User Guidelines for
HT-MS | High Throughput Mass Spectrometry Core Facility

1. Preamble

In 2019, the Core Facility "High Throughput Mass Spectrometry" (short: HT-MS) was founded as a Core Facility, and thus as a central research service provider of the Charité, to meet the increased demand for large proteomic and metabolomic sample series in fundamental biomedical research. The HT-MS focuses primarily on quantitative proteomics. To this end, automated sample preparation methods, as well as ultra-high-throughput measurement techniques are developed and applied.

The facility is specifically designed to analyze large sample series (> 500 samples) as required for systems biology experiments as well as clinical and epidemiological studies. These include the analysis of body fluids such as plasma, serum, urine and cerebrospinal fluid, cells and tissue. The facility extends the range of services already available through the BIH Core Units Metabolomics and Proteomics.

2. Contact person

Only qualified and trained staff operate the equipment. The Core Facility is closely linked to the Institute of Biochemistry and the research group "Biochemistry and Systems Biology of Metabolism". The synergy in technical and personnel resources secures the equipment of the CF and ensures operation and technical support of the devices (e.g. maintenance).

Scientific and project management
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The Core Facility is represented via the following websites:

https://biochemie.charite.de/facilities/ht_ms_high_throughput_mass_spectrometry_core_facility/
https://iris.charite.de/Landing/Resource/9136

In case of damage/breakdown and unavailability of facility staff, contact the CFM: 030-450-575444

3. Equipment

Name *manufacturer; year of purchase*	***Description***	***Usage time per year***	***Assignment***
Biomek i7 *Beckman Coulter 2019*	Pipetting robot for sample preparation with 96-channel pod and robotic arm, plate reader, barcode scanner, shaker, thermal shaker, wash station, fan	2000 hrs	Charité core-funded
Biomek i5 *Beckman Coulter 2020*	Pipetting robot for reformatting samples	1000 hrs	BUA Link-Lab
LE220Rsc *Covaris 2020*	Focused ultrasonic sonicator protein extraction	1000 hrs	BUA Link-Lab
TripleTOF 6600 / 1290 Infinity II LC *SCIEX / Agilent 2020 / 2020*	Hybrid quadrupole-time of flight electrospray mass spectrometer / normal flow chromatography system	750 hrs	SCIEX; collaboration
TripleTOF 6600 / 1290 Infinity II LC *SCIEX / Agilent 2016 / 2020*	Hybrid quadrupole-time of flight electrospray mass spectrometer / normal flow chromatography system	750 hrs	BBSRC (AG Ralser)
timsTOF Pro / Ultimate 3000 RSLCnano *Bruker / Thermo Scientific 2020 / 2020*	Hybrid trapped-ionmobility-quadrupole-time of flight electrospray-massenspektrometer with ion trap mobility / nanoliter flow chromatography system	250 hrs	MSTARS (AG Ralser)
timsTOF Pro / Ultimate 3000 RSLCnano *Bruker / Thermo Scientific 2020 / 2003*	Hybrid trapped-ionmobility quadrupole time of flight electrospray mass spectrometer with ion trap mobility / capillary flow chromatography system	250 hrs	MSTARS (AG Ralser) / BIH
Q Exactive Plus / Ultimate 3000 RSLCnano *Thermo Scientific 2016 / 2016*	Hybrid quadrupole-orbitrap electrospray mass spectrometer / nanoliter flow chromatography system	2000 hrs	DFG GG 91b (2016)
Agilent 6470 / 1290 Infinity *Agilent 2016 / 2016*	Triplequadrupole electrospray mass spectrometer / normal flow chromatography system	250 hrs	ERC (AG Ralser)

The location for all devices is at Charité Campus Mitte, Charitéplatz 1, 10117 Berlin; internally: Charité-CrossOver Virchowweg 6.

4. Usage models

The service of the facility can, in consultation with the user, cover all areas from experimental design, sample preparation, measurement, raw data analysis, statistical and functional evaluation—or advise the user in this respect. It is important to us that the mass spectrometric analysis is understood as part of a workflow for which the quality of the preceding and subsequent work is essential.

The use of the Core Facility will be possible as follows, depending on the service demanded and the user's requirements:

- Service model / operation

  The service model allows the client to use the workflow of the mass spectrometric analysis as a complete package, including experimental design, sample preparation, measurements and elementary data evaluation. Services can also be booked independently, e.g. only the measurements on the instrument, with sample preparation and data evaluation performed by the user—if necessary with support from the Core Facility and in compliance with guidelines communicated to the user. Advanced data analysis (see § 7.8 & § 8) can be offered as a service only if sufficient capacity is available. A data analysis plan would need to be agreed on with a defined time frame and clear deliverables. Scientific interpretation of the results is not considered as service.

- Cooperation model / application operation

  Only qualified users will be able to make direct bookings of large-scale equipment.

5. User / Access

The core facility provides services to both internal and external users. Operation and technical support for the equipment are provided by Core Facility staff and qualified personnel assigned to the Core Facility.

Qualified users may also use equipment themselves should this be beneficial to the successful completion of a project. The assessment of their professional qualifications is the responsibility of the Core Facility. For equipment used for sample preparation, this can be acquired through instruction or training.

5.1 Prioritization

The Core Facility HT-MS can be used by the following groups in the following priority and with different fees:

(1) highest priority	Projects of the researchers of the Charité and associated institutions
(2) medium priority	Projects of other academic (non-profit) institutions
(3) lowest priority	non-academic projects

6. Availability of equipment

The Facility aims for maximum utilization of the equipment. Independent use on weekends and holidays by external qualified users is precluded.

7. Project realization

7.1 Project request

New projects or requests for individual measurements need to be made via the OpenIRIS portal (https://iris.charite.de/Landing/Resource/9136). We require the client to fill a questionnaire before the initial project meeting. The information is then used in the meeting to discuss the feasibility and scope of the project, the requirements for necessary equipment, service, safety aspects and any training that may be required for the project. Subsequent projects are usually submitted via OpenIRIS based on a brief project outline and are reviewed and approved by Core Facility management. The Core Facility decides which method is suitable for the desired investigation.

A cooperation (with co-authorship in case of a publication) with the staff of the Core Facility might be beneficial in case of special requirements, e.g. development of new protocols.

7.2 Project evaluation and prioritization of projects

The projects are evaluated and prioritized according to their feasibility as well as the scientific objective and relevance by the management of the Facility and, if necessary, after consultation with the User Council/Advisory Board. The Facility can only accept projects that can be realized with available methods and equipment. In general, samples are scheduled for analysis in the order of their date of complete receipt. This includes confirmation of the prepared proposal with planned deliverables, delivery of samples that are checked against a complete and accurate sample list, and a complete listing of relevant metadata. In the event of capacity limits, the samples will be processed according to the order of priorities mentioned under Section 5.1 and above. In the case of capacity limits, the decision on prioritization lies with the User Council.
If data are required for particularly important reasons, e.g. for the re-submission of a manuscript, these samples will be analyzed with priority at the request of the user.

7.3 Quotations

After the project has been approved, the facility management creates a quotation based on the project summary and the first discussions. The respective offer, as well as the user regulations, must be signed and handed over to the facility before the start of the project. The quotation includes the scope of the service, when the service is provided by, and a first calculation of fees. Internal projects must indicate the cost center on the quotation. It needs to be signed by the project manager and the person responsible for the cost center. Quotations for external clients need to state a billing address. The calculated fees are an estimate and can change according to actual incurred costs and effort. If it is likely that fees deviate more than 20% from the offer, the project manager will be informed in order to discuss a continuation, adjustment or, if necessary, termination of the project.

7.4 Usage time / booking

Qualified users can book services on OpenIRIS. The booking needs to be approved after consultation with the person responsible for the equipment and in consideration of other projects.

7.5 Training

Instruction and training are based on the qualification of the person. The personnel and material costs are allocated to the users based on the cost catalog in § 8.

7.6 Cancellation

In case of cancellation of a scheduled project, the Core Facility reserves the right to charge all material costs already incurred as well as work performed, such as project management.

If the booking of a device is not canceled at least 24h before use, the full price will be charged.

7.7 Sample management

Sample transfer

Users must provide a complete sample description including relevant metadata and instructions for safe handling and storage.

It is the responsibility of the project manager to organize sample transport in a way that guarantees sample integrity as well as necessary safety precautions, e.g. personal protection and prevention of accidental release. The Facility can assist in the planning.

Sample drop-off is possible only after prior notification and confirmation of the appointment (Tel.: 030-450-528317, contact via OpenIris).

Samples can be shipped to the Core Facility. We expect to receive a tracking number to monitor shipment.

Core Facility - High Throughput Mass Spectrometry
Charité - Universitätsmedizin Berlin
Charitéplatz 1, 10117 Berlin
(intern: Virchowweg 6, Geb. 2360, R. 04.312)
Tel.: 030 450 528317 / 030 450 528415

Storage

The samples are stored under the agreed conditions, which ensure the integrity of the samples as best as possible. A sample management system allows clear allocation and tracking of the sample and its derivatives. Storage is usually only possible for the duration of the service performance.

Destruction and return

Samples and their derivatives will be destroyed or returned upon completion of the project and written confirmation. Early destruction or return may be requested by the user at any time. The Facility reserves the right to charge for labor and shipping costs.

7.8 Data management

Data storage

Raw data are transferred to a server 20 min after complete recording. At this stage, data can still be modified or deleted (read/ write rights).To ensure the integrity of the file, a CheckSum is calculated beforehand and confirmed after transfer. If necessary for further use, files are automatically converted to the desired format. Before the file is copied to a storage server for permanent storage, the correct naming and completeness of the study is checked. Eventually, the raw data are deleted from the operating computers after the integrity of the files on the storage server has been verified once again. Clinical data, as well as communications with clients, are stored on the Charité servers in a standardized directory structure. Each study receives an identification number for this purpose. The data can only be read by members of the Core Facility and assigned personnel. For data exchange with clients, Charité internal read/write rights can be set on special incoming and outgoing folders.

Data transfer

For the transfer of measurement data, users are provided with a transfer server with individual server segments specially set up by the IT division for the Core Facility. These segments are located on a server managed and secured by Charité and only pre-approved users are authorized to access them. The data stored on these individual segments can be transferred to the user's own storage media/server locations. This prevents the use of unsuitable media (i.e. transportable, non-encrypted hard disks) for data transfer. Raw data, without clinical or other metadata, are automatically transferred to a secure server at the Berlin Institute of Health. Each user is responsible for the permanent storage of the data; this is also specified in the usage regulations. However, the Core Facility can advise users on the necessary storage space and also involve the IT department of the Charité in this regard. The latter is responsible for providing sufficiently secure storage space.

Data deletion

The sample documentation is stored for at least 5 years in the Core Facility Mass Spectrometry. All data are available to the users. They can be transferred at any time and deleted if desired. It should be noted that large amounts of data are generated and therefore appropriate storage media are required. The raw data is stored permanently. These do not contain any relevant project data in order to exclude misuse by third parties.

Data analysis

We see data analysis as an essential part of mass spectrometric analysis. The Core Facility identifies appropriate programs, tools and bioinformatic methods that are used in a standardized way to guarantee the quality of the analysis and to facilitate comparability between different experiments and studies. The Facility service provides raw data processing (computational mass spectrometry) and elementary bioinformatic analysis of the data. This typically includes quality control and outlier analysis, normalization, imputation, an analysis of provided metadata, and exploratory evaluation.

Advanced data analysis can be offered as a service only when sufficient capacity is available and according to a written agreed data analysis plan with a defined time frame and deliverables. This includes, but is not limited to, statistical modeling, integration of different data sets, advanced exploratory and functional analysis, and development of models e.g. for classification or prediction.

7.9 Miscellaneous

Only genetic safety level 1 and biological safety levels 1 and 2 samples can be accepted by the Facility unless they have been inactivated by approved methods. It is also desirable that samples of safety levels 2 are inactivated before sample transfer, if the method is compatible with the workflows of the Core Facility.

It is the responsibility of the project leader to comply with all necessary requirements in the areas of animal welfare, ethics committee, data protection, biological and genetic safety etc. and to ensure necessary measures. The Core Facility High Throughput Mass Spectrometry reserves the right to reject or cancel projects if these requirements are not fulfilled. Costs already incurred will be charged to the users.

8. Service catalog/usage fees

The use of the services of the Core Facility High Throughput Mass Spectrometry is chargeable for all users. For internal billing via ILV, a cost center to be debited and, in the case of external users, a billing address must be specified on the quotation.

Fees are calculated individually, based on material costs and required working hours. The fees are calculated as an example, for Charité internal service fees, for all offered services and experiments with 80, 160, 480 and 960 samples. Material costs for sample management, sample preparation, measurement and logistics are charged to the client. The prices are updated regularly, based on the purchase costs. The associated work is divided into administration, sample preparation, instrumental analysis, computational mass spectrometry, and data analysis. The hourly rates are calculated based on assigned personnel. Because the workflows are specifically designed for large numbers of samples, costs for smaller studies cannot be substantially reduced.

Invoicing takes place after completion of the project and for larger or long-term projects at the end of each quarter. The user fees are to be paid within 14 days after receipt of the invoice.

Support for grant application

Project leaders can request the user fees in funding proposals (in DFG proposals under the item "Requested other costs"). The scientific management of the Core Facility will be happy to assist you with the corresponding cost estimate in the application phase.

In general, the flat rate (Pauschale) as suggested by the DFG for mass spectrometry is not appropriate for large-scale, high-throughput studies, and its use is mandatory. Costs for our services can be fully compensated, but need to be listed in detail to allow transparency. We are happy to provide you with a cost calculation that can be attached as appendix/supplement to your proposal.

As a rule, the project should be discussed with the facility before submitting the application.

SERVICE	DESCRIPTION	INSTRUMENT	COST PER SAMPLE PER SAMPLE SET OF*			
			80	160	480	960
PLASMA AND SERUM PROTEOMICS	200 – 300 proteins in 5 min	SCIEX 6600 TripleTOF	40 €	25 €	20 €	15 €
MICROBIAL PROTEOMICS (IN-SOLUTION DIGEST)	High abundance proteome in 5 min	SCIEX 6600 TripleTOF	45 €	30 €	25 €	20 €
CELLLINE BASED COMPOUND SCREENING	~ 4000 proteins in 5 min	SCIEX 6600 TripleTOF	45 €	30 €	25 €	20 €
TISSUE PROTEOMICS FRESH FROZEN & FFPE	~ 2.500 proteins in 5 min	SCIEX 6600 TripleTOF	40 €	30 €	25 €	25 €
	~ 4000 proteins in 2 hrs	Thermo Scientific Q-Exactive Plus	50 €	40 €	35 €	30 €
	~ 6000 proteins in 2 hrs	Bruker timsTOF Pro	50 €	40 €	35 €	30 €
SCREENING FOR CHANGES IN FREE AMINO ACIDS	19 proteinogenic, 6 additional amino acids; no cysteine	Agilent 6470	35 €	20 €	15 €	10 €
SCREENING FOR CHANGES IN CENTRAL METABOLISM	65 metabolites of glycolysis, TCA, PPP, cofactors, nucleotides, amino acids in 11 min	Agilent 6470	35 €	25 €	20 €	15 €

Costs do not include data analysis or project administration etc. and refer to sample preparation and mass spectrometric measurement, as well as raw data processing.

Description *Code*	***Fees Cat. I ILV***	***Fees Cat. II academic projects***	***Services***
Data Analysis *DA*	51 €	74 €	Data Analysis (DA) includes, but is not limited to, quality control and outlier analysis, normalization, imputation, metadata analysis, and exploratory evaluation. Advanced data analysis can be enabled as a service only if there is sufficient capacity and according to a written agreed data analysis plan with defined time frame and deliverables. This includes, but is not limited to, statistical modeling, integration of different data sets, advanced exploratory and functional analysis, and development of models e.g. for classification or prediction.
Computational Mass Spectrometry *COMP*	53 €	77 €	Computational Mass Spectrometry (COMPT) includes, but is not limited to, the following activities: signal integration, metabolite/peptide/protein identification, database search, quantification, and data export.
Sample Preparation *SP*	39 €	56 €	Sample Preparation (SP) includes, but is not limited to, the following activities: sampling and documentation, balancing of experimental groups and reformatting, sample extraction, sample processing, clean-up and conditioning.
Analytical Instrumentation *INSTR*	54 €	79 €	Analytical Instrumentation (INSTR) includes, but is not limited to, the following activities: operation of analytical instrumentation, generation of quality control, internal and external standards, system suitability testing and calibration, data acquisition, initial quality control and data backup.
Project Administration *PA*	51 €	74 €	Project Administration (PA) includes, but is not limited to, the following activities: meetings, sample and information management, data management and report writing.
Special Item – Material *MAT*	1.00 €	1.45 €	Special Item - Materials (MATS) contains the consumables that are required for the various services. These are roughly broken down in the quotation and invoice.
Special Item – Labor *LAB*	1.00 €	1.45 €	Special Item - Labor (LAB) includes activities necessary to fulfill the contract that can only be performed by higher-skilled personnel, e.g. method development, specialized analysis etc.

The hourly rates for the activities are calculated based on assigned personnel.

9. Rights & duties

All users

Users may only be in the rooms of the Core Facility High Throughput Mass Spectrometry after prior safety instruction. The safety briefing is carried out by the head of the Core Facility and confirmed in writing.

Each user is responsible for the proper performance of the investigations in accordance with the relevant guidelines/regulations (e.g. genetic engineering, animal protection, infection control, radiation protection, etc.).

Qualified users

Qualified users have the necessary expertise in the field of mass spectrometry. They are authorized to operate the equipment independently after detailed instruction and familiarization. These users comply with the regulations on measurement routines, data storage and data management that have been made known to them. Furthermore, they carry out regular maintenance tasks. After successful training, qualified users receive a personal authorization (activation of the transponder) from the operational management. The transponder may not be passed on to third parties. Users must ensure that no unauthorized persons have access to the rooms/devices.

10. Laboratory rules

Ongoing operation

Users are required to follow the principles of Good Laboratory Practice (GLP). The devices and the associated equipment are to be kept in perfect condition.

Technical faults and/or defective equipment must be reported immediately to the persons listed in § 2 of these regulations. Independent installation or replacement of spare parts may only be carried out after prior instruction and consultation.

Before the start of each measurement, the users must have familiarized themselves with current operational changes/disruptions via OpenIRIS and/or the laboratory book, which is available at the devices. The booking of the device must be confirmed. After completion of the experiment, the rooms/devices must be left in a tidy and hygienic condition.

Resources

Standard consumables such as gloves, solvents, tips, HPLC vials etc. are provided by the facility at no additional charge. Each user is responsible for providing other work equipment.

11. Exploitation rights and authorship

All exploitation rights belong to the respective work group that made the invention, unless otherwise agreed. Restrictions apply for employees of the Charité through the regulations of the Technology Transfer Office of the Charité and the corresponding legal regulations (e.g. in the ArbnErfG, UrhG etc.). This does not apply to technical developments that affect the analytical platform.

When publishing data, the involvement of the High Throughput Mass Spectrometry Facility must be clearly indicated. Users are obliged to state the facility in the acknowledgement. Example: "We thank the Core Facility High Throughput Mass Spectrometry of the Charité for support in acquisition (i.a. and analysis) of the data." In case of scientific involvement, e.g. development of new methods, experimental design, extended data analysis or scientific interpretation of the results, the involved collaborators should be considered as co-authors in the sense of good scientific practice and should be involved in the preparation of the manuscript. Prior to submission of a manuscript/patent, it should be submitted to the Core Facility for comment, e.g., to review the technical details.

The funding sources of the studies should be identified in accordance with good scientific practice, usually in the acknowledgements.

12. User liability

There is no insurance for the equipment operated by the Facility. Therefore, each user who is allowed to work independently on the equipment is responsible during the booked measurement/analysis time for the equipment and can be held liable for damages. If equipment is damaged due to misconduct, the user and, if applicable, the project manager will be liable for the damage and, if applicable, consequential damages resulting from equipment failure.

Each research group is responsible during its measurement period for i) compliance with legal requirements, ii) set-up and adherence to SOPs, and iii) proper handover of laboratories and equipment.

All users are liable for damages and consequential damages caused due to gross negligence or under intent. External users must provide proof (letter from insurance company or copy of policy) that their insurance covers the amount of eligible equipment in the event of damage prior to first use of the equipment/premises.

In the event of damage, notify Core Facility management immediately. If this is not possible, contact the Charité Facility Management (CFM, Hotline: 030 450 575 444).

13. Core facility liability

Claims for damages against the Core Facility High Throughput Mass Spectrometry are limited to intent and gross negligence. Liability for consequential damages is excluded. The limitation of liability does not apply to personal injury.

The Core Facility High Throughput Mass Spectrometry is not liable for damages and consequential damages resulting from the fact that the facility cannot be maintained to the extent foreseen or that its operation must be restricted or discontinued due to official requirements. The Core Facility High Throughput Mass Spectrometry is also not liable for equipment failures and for damages resulting from the fact that the technical equipment is not available to the extent foreseen or has not been used properly. Furthermore, the Core Facility is not liable for damages caused by a user's failure to follow safety instructions.

The Core Facility cannot accept liability for stored samples and stored data.

14. Severability clause and validity of the user regulations

Should individual provisions of the user regulations be invalid, this shall not affect the validity of the remaining provisions. The invalid provision shall be replaced by a provision that comes as close as possible to what the Core Facility High Throughput Mass Spectrometry intended or would have intended if it had been aware of the invalidity of the provision. The same shall apply to any loopholes in the contract.

The user regulations are binding for all users of the Core Facility High Throughput Mass Spectrometry. Additional agreements are made in particular with external users and must be in writing. The User Regulations are valid in the respective version for an unlimited period of time until they are replaced by a new version or become obsolete due to the dissolution of the Core Facility.

15. Signatures

We have taken note of these user regulations and accept the conditions listed here

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