Guideline

on using the technology platform in the

COVID-19 Research Network Lower Saxony (COFONI)

– Animal Models –

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COVID-19
FORSCHUNGSNETZWERK
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The German version of this guideline is the only legally binding version.
The translation is for information purposes only.

Content

Preambel

The basic idea of the COVID-19 Research Network Lower Saxony (COFONI) is the networked grouping of complementary site expertise around a central technology platform. The technology platform lays the scientific foundation for interdisciplinary research projects that were previously only possible to a very limited extent due to financial and technical limitations. The central technology platform is divided into three sub-areas (1) animal models and test systems, (2) research biobank and (3) research databases. They provide the research network with cross-cutting methods and animal models as well as data and biobanks with maximum efficiency for all participants to share.

The aim of the guideline for the use of the technology platform is to enable and promote the scientific use of the data collected and biospecimens obtained in COFONI projects. It is COFONI's concern to obtain the maximum benefit for medical research from the collected data and biospecimens.

This guideline includes the general regulatory purpose and specific regulations of the Technology Platform “Animal Models” (Chapter I) as well as general templates and recommendations for central elements of animal experiment applications to standardize the framework conditions in the “Performance of Animal Experiments” (Chapter II). The regulations which have been made apply to all COFONI-funded projects and COFONI Utilisation Projects in accordance with this guideline.

This guideline is valid for everyone who uses the Technology Platform “Animal Model” at the sites University of Veterinary Medicine Hannover, Foundation, TWINCORE - Centre for Experimental and Clinical Infection Research (Hannover), Helmholtz Centre for Infection Research (Brunswick) and German Primate Centre, Leibniz Institute for Primate Research (Göttingen). Users are researchers who in the framework of COFONI perform animal experiments at the respective involved institutions funded by COFONI or use any samples or data generated from such research. Users of the technology platform "Animal Models" comply with existing operating instructions and biosafety guidelines of the respective institution. The guideline does not regulate questions regarding utilisation and "intellectual property". This is left to a separate process to be coordinated with the participating institutions and project leaders and, if necessary, to individual agreements based on this.

I. Guideline on the Use of the Technology Platform Animal Models

§ 1 Definitions

(1) **COFONI Utilisation Project**: project that uses data and/or samples which were compiled within the context of a COFONI funded project.

(2) **Project leader**: applicants of the COFONI funded projects who have initiated the performance of the animal experiments in question.

(3) **Users**: scientists who would like to use the data, biosamples or findings from the COFONI funded projects further for supplementary scientific questions in a COFONI utilisation project.

(4) **Contributors**: numerous persons who are involved within the context of the projects in the preparation or performance of the animal experiments and further sample processing.

(5) **Data**: All collected and obtained data and findings like for example clinical data, biosample data, image data as well as analysis data.

(6) Biosamples: numerous biological materials which are gained from the animal experiments of the COFONI funded projects. These include tissue, blood, serum, plasma, saliva, bronchoalveolar lavage and materials further extracted from them, such as DNA/RNA.

(7) Findings: all information and derived variables obtained from submitted data and biospecimens and suitable for further analysis.

§ 2 Regulatory Purposes and Regulatory Needs

(1) With these regulations of use, a transparent, efficient and most fruitful use of the data and the biosamples is achieved within the framework of the freedom of research protected by the Basic Law, while at the same time safeguarding animal welfare and implementing the 3R concept ("Reduce- Refine-Replace") as well as the interests of the institutions involved in the implementation of COFONI projects.

(2) In addition to these usage regulations, the superordinated regulations listed below must be observed in the respective applicable version:

(a) guidelines on good scientific practice [1]
(b) the provisions of the cooperation agreement with the COFONI partners in the respective applicable version as well as other internal regulations
(c) requirements under grant law (grant letters and forwarding agreements incl. annexes)
(d) the COFONI Publication Regulations in the respective applicable version
(e) regulations for biosafety and animal welfare law and the documentation obligations required thereby

(3) The right of the data collecting/data obtaining institutions to use self-collected/self-obtained data and findings for internal purposes in research and teaching remains unaffected at all times. It is irrevocable, non-exclusive and free of charge.

§ 4 Guidelines of the Technology Platform Animal Models

(1) When processing or using the data, the existing operating regulations and biosafety guidelines as well as animal protection guidelines of the respective institution must be adhered to. Data maintenance with regard to biomaterials, genetically modified organisms and animal testing must be carried out in accordance with regulatory guidelines.

(2) All in vivo infection experiments in the case of SARS-CoV-2 infections must be performed under biosafety level 3 practices. Native specimen material that poses a risk of infection can only be stored in biobanks designated for BSL-3.

(3) For already published data, the general quality requirements apply in accordance with the “Guidelines on Good Scientific Practice”1. Access to and availability of generated material and data is regulated/guaranteed by the publication prerequisites of the scientific journals. Adhering to the FAIR principles of the publications is compulsory.

(4) For non-published, relevant data applies that these can be made available to the researchers and the users in COFONI by means of a databank like for example the REDCap databank in order to keep the number of animal experiments to a minimum.

[1] Codex “Guidelines on Safeguarding Good Scientific Practice“, DFG, DOI 10.5281/zenodo.3923601

(5) Samples with their availability, which have been generated in COFONI-funded projects or COFONI Utilisation Projects, shall be entered into a facility-specific database. The visibility of the samples in the database and the availability of these is regulated as follows

(a) Access to the sample database is granted to each potential user individually after approval by the respective project managers. For this purpose, the application for sample and data use of the Technology Platform Animal Models (Appendix 1) must be completed in advance and submitted to the contact person of the Technology Platform. The contact person will inform the COFONI coordination office (cofoni@med.uni-goettingen.de), which will report the use to the COFONI steering committee.

(b) Release of samples to users is granted after approval by the respective project leader, taking into account and complying with the valid operating instructions and biosafety guidelines of the respective facilities.

(c) The regulations specified in (a) also apply to all sample and data uses that extend beyond a previously approved COFONI project. Project leaders must indicate the extended use by means of Appendix 1

(6) Users of the data, biospecimens and results from the databases undertake to notify the respective project leader of the scope and type of use and also to deposit corresponding information in the database of the technology platform of the participating institutions.

(7) After completion of the analysis and processing of the data from the COFONI Utilisation Projects, users shall make the results available to the project leader immediately and in full in a suitable electronic form.

(8) The project leader communicates information about the use by other users to the contributors in the respective project in order to enable author attributions in accordance with the criteria of the COFONI publication regulations, if applicable.

(9) The project leader communicates information about the use by further users to the COFONI Coordination Office (cofoni@med.uni-goettingen.de).

(10) In connection with the provision, processing, storage and transfer of data or biosamples at the respective institutions, any additional expenses (e.g. material, personnel, transport costs) are generally to be borne by the users.

(11) Data or biospecimens will not be sold for a fee.

§ 5 Use and Access Committee (UAC)

The COFONI Steering Committee provides the permanent representatives of the Use and Access Committees (UAC). The UAC shall be informed by the COFONI Coordination Office about all COFONI Utilisation Projects by the provision of the request for sample and data use (Appendix 1). The UAC can ask questions regarding the COFONI Utilisation Projects to check the adherence of the corresponding guidelines and regulations.

§ 6 Scientific Publications

(1) Authorship of scientific publications

In accordance with the COFONI Publication Regulation, COFONI strongly recommends the coordinators/contact partners of the technology platform be offered to contribute to the

manuscript (author's credentials), as they make a large, important, long-term and time-consuming scientific contribution to the success of the COFONI technology platform.

(2) Details in the acknowledgement of scientific publications
In accordance with the COFONI Publication Regulation, the wording for a COFONI Utilisation Project reads:

"Data and/or samples were provided by the COVID-19 Research Network of the State of Lower (COFONI) from the COFONI data and sample collection funded by the Ministry of Science and Culture of Lower Saxony in Germany (14-76403-184)."

„Daten und/oder Proben wurden durch das COVID-19 Forschungsnetzwerk Niedersachsen (COFONI) aus der COFONI-Daten- und Probensammlung zur Verfügung gestellt, welche mit Mitteln des Niedersächsischen Ministeriums für Wissenschaft und Kultur (14-76403-184) gefördert wird."

II. Guideline on Performance of Animal Experiments

§1 Regulatory Purposes and Regulatory Needs

(1) The regulations made in Chapter II (Performance of Animal Experiments) serve the purpose of standardizing the framework conditions for the application of animal experiments within the Technology Platform Animal Models of the COVID-19 Research Network Lower Saxony in the interest of research.

(2) General templates and recommendations for key elements of animal experiment applications, such as scoring and experimental protocols, are intended to ensure better comparability of data and favor the quality of studies. Animal study application processes should be simplified and streamlined through standardized general templates and recommendations for specific items. Any changes in forms and laws will be adapted in a timely manner.

(3) In addition to these guidelines, the following superordinate regulations must be observed:

(a) The provisions of the cooperation agreement with the COFONI partners as amended from time to time including the annexes (such as Annex 4 Employee-Inventor Declaration) as well as other internal regulations.
(b) Animal Protection Act and the Animal Protection Experimental Animal Ordinance of the State of Lower Saxony in the respective current version available online.
(c) GV-SOLAS publications: e.g. animal husbandry, recommendation for administration of substances to laboratory animals in the respective current version available online.

(4) These guidelines are valid for everyone who would like to apply for animal experiments at the sites University of Veterinary Medicine Hannover, Foundation, TWINCORE - Centre for Experimental and Clinical Infection Research of the Helmholtz Centre for Infection Research (Hannover) and Deutsches Primatenzentrum GmbH - Leibniz Institute for Primate Research (Göttingen) within the framework of COFONI.

(5) This guideline serves the qualitative optimisation of animal experiments as well as the improvement of the comparability of animal experiments. This has a positive effect on animal welfare and the implementation of the 3R Concept ("Reduce-Refine-Replace").

(6) All in vivo experiments must be performed under BSL-3 conditions, which requires special regulation.

§2 Guidelines on Performance of Animal Experiments

(1) In general, applications for animal experiments must comply with the applicable Animal Welfare Act and the Animal Welfare Experimental Regulations.

(2) The recommendations of the GV-SOLAS on the conduct of animal experiments must be followed as far as possible for the application and conduct of animal experiments. Deviations must be specifically justified.

(3) In accordance with legal requirements, all applications are submitted for comment to the Animal Welfare Officer of the respective facility in which the experiment takes place.

(4) In addition, the applications are submitted to the management of the husbandry (§ 11 TierSchG Erlaubnis) of the respective facility for the definition of the husbandry conditions in accordance with § 7 para. 1 cl. 2 no. 2 TierSchG i.V.m. § 31 para. 1 cl. 2 No. 1j TierSchVersV with special consideration of the BSL-3 conditions before submission to LAVES. The management of husbandry (§ 11 TierSchG Erlaubnis) must give its consent to the performance of the experiment in the respective husbandry.

(5) Applications must be submitted to the appropriate COFONI technology platform contacts/coordinators at the respective facility prior to submission to LAVES, which will allow for reconciliation and standardisation of for example scoring, biometric design (type I and type 2 error, power, the biologically relevant difference and standard deviation), and husbandry conditions.

(6) Animal species-specific training for experimental participants is mandatory. For primate experiments where training on animals is not legally possible, training is provided by adequate substitute and supplementary methods. The respective individuals must be able to demonstrate, by means of certificates and/or proof of training and/or exemptions (attach testimonial), that they have acquired and can apply the required knowledge for the respective animal species and procedures.

(7) Where possible, standard protocols/procedures should be defined and used in animal studies. After consultation with the contact persons of the technology platforms, individual templates are available, which have to be individually adapted to the respective purpose of the animal experiments to be applied for. Furthermore, some points in the templates have to be adapted specifically for the respective institution. Standards should ensure the highest possible comparability of the following points and simplify the approval of the experiment applications for all persons involved:

   (a) Husbandry: see "Technical Information from the Committee for Animal Welfare in Laboratories (GV-SOLAS").
   (b) Implementation of the 3R Concept (such as "The Principles of Humane Experimental Technique"; European Directive 2010/63/EU; Animal Welfare Act; Animal Experimentation Regulations; handout from the Permanent Senate Commission on Animal Protection and

Experimentation at the German Research Foundation (DFG); Working Group Berlin Animal Welfare Officers; Arbeitskreis Berliner Tierschutzbeauftragte).

(c) Handling: see "Technical Information from the Committee for Animal Welfare in Laboratories (GV-SOLAS"). The current specific technical information for the respective laboratory animal species must be observed. Further recommendations for the protection of the staff and the welfare of the animals: the animals should be acclimatised in advance for at least one week (preferably two weeks) to the new environment, to the protective clothing provided in the experiment, to the handling and scoring. The stress of the animals should be reduced to a minimum and handling should be as contactless as possible (e.g., transferring rodents using tubes).

(d) Scoring (Score Sheet)

(e) Anaesthesia

(f) Euthanasia

(g) Substance applications: see "Recommendation for Substance Application in Laboratory Animals", GV-SOLAS

(8) Each animal experiment application is subject to a case-by-case review. Therefore, the explanations on the scientific indispensability, the indispensability of the animal numbers, the selected animal model and the expected burdens, and the harm-benefit assessment must be formulated on a project-specific basis for each individual case.

(9) For the animal experiment application, the following documents must be available as described in items (3) - (5):

(a) Score Sheet

(b) Financing Supplement

(c) Bibliography

(d) Template for recording results

(e) Biometric planning/expertise

(f) Statement of Animal Welfare Officer

(g) Non-technical Project Summary(NTP)

(h) Permits and proof of keeping according to § 2 TierSchG and § 1 TierSchVers and performance of the experiments (in case of already existing permit, indication of the file number is sufficient as proof)

(i) Load chart (optional)

(10) Evidence of "knowledge and skills required for the care or killing of animals or the planning or performance of animal experiments (TierSchVersV Annex 1 to § 2 paragraph 1 clause 1 no. 2, § 3 paragraph 1 clause 1 and § 16 paragraph 1 clause 1 and paragraph 3)" is required.

(11) All discussion contents and any communication of the following points should be forwarded to the coordinators of the technology platform of the respective facility for information:

(a) Personal communication with LAVES should only take place after consultation with the technology platform coordinators and corresponding contact person of the respective facility (see below) as well as the Animal Welfare Officer.

(b) Each change in the trial procedure must be submitted to LAVES by means of a separate trial change notification and approved as well as submitted to the corresponding contact persons/coordinators of the COFONI technology platform, the Animal Welfare Officers and,

depending on the facility, additionally the management of the husbandry before submission to LAVES.

(12) Irrespective of this guideline, the operating instructions and regulations of the respective facility where the experiments are carried out must be observed.

(13) The management of the animal experimentation project is fully liable to control as well as exclusively authorised to give instructions to the performers in the experimentation project and must have full access authorisation including the required biosafety training in addition to all performing persons in order to be able to perform their tasks within the framework of the project at any time. The management of the animal experimentation project is therefore actively involved as a cooperation partner in the respective COFONI projects.

(14) All anomalies/deviations that are not described in the approved animal experiment application must be reported immediately by the animal experiment management to the Animal Welfare Officer and, if necessary, additionally to the animal husbandry management, depending on the institution.

(15) The animal experiment project management is required to provide appropriate training (including scoring and specific measures) to all performers in the specific experiment project prior to the start of the experiments in a project kick-off meeting and to document the training accordingly.

(16) During the experiment, all experiment-specific scorings must always be documented in writing by the respective person performing the experiment, including daily checks by the experiment management or responsible persons named in the animal experiment application.

(17) All animal experiment data generated within the framework of COFONI must be stored centrally at the respective facilities where the animal experiment is performed and in consultation with the coordinators of the technology platform. This includes the submitted animal experiment documents, correspondence with LAVES, the information on the execution (incl. detailed protocols, time and personnel schedules), the raw data as well as the evaluation of the data (see Chapter I).

(18) The cooperation agreement between the COFONI partners regulates old rights (§ 6) as well as new rights (§ 7) (e.g. patent applications). Pursuant to § 7 (2) of the cooperation agreement, the COFONI partners which are universities are obliged to commission employees who fall within the scope of § 42 ArbnErfG with the implementation of a project or to involve them therein only after they have assumed the obligations arising from the cooperation agreement by means of a declaration in accordance with the sample attached as Annex 4 "Employee-Inventor Declaration". Annex 4 of the cooperation agreement must be signed by all participants who are employed at universities.

(19) The exact cost calculations of the execution of the trials must also be submitted to the contact persons of the technology platform.

III. Coming into Force

All coordinators of the Technology Platforms and the COFONI Steering Committee unanimously agreed to the guideline on the Use of the COFONI Technology Platform Animal Models; it came into force on 14.01.2022 and was updated to version 1.1 on 13.05.2022. The German version of this guideline is the only legally binding version. The translation is for information purposes only.

IV. Appendix

Appendix 1: Form for Request for Sample and Data Use

V. Coordinators of the Technology Platform Animal Models

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