Terms of Service
BIH Core Unit pluripotent Stem Cells and Organoids

Valid from 1.1.2023

These Terms govern your access to and use of BIH Core Unit pluripotent Stem Cells and Organoids (CUSCO) services and equipment. Our Services are offered subject to your acceptance, without modification, of all the terms and conditions contained herein and all other operating rules, and procedures that may be published from time to time by us. You agree that we may automatically upgrade our Services, and the Agreement will apply to any upgrades. Please read the Agreement carefully before accessing or using our Services. By accessing or using any part of our Services, you agree to become bound by the Agreement. If you do not agree to all the terms of the Agreement, then you may not access or use our Services.

Your Account

The use of our Services requires an account in the openIRIS system (http://iris.charite.de), hence, you agree to provide us with complete and accurate information when you register for an account and keep the information current. This is important because sometimes we may need to send you notable updates. You will be solely responsible and liable for any activity that occurs under your account. You are responsible for keeping your account information up-to-date and for keeping your password secure. You are responsible for maintaining the security of your account and you are fully responsible for all activities that occur under your account and any other actions taken in connection with our Services. You shall not share or misuse your access credentials. You must immediately notify us of any unauthorized uses of your account or of any other breach of security. We will not be liable for any acts or omissions by you, including any damages of any kind incurred as a result of such acts or omissions. Your account will be active for one year and can then be prolonged.

In addition, the following must be observed *before the account is created*:

a) Before use, a free consultation must take place to assess the need and scope.

b) Project-related support must be submitted using a project registration in openIRIS and include project title, description of the expected services, and the client.

c) Access to the Infrastructure and Services of CUSCO is approved only to the Users who have registered their projects and themselves as USERS via openIRIS system and receive the specific introduction by the CUSCO personnel.

Following account activation, you as a CUSCO user, agree to adhere to the following obligations:

a) to comply with the regulations of the user rules and the specific laboratory and equipment rules (see Service and Equipment).

b) to attend the annual safety instructions for the necessary laboratory safety levels.

c) to strictly follow the instructions of the CUSCO staff in the CUSCO rooms and when using the equipment.

d) to make the CUSCO staff aware of the existence of safety risks related to the experimental material (e.g., pathogenic, infectious, toxic, or radioactive properties or according to *Biostoffverordnung (BioStoffV)*).

e) if necessary, to provide evidence of corresponding notifications and approvals (here in particular the approval of the genetic engineering experiments to be carried out or experiments on animals or humans, if necessary, with the approval of the ethics committee) of research projects and experiments. Patient data are to be handled by the user in compliance with the relevant data protection regulations and are to be handed over to CUSCO exclusively in anonymized form.

f) any work with genetically modified organisms (according to Gentechnikgesetz (GenTG)) is only allowed after a prior approval with the CUSCO director.

g) if necessary, authorize CUSCO to perform the experiments.

h) Operate the equipment and perform the experiments only after the instruction of CUSCO staff.

Service and equipment

Within the framework of its available capacities, the CUSCO performs the following services in particular:

- Project consultation and support
- Isolation of primary cells from patient material
- Reprogramming of cells into human induced pluripotent stem cells (hiPSCs)
- Banking, characterization, and quality control of hPSCs
- Genome editing using CRISPR/Cas
- Establishment of differentiation protocols
- Provision of cells differentiated from hiPSCs
- Establishment of methods for organoid generation and analysis
- Provision of hiPSC reference cell lines
- Provision of reagents
- Provision of infrastructure and equipment
- Training

In addition, CUSCO manages access to and supports, the shared equipment (specific equipment available is listed in openIRIS).

Equipment managed by CUSSO is available to all CUSCO registered users. By accepting these Terms of Service, the users agree to adhere to the following rules of the equipment use:

a) Equipment access and training must be requested through openIRIS. Approval of access will be granted only to the users that completed the training.

b) All equipment available at CUSCO must be booked through openIRIS before use. Use of equipment without booking is strictly forbidden.

c) Equipment booking expires 30 min after the booking time has begun if the user is not present, but usage fees will apply.

d) In case the use time exceeds the booking time, additional time must be booked in openIRIS.

e) Bookings can be made up to a maximum of 14 days before planned use. Cancellation of a booking can be made up to 24 hours before the start of the booked period. Cancellations made after this time may result in usage fees if no other user books this period.

f) Note that repeated absence during booked time and/or use of device without booking will result in <u>user access cancellation</u>.

g) Users are responsible for immediate removal of data from the CUSCO computers. CUSCO is not responsible for data storage and safety. All data older than four weeks will be automatically deleted from the PCs without further notice.

h) It is not allowed to store any kind of data anywhere else on the CUSCO computers other than in the respective directories. All data in other locations (for example on the desktop) will be deleted without further notice.

i) Equipment manuals and accessories must remain with the respective device at any time (PDFs of manuals can be provided on request by CUSCO).

j) In case of a device malfunction, the CUSCO personnel must be immediately informed. Error messages must be copied or documented by a screenshot and uploaded as an "issue" through openIRIS.

Liability

All users are liable according to the legal regulations. This applies in particular to damage caused by failure to comply with the obligations incumbent on the users, by non-clarification of security risks or by non-compliance with binding instructions issued by the staff. The responsibility for the quality of the incoming material or incoming data of a project lies with the user.
The liability of CUSCO towards users is limited to intent and gross negligence. The CUSCO do not assume any warranty for the test material.

Publications

Users are obliged to take due account of the work of CF Stem Cells in publications following the generally accepted rules of scientific practice:

a) In principle, any external work, e.g., the work of CF Stem Cells, must be identified at the appropriate points in scientific work, e.g., in the material and method part. The payment of fees or charges resulting from service <u>does not</u> replace the corresponding labelling of technical or scientific work.

b) Depending on the scope and complexity of the work or in the case of corresponding collaboration agreements, the CF Stem Cells or individual employees must be considered by mentioning them in the acknowledgment[1] or within the framework of a co-authorship. Co-authorship of CF stem cell scientists usually requires a scientific contribution that goes far beyond the mere performance of experiments or analyses.

c) The CF Stem Cells should be notified before submission of the publication. If necessary, the corresponding files must be made available for inspection beforehand. Also, a copy of the publication in electronic form must be sent to the head of CF Stem Cells after publication.

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[1] Please refer to the following formulation example: „This work was supported by the Core Unit pluripotent Stem Cells and Organoids of the Berlin Institute of Health (BIH) at Charité – Universitätsmedizin Berlin."

Exclusion and restriction of use

In particular, the approval for use may be refused, revoked, or further restricted if

a) no proper application has been submitted

b) the information in the application is not or is no longer correct

c) a fixed usage fee is not paid

d) the regulations for use, the specific laboratory and equipment rules or instructions of the CF Stem Cells staff are violated

e) CUSCO is not mentioned or adequately considered in publications according to chapter „Publications".

The user is not entitled to claims for damages due to the refusal, revocation, or subsequent limitation of admission.

Service Catalogue / Usage Fees

- The fees to be paid by the users for CUSCO services can be found in the current list of fees. Special rates apply to external users.
- For projects regarding technology or method development, including feasibility studies, within the framework of a cooperation b, the prices can be reduced or, in exceptional waived at CUSCO staff discretion. Co-authors of CUSCO are expected to be considered in the resulting publications according to their scientific or technical contributions.
- The user fees are charged after receipt of the services. In the case of internal customers, this is done via internal service charging (interne Leistungsverrechnung, ILV). External users always receive an invoice.
- Project leaders can request user fees in funding applications (in DFG applications under the item „Requested other costs", CUSCO is registered in the DFG Database). The team of CUSCO will be available to assist you with the appropriate cost estimation during the application phase.
- CUSCO reserves the right to issue a partial charge on the failed services. Due to underlying biological limitations, CUSCO is unable to always guarantee the success of the following services:
  - ➢ Reprogramming
  - ➢ Genome editing
  - ➢ Differentiation

CUSCO staff guarantees to perform necessary experimental steps to fulfil the service request. However, in an unlikely event of the service failure, the number of further attempts will be limited as defined by individual service descriptions and the services will be continued only after an explicit confirmation from the User. The user agrees to the payment of charges according to the steps completed by CUSCO in the attempts to fulfil the service.

➔ *The current list of fees is attached as Appendix 3.*

Severability clause and validity of the user regulations

The user regulations are binding for all users of CUSCO. Agreements beyond the scope of these Terms of Service are made with external users and must be issued in writing. The Terms of Service are valid in the respective version without limitation until they are replaced by an updated version.

Contact

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Appendix 1: **Specific rules for equipment use**

MACSQuant VYB:
- Users must use personal accounts. Account sharing is not allowed.
- Personal account will be assigned immediately after user introduction.
- Calibration of the machine is performed by the CUSCO personnel once a month.

MACSQuant Tyto FACS Sorter:
- Users must use personal accounts. Account sharing is not allowed.
- Workspace set-up and advanced training cannot be provided by CUSCO and must be requested by the user to Miltenyi directly. CUSCO only provides access to the Sorter, an account, and general recommendations for equipment use.
- Accessories, like Tyto magnet for cartridge load, must be used at CUSCO lab. It is strictly forbidden to remove equipment from CUSCO lab space.
- Data must be saved in a folder named after the group/username in the following location: "D:> cap_0.5.1.4182005e > folder *[username]"*

QuantStudio 6:
- Data must be saved in a folder named after the group/username in the following location: "D:\Users\Public\Documents\QuantStudio Real-Time PCR software\experiments\[Group Name]\[user name]"

Opera Phenix, Operetta and Columbus Server
- No gloves are permitted when working with the system.
- The computers operating this equipment must not be switched off. It is critical for the instrument operation that the computers stay active.
- Use of the computer for applications other than device control is not allowed.
- The use of USB storage devices is prohibited.
- New users must be trained in the operation of the unit by an experienced user. After this training, CUSCO staff will evaluate the ability of the user to operate the unit properly and permit access.
- Measurement data must be transferred to the Columbus server (http://columbus.charite.de) or OMERO Server (https://omero.charite.de) immediately after the measurement and removed from the measurement computer.

Leica inverted Microscope (User Lab):
- Data must be saved in a folder named after the group/username in the following location: "Dieser PC > Dokumente > Folder [Group Name] > [username]"
- All image data should be moved immediately after acquisition to the central OMERO Server (https://omero.charite.de) of the Charité

Picking hood Microscope (User Lab):
- Data must be directly saved in external source (USB stick) and/or deleted immediately from the computer hard disk after transfer.

Chromium Controller
- Only the use of the Controller and accessories ad-hoc are allowed (chip holder and vortex with adaptor for beads rack).
- Accessories must be used at CUSCO lab; it is not allowed to move them somewhere else.

Molecular biology work bench rules

- Molecular biology bench must be booked via openIRIS when Chromium Controller is used.
- This bench is reserved for single cell experiments and any molecular biology work like RNA isolation, qPCRs.
- Pipettes marked as "molecular" MUST not be used for other protocols (WB, IF, etc.).

Cryostat

- It is mandatory to clean up the device after use with ethanol 70% as it was instructed during the training. Remnants of embedding medium can damage the device.

Leica LSM SP8

- Use of the computer for applications other than device control is not permitted. Furthermore, the use of USB storage devices is prohibited.
- All image data should be moved immediately after acquisition to the central OMERO Server (https://omero.charite.de) of the Charité

Appendix 2: **Specific rules for use Cell culture labs**

- It is mandatory to book cell culture safety cabinet in openIRIS before use. In case the use time exceeds the booking time, additional time must be booked in openIRIS.
- Use of PPE (lab coat and gloves) is mandatory in the cell culture labs.
- User responsibilities:
  - Refill general consumables, for example: 70% ethanol, paper tissues, glass pipettes, plastic material, etc.
  - Dispose of trash as indicated during lab introduction (white bins, yellow glass containers, already full trash bags).
  - Empty liquid waste (vacuum container).
  - Inform CUSCO personnel if reagents or consumables are running out (use the white board outside of the cell culture room to leave notices). Provide enough time before the material is completely consumed.
  - Inform CUSCO personnel if any issue with equipment or space is encountered.
  - Keep safety cabinets, incubators, water bath and general space clean.
  - Re-fill water in incubator if needed using deionized autoclaved water (red cap bottles).
  - Only pipette tips with filter are allowed in the cell culture safety cabinets. Please store only one box of pipette tips per size for each bench and make sure they are closed properly when removed from the safety cabinet.

- The usage of reagents provided by CUSCO (e.g., media, supplements) must be documented by each user (list on fridge) according to the amount pre-ordered via openIRIS.
- It is not allowed to stock alarge number of aliquots of reagents from the user projects in the fridge/freezer of the user lab. Keep only what is needed for a month. Space is limited.
- All reagents, plates, boxes, etc. must be properly labelled. CUSCO personnel will discard all unidentifiable material without further notice.
- It is not allowed to store samples (DNA, RNA, cell pellets, imaging plates, etc.) in fridge/freezer of the user lab for long term. When a user is not working in the facility anymore (not active) and after notification, we will remove and discard all reagents/samples of the user. Do not store any belongings on the benches/cupboards, they will be removed. It is a common working area.

- After completion of work:
  - Clean bench and disinfect the surface with 70% ethanol!
  - Clean the tube of the pump first with deionized water and subsequently with 70% ethanol after usage
  - Switch off lamps of the microscopes according to the introduction!
  - If necessary (last user in the cell culture lab), switch off the bench, pump, water bath and microscope.

- The following materials will be provided by CUSCO and are included in the bench usage fee:
    - Serological Pipettes (5ml, 10ml and 25ml)
    - Falcon Tubes (15ml and 50ml)
    - Plates (6-wells and 12-wells)
    - Filter Tips
    - Ethanol
    - Yellow waste bins
    - Gloves
    - EDTA solution
    - Eppendorf tubes

    Furthermore, the following reagents are provided but must be purchased in openIRIS prior use:
    - Vitronectin
    - ROCK inhibitor
    - mTeSR medium
    - E8 medium

Appendix 3: **Price list of CUSCO (valid from 01.01.2023)**

Description	Unit	Preis [€]
Generation of iPSCs, Banking and Characterisation		
Primary cell Isolation	Donor	90,00
Derivation of iPSCs from primary cells	Donor	3580,00
Banking of iPS cell line (48 vials)	cell line	610,00
QC and Characterisation - full Panel	cell line	2110,00
QC and Characterisation - reduced Panel	cell line	1140,00
Cell Line Identity (STR Analysis)	cell line	140,00
Virtual Karyotyping using a SNP Array	cell line	250,00
G-Banding Karyotyping	cell line	430,00
Morphology and Viability	cell line	280,00
Sterility and Mycoplasma testing	cell line	70,00
Marker for undifferentiated iPSCs (IF)	cell line	310,00
Marker for undifferentiated iPSCs (FACS)	cell line	370,00
Differentiation capacity of hPSCs	cell line	610,00
Confirmation of gene editing	cell line	80,00
Virologic testing of cultured cells	cell line	480,00
Differentiated Cells and Organoids		
Generation of endothelial cells	BATCH	1230,00
Generation of neural stem cells	BATCH	1360,00
Cerebral organoids - StemCellTech Kit	BATCH	1440,00
Gene editing and complex projects		
Supervision	hour	36,00
CRISPR Design	cell line	180,00
gRNA efficiency testing	cell line	660,00
CRISPR experiment	cell line	530,00
Single cell cloning with IOTA	cell line	910,00
Clone Validation	cell line	1510,00
Provision of reagents		
E8 Media (500ml) - own production	BOTTLE	111,00
mTeSR Media (500ml) - own production	BOTTLE	140,00
mTeSR Media (500ml)	BOTTLE	393,00
Geltrex Aliquots (10 ml)	Aliquot	83,00
Vitronectin Aliquots (600 µl)	Aliquot	86,00
ROCK Inhibitor Y-27632 (1 ml)	Aliquot	66,00

Provision of cells		
Provision of live iPSCs	WELL	20,00
Cryopreserved iPCSs	VIAL	72,00
Cryopreserved iPCSs - own bank	VIAL	13,00
Cryopreserved iPCSs - external	VIAL	344,00
Cryopreserved Neuronal Stem Cells	VIAL	27,00
Cryopreserved Endothelial Cells	VIAL	43,00
Devices		
FACS Analyzer MACS Quant VYB	hour	13,00
FACS Sorter MACS Quant Tyto	hour	26,00
Real-time PCR Quantstudio6	hour	8,00
10X Chromium Controller	hour	63,00
Leica Confocal SP8	hour	13,00
Opera Phenix High Content Screener	hour	16,00
IsoCell	hour	27,00
TapeStation	hour	8,00
Incucyte SX5	hour	13,00
Cell3Imager Duos	hour	13,00
Bench fee - User-Lab	hour	10,00
Training		
Equipment training	hour	42,00
Hands-on training - basic hPSC culture	training	540,00