# LEOSS: GOVERNANCE, DATA USE AND ACCESS POLICY

Version 2.1, 28th of January 2021

## 1. INTRODUCTION

The Lean European Open Survey on SARS-CoV-2 (LEOSS) is an international registry set up in March 2020 to overcome the lack of knowledge on epidemiology and clinical course of SARS-CoV-2 infection. The aim of this registry is to further develop evidence-based diagnostic and therapeutic recommendations based on the collected data. Data collection is performed retrospectively and anonymously, while only data from standard of care treatment is documented (secondary data use). The LEOSS study group will provide basic statistics on included cases, sociodemographic characteristics, clinical courses, correlation of treatment strategies with the before-mentioned factors as well as time to event analyses on regular basis (daily - weekly). The latest statistics will be publicly available on https://leoss.net.

There are four variations of the LEOSS data-set:

- **Public (Public Use File, PUF)**: openly available condensed data-set including limited variables on all cases entered into LEOSS as defined by the study's protocol
- **Scientific (Scientific Use File, SUF)**: extensive data-set for research purposes with a vast variable set as defined by the study's protocol. Anonymization processes developed with experts will ensure patient anonymity by aggregating variables or dropping cases
- **Local**: the data-set of a specific study site that includes all records created by this specific site in the LEOSS database
- **Secure**: full data set, not for scientific use, waiting for second anonymization

This Data Use and Access Policy's main purpose is to define how the scientific data-set of the LEOSS registry can be requested from researchers and which criteria and conditions apply for acceptance of the data request. Details on the LEOSS governance and dedicated sections for the study site data-set as well as the public data-set are provided too.

The Data Use and Access Policy shall be re-evaluated when the total case count of the LEOSS registry surpasses 10,000.

## 2. ETHICS REQUIREMENTS

### 2.1. ETHICAL CONSIDERATIONS

The underlying principle of the LEOSS registry is that data collected as part of routine treatment should contribute to evidence-based medicine, and be leveraged to improve diagnostic and therapeutic recommendations as well as prognostic models for SARS-CoV-2 infected patients. However, regardless of whether this use is for quality improvements, data evaluation, or research, all activities must always be conducted according to ethical principles and guidelines**.** Secondary analyses of LEOSS data may warrant approval of the Institutional Review Board (IRB) based on local laws and regulations. Potential considerations that would require a formal ethical review include:

- Use of data beyond the initial scope or purpose of data collection in LEOSS
- Targeted data analysis involving minority groups which are separated from the main body of data

Investigators requesting data from LEOSS will have to guarantee that a formal IRB approval will be obtained prior to the analysis, if necessary (see Research Outline and Data Request form). The LEOSS study group does not take any responsibility for secondary data use.

## 2.2. PROTECTION OF ANONYMITY

Comprehensive measures have been taken to rule out the risk of re-identification for patients registered in the LEOSS study. Details on the respective measures can be found in the study protocol. Tailored datasets for secondary research use will be provided to researchers after acceptance (see below).

# 3. LEOSS GOVERNANCE

All centers caring for patients with SARS-CoV-2 infection and all medical and scientific societies with special interest in SARS-CoV-2 are invited to participate in this study and to use the data of LEOSS' scientific database. The community-based governance structure of LEOSS has the aim of allowing as dynamic and fast scientific use of the data as possible, while maintaining high scientific quality as well as responsible public communication.

## 3.1. PRINCIPAL COORDINATING INVESTIGATOR (PCI)

The Principal Coordinating Investigator (PCI) of the study takes responsibility for the overall conduct of the study. She or he will serve as speaker and make day to day management decisions. She or he will inform all levels of study governance on major developments and changes in policy or procedures on a regular basis. The PCI can vote in the Global Board of Investigators, and her/his vote can decide split decisions.

## 3.2. COUNTRY COORDINATOR

Country coordinators will liaison with scientific societies and other epidemiological studies in all countries contributing patient cases. They coordinate contributing centers and reach out to local government and interest groups on a national basis. In general, one or two coordinators per country should suffice. The country coordinators are elected by the National Board of Investigators upon formation.

## 3.3. GLOBAL BOARD OF INVESTIGATORS (GBOL)

Sites enrolling at least 10 patients and at least 2% of the overall study population recruited in the past 3 months (monthly evaluation) will be invited to send a delegate to the Global Board of Investigators (GBoI). If sites later fall below the threshold of 2%, members of the GBoI will retain membership status for one further year. During April and May 2020, recruitment numbers will be re-evaluated on a weekly basis, then on the last day of the month. Two extra positions in the GBoI will be created for ESCMID and/or EITaF board members and one for the PCI. The GBoI will vote on all major decisions, research proposals, and scientific publications. Should the PCI step down from her or his position, become unable to fill the position or receive a vote of no confidence by 2/3 of the GBoI, the GBoI can decide to elect a new PCI. During the early phase April/May 2020, votes have to be cast within two working days (Mo-Fr) based on email notice and there will be no quorum. Starting June 2020, the voting period will be extended to five working days.

## 3.4. GLOBAL SCIENTIFIC COUNCIL (GSC)

Each collaborating medical society/field that explicitly recommends documenting cases in LEOSS to its members is welcome to send up to two delegates to the Global Scientific Council (GSC). In case that medical and scientific societies are different institutions in a given field, each should receive one seat in the council. All collaborating medical societies of LEOSS are asked to contribute with their expertise to research projects as members of the GSC. The GSC will be informed about all changes of data items, requests for data and analysis, and publications and has a chance to comment in the same time-frame as the Board of Investigators. In case a research proposal has endpoints exclusively relevant for members of the GSC, these members may vote to block a request for a period of 6 weeks.

### 3.5. NATIONAL BOARD OF INVESTIGATORS (NBOI), NATIONAL SCIENTIFIC COUNCIL (NSC)

Countries counting at least 5 national sites and 100 registered cases are invited to call for a separate data access structure, and to convene a National Board of Investigators (NBoI) as well as a National Scientific Council (NSC). LEOSS will make country-specific statistics available to the national group to allow specific communication and analysis.

The NBoI can define it's own code of conduct, which must be voted on and reported to the LEOSS study group, otherwise it will default to the same procedures as in the GBoI with respect to the national case numbers. Upon convening the NBoI, a Country Coordinator is elected by simple majority. The NBoI has full autonomy on data use of patients documented in the respective country and can decide not to participate in projects promoted by the GBoI. The Country Coordinator must inform the LEOSS study team of planned national projects to allow planning of resources and connection with other projects.

At the discretion of the NBoI, additional councils such as an NSC may be convened.

Countries not fulfilling the requirements or not explicitly calling for a separate data access structure are automatically included in the global structures.

### 3.6. HEROINES AND HEROES OF LEOSS (HOL)

Participants of the LEOSS registry that have been significantly involved in the design or conduct of the study, can be named a Heroine or Hero of LEOSS and act as part of an informal board that receives all non-confidential information in the same way as the GSC and has the right to inform the GBoI of any comments they have. The GBoI will vote whether a contribution was meaningful enough to justify appointment.

## 4. REQUESTING THE PUBLIC DATA-SET OF THE LEOSS STUDY

The public data-set will be regularly and openly published on https://leoss.net. Before downloading the public data-set any user has to agree to the following public data set terms of agreements:

1. This work is licensed under the Creative Commons Attribution Non-Commercial 4.0 License and I agree to include a proper acknowledgment of the LEOSS study group in any work based on the dataset. To view a copy of the license, visit https://creativecommons.org/licenses/by-nc/4.0/

2. I agree to maintain the confidentiality of the dataset at all times and to not attempt to compromise or otherwise violate the privacy of the patients described.

3. I confirm that I have the necessary expertise to analyze and interpret the dataset based on statistical guidelines.

## 5. REQUESTING THE STUDY SITE'S DATA-SET

Each study site has the full rights to its own data-set. It can be requested any time by the study site coordinator from the LEOSS study group. The LEOSS study group will provide access to the full data-set of the respective study site within 5 working-days via an enrypted file transfer service. The survey provider QuestBack is working on a solution allowing direct download of all documented patients.

## 6. RESEARCH OUTLINE AND DATA REQUEST FORM

To request a scientific data-set, registration can be performed https://leoss.net, the project proposal form includes the following points:

- Responsible investigator and contact details of research group
- Outline of research goal in alignment with LEOSS protocol

- Methods of statistical analyses intended to be used
- Required LEOSS data elements for answering the research question

## 6.1. REVIEW PROCESS

**1. The request will be checked for formal issues by the LEOSS Project Coordinators (PCos) within three workdays. This administrative assessment will include the following points:**

a) Verification of the accreditation of the requesting researcher (track record in public health, epidemiology, infectious diseases or related clinical care)*
b) Check whether requesting researcher is a cooperating partner in the LEOSS study*
c) Check if goal of requested research aim is in alignment with the LEOSS protocol
d) Check for overlap with ongoing or previously requested research aims (submitted within the last 12 months)
e) Check whether primary or other key endpoints lie within the scope of one of the participating societies / specialties

*) Criteria marked with an asterisk serve prioritization, but will not cause formal exclusion

2. After administrative review, the request will be forwarded electronically to the responsible Board of Investigators (GBoI or NBoI) and Scientific Council (GSC or NSC) and, if considered non-confidential, to the HoL. The responsible boards will be chosen according to the kind of data requested:

a) Request of global dataset (data from all sites participating in study): Global Board of Investigators (GBoI) and Global Scientific Council (GSC)
b) Request of country-specific data for the country, in which the cooperating institute/partner is located: National Board of Investigators (NBoI) and National Scientific Council (NSC)
c) Request of country-specific data for countries without established NBoI and NSC: Global Board of Investigators (GBoI) and Global Scientific Council (GSC)

If the intended study lies within the scope of one of the participating societies / specialties (see 1e), the representatives of that specialty can use their right of postponement (see GSC/NSC) within the given timeframe.

### THE FOLLOWING VOTING OPTIONS WILL BE PROVIDED:

1. Accept request as it is
2. Accept request after revisions (necessary revisions should be specified)
3. Request additional time for review and discussion of complex request
4. Decline request (must provide reason)

### THE FOLLOWING POINTS WILL BE CONSIDERED DURING REVIEW OF THE RESPONSIBLE SCC/BOI:

- Feasibility of research aim based on LEOSS data elements requested
- Research goal in alignment with LEOSS protocol
- Methods of statistical analyses being used
- Presence of potential conflicts of interest

The LEOSS PCos will inform the requesting investigator about the decision via email. In case the request was accepted, the requesting investigator will receive details to get in contact with the LEOSS data management (see paragraph 4).

### 6.2. COMPETING INTERESTS:

Modern and standard epidemiology resulting in hazards-, risks-, or odds-ratios with P values and/or confidence intervals will be considered *competitive*, since repeated inference from the same data-set will inflate the risk of false conclusions and contradictory messages. Such projects should receive special consideration, since projects in this area with identical endpoints should be limited to one group. Such projects should be placed on defined time-lines with the option to reissue a project to a different group in case of project delays. Deep learning, other AI approaches, score calculations with complex or abstract models, where development of an inference machine can be considered the principle science of the project, are generally considered *non-competitive*. This means that time-lines can be more lenient and that multiple projects with comparable goals can be permitted concurrently.

### PROCESS:

The full process to request the use of LEOSS data is shown in the overview chart below (Figure 1):

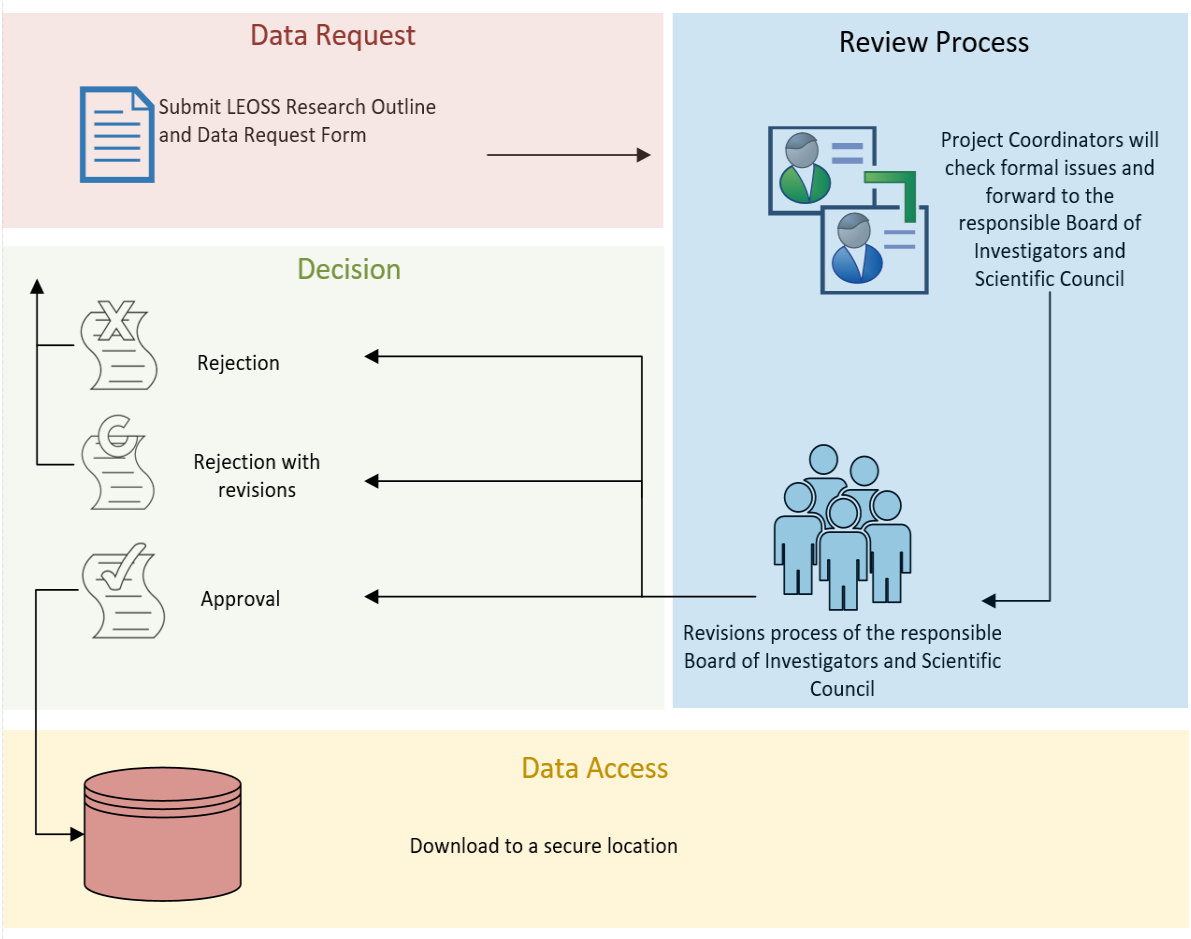


**Figure 1 - LEOSS data access process**

## 7. ANALYSIS OF REQUESTED LEOSS DATA

Analysis of LEOSS data should be performed in a secure location under control of the requesting investigator or via the LEOSS JupyterHub as an alternative. Everyone performing analyses is encouraged to share and publish statistical scripts for community peer review. Analysts and scientists are encouraged to coordinate activities with the BoI and GSC/NSC to align with the publication strategy of the BoI.

## 8. AUTHORSHIP POLICY

Peer-reviewed journal publications of the data set should follow the overall principle of having named authorships for the investigators behind the analysis and the project statistician and as many members of the contributing study sites as possible based on ICJME recommendations. Scientific members of the project infrastructure should also be invited in an appropriate manner. Members who cannot take part in one publication will receive higher priority for the next project. The named group will add “on behalf of the LEOSS study group” with a list of study sites which contributes more than 5 per mille to the analysed cohort and the LEOSS infrastructure in the acknowledgments.

## 9. EVALUATION OF DATA USE AND ACCESS POLICY

Once the study population includes 10,000 cases, this Data Use and Access Policy will be re-evaluated and revised consulted by the BoI and the GSC.

## 10. PUBLICATION OF DATA

The full anonymized data-set of LEOSS will be published on adequate scientific platforms six months after conclusion of the study.

## 11. RESEARCH OUTLINE AND DATA REQUEST FORM (EXAMPLE TEMPLATE)

| **Project Proposal LEOSS** | |
|---|---|
| Title | |
| Working group | |
| Contact details | |
| Background | |
| Aim of the project | |
| Methods | |
| Required data/variable (a list of the required variables will be filled out separately) | |
| Start- and end date of the project | |

## 12. DATA ACCESS APPLICATION FORM FOR SCIENTIFIC USE FILE

Title of the project: _____

Name, Affiliation, Position: _____

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1. I guarantee that the data provided will be only used for the purpose for which this request has been approved.
2. I guarantee that the data provided will not be used for analyses primarily targeted at describing effects or side-effects of drugs or medical devices or to replace or substitute any inference that requires a study based on drug or medical device regulations of the European Union and the local authorities.
3. I guarantee, that I will do not grant access to the data to any person not working under my direct authority, i.e. a dependent employee. It is my responsibility to ascertain that subordinates I assign with tasks related to the data adhere to the same rules as stated in this document.
4. Although comprehensive effort has been taken to anonymize the provided data, I will handle the file as if it was containing personal data and maintain security measures for the protection of the data extract that are equivalent to information security best-practices used for personal data and are compliant with the of the EU General Data Protection Regulation (use BSI guidelines).
5. I agree that I have expertise to analyze and interpret the LEOSS data based on statistical guidelines.
6. I will only use statistical models / inference systems in the manner described in my request and will not publish any statistical correlations without adequate controlling for bias and confounders.
7. I agree to recognize the contribution of the LEOSS study group and to include a proper acknowledgment in any work based on the LEOSS data.
8. I will include the LEOSS study group as coauthors on any publication or presentation arising from use of data from this project, as outlined in the LEOSS Authorship Policy or otherwise agreed upon in writing (electronic agreement acceptable).
9. Upon request, I will provide the LEOSS study group as well as the respective data protection control and supervisory authority with any material using the requested data for publication or presentation.
10. I will not try to re-identify patients included in the provided data-set.
11. I agree to notify the LEOSS study group as soon as I become aware of a breach of the terms or conditions of this agreement.
12. I guarantee to delete the provided data completely at the latest 10 years after having completed the above indicated project or directly in case of quitting the research project.

_____ _____

**Date, Place** **Signature of applicant**