative to their projects. They are responsible for the statistical treatment and analyses of these data, their scientific publication and all other dissemination of the results, in compliance with good epidemiological practices. In the case of supplementary data collection, the PI of each research project undertakes to provide to the Constances Director all the information needed to assess the quality of the data in order to decide whether they can be included in the Constances database.

2.11 DISSEMINATION OF RESEARCH RESULTS

2.11.1 Scientific publications

The results from the projects using Constances data must be made public through publication in scientific journals, reports, thesis, etc. If needed, a confidentiality period can be defined in the memorandum of agreement.

PIs of research project can publish their results and thus provide the scientific community with this information in any form they choose. They are entirely responsible for such publication and must take into account the standard professional practice rules in this area.

PIs of research projects are required to provide a copy of each manuscript to the Constances Director at the moment of its submission; the Constances Director can require the inclusion in the manuscript

of a statement that she is not responsible for the data analysis or the interpretation of the results.

Because of the very substantial scientific and technical activity of the Constances team in the development and management of the cohort, the signature of members of the Constances team, at least the project referent, must appear in any scientific publication or communication from these research projects, in compliance with the publication standard rules; these modalities shall be specified on a case-by-case basis between the PI and the Constances cohort Director.

A statement that the research was conducted in the Constances cohort must be included in every scientific publication or communication and the word "Constances" must appear in the title or at least in the abstract of any publication, as well as the DOI: doi.org/10.13143/inserm_constances

After publication, PIs are required to provide to the Constances cohort a copy of all publications and reports resulting from the project.

Important notes

Publications in scientific journals should be Open Access whenever possible.

Under French law, articles must be deposited in an open archive if the research from which they originate is at least half publicly funded. Research organizations and the majority of French universities use the HAL public infrastructure (https://hal.science/).

European law also requires articles to be published in an open archive if at least half the research is financed by European funds.

2.11.2 Acknowledgements and Funding

Acknowledgements and sources of funding for Constances are available on the Constances website on the “You're about to publish” page of the Scientific Area (https://www.constances.fr/en/scientific-area/youre-about-to-publish/).

Nominative acknowledgements of the researchers who contributed to the development of the Constances cohort protocol may also be added, depending on the data used in the research project. Where appropriate, the specific role of one or several other partners may be specified.

2.11.3 Reference to the Constances project

Every publication must refer to at least one of the methodological articles presenting the study protocol and published by the Constances team. Depending on the theme of the project, the references to be cited are those available on the Constances website on the “You're about to publish” page of the Scientific Area (https://www.constances.fr/en/scientific-area/youre-about-to-publish/).

2.11.4 Dissemination to cohort volunteers and the public

The research project PI is required to prepare, in liaison with the Constances team, documents intended to disseminate their results to the cohort volunteers and to both medical and non-medical audiences, especially via the Constances cohort website. At the request of the Constances Director, research project teams are also required to present the progress and results of their work during the annual scientific meetings of the Constances cohort.

Important note: no use of these results for commercial purposes, by research project PIs or their financial partners, is allowed without the written agreement of the Constances Director, after consulting the governing bodies of the Constances cohort.

2.11.5 Constances cohort website

The Constances cohort website makes public some information about the PIs of associated research projects. This information concerns the project (title, description, keywords, publications, etc.) as well as the name and postal address of the researchers.

2.12 COHORTE CONSTANCES

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