



Technicians from Biobank Graz process and store patient's liquid samples on Hamilton platforms

Automating the Processing and Storage of Liquid Samples from Patients Recovered from COVID-19

Authors: Veronika Perzt¹ and Gabriela Boza-Moran^{2*}

¹ Biobank Graz, Neue Stiftingtalstraße, 8010 Graz, Austria

² Hamilton Bonaduz AG (Robotics), Via Crusch 8, 7402 Bonaduz, Switzerland

* for correspondence: mboza-moran@hamilton.ch

Summary

Biobank Graz is a central research infrastructure of the Medical University of Graz and one of the largest clinical biobanks in Europe. Driven by the need to ensure full traceability of the patient samples during processing and storage, Biobank Graz decided to automate both processes in two customized Hamilton Microlab® STAR™ liquid handlers and a Hamilton BiOS® Storage system. In this case study, we describe how these systems are being used for establishing a biobank cohort of liquid samples from patients that have recovered from COVID-19.

About Biobank Graz

Biobank Graz is a publicly funded, non-profit organization of

the [Medical University of Graz](#), Austria. The institution is one of the largest clinical biobanks in Europe, holding more than 20 million human samples of body fluids, fresh frozen tissues and formalin-fixed paraffin-embedded (FFPE) tissues.

Biobank Graz has a well-renowned reputation worldwide. The organization is an active member of various key national and international Biobanking networks, including the Biobanking and BioMolecular resources Research Infrastructure Austria ([BBMRI.at](#)), the Biobanking and BioMolecular resources Research Infrastructure – European Research Infrastructure Consortium ([BBMRI-ERIC](#)), the International Society for Biological and Environmental Repositories ([ISBER](#)) and the European, Middle Eastern and the African Society for Biopreservation and Biobanking ([ESBB](#)).

Biobank Graz core activities

- Provision of high-quality patient samples and data for research
- Project development and coordination of research studies
- “Biobanking on demand” - Planning and realization of prospective sample cohorts
- Collection and storage of patient samples
- Consultancy on topics related to biobanking
- Networking and collaboration with other biobanking organizations



[Learn More about Biobank Graz](#)

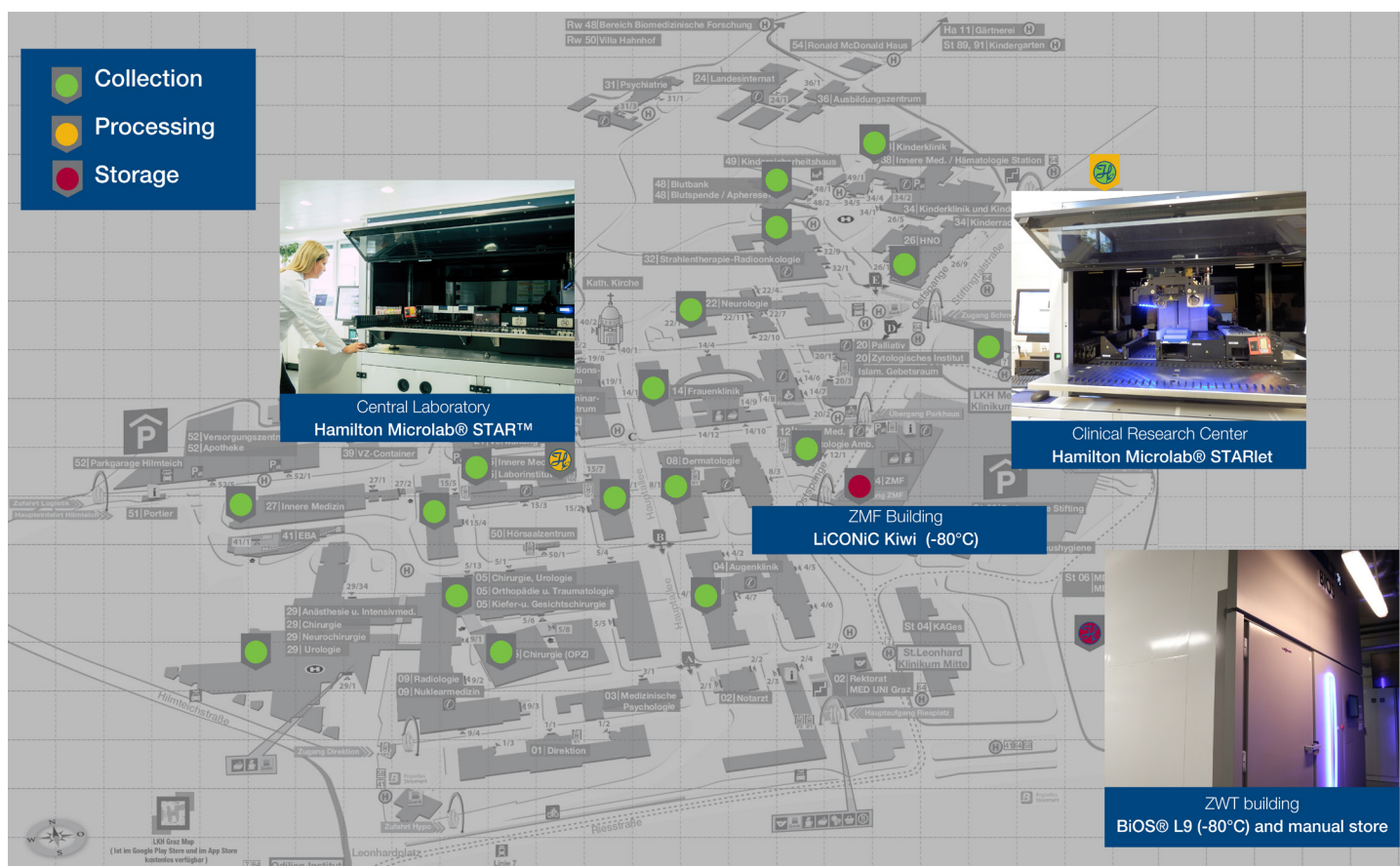


Figure 1: Sites and automated platforms for the collection, processing and storage of liquid samples in the University Hospital Graz

The role of biobanks in medical research

The primary role of biobanks is to improve the understanding of different factors influencing human health by enabling the study of samples from specific, well-characterized cohorts. The ultimate goal is to use this information to improve or create new preventive, diagnostic and therapeutic interventions.

Biobank Graz has supported several successful research projects, including the “Interfast” study and the reproductive medicine studies from the Kinderwunsch Institut. The “Interfast” study is an internal project from the Medical University of Graz investigating the effect of alternate day fasting on human health. The first results from this study were published last year in [Cell Metabolism](#). For the reproductive medicine studies from the Kinderwunsch Institut, Biobank Graz acts as an external partner supporting the collection and storage of the samples from the “reproductive medicine” cohort. These studies aim to elucidate the mechanism of infertility and to improve the success of fertility treatments. For more information about this cohort, see <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5306411/>.

From manual to automated sample processing

In 2007, after several decades of separately collecting samples at various departments, the biobanking activities

were centralized and Biobank Graz became an institutional and central research infrastructure of the Medical University of Graz.

To optimize the workflows and avoid documentations errors, Biobank Graz decided to automate the steps for the processing and storage of liquid samples. Today, the ISO 9001:2015 certified biobank processes the majority of its liquid samples with two [Hamilton Microlab® STAR platforms](#) (a STAR and STARlet). Processed liquid samples are then stored in a [Hamilton BIOS® L9 automated storage system](#), a LiCONiC Kiwi automated storage system or a manual storage, depending on the specifications defined in the project (Figure 1).

The preparation and storage of tissue samples (FFPE and cryopreserved tissues) is done manually.

Biobanking Cohort: COVID-19 recovered patients

Biobank Graz is currently building a cohort of liquid samples from patients that have recovered from COVID-19 (COVID-19 convalescent cohort; ethics approval 32-423ex19/20). These samples are available to researchers worldwide on a collaborative basis, subject to the approval of the local ethics committee and the consent of the local cooperation partners. The procedure to access samples from this cohort

is the same as the procedure to access any other sample at Biobank Graz. For more information: <https://biobank.medunigraz.at/>

Dr Veronika Perz, Project Officer at Biobank Graz explains the project:

“The purpose of this cohort is to investigate the course of the COVID-19 disease, identify diagnostic or prognostic biomarkers and develop/validate antibody-testing procedures. As part of this project, our researchers investigate the development of antibody titers over time and compare the performance of various antibody tests against the two major antigen determinants of SARS-CoV-2. This information will allow researchers to study important traits of the disease, such as how its severity correlates with antibody titers. Furthermore, Biobank Graz provides researchers and companies with access to these well-characterized, high-quality samples to enhance the development of new antibody tests and neutralization assays.”

There are several departments involved in the collection of the samples for this cohort. Volunteers that have recovered from COVID-19 are invited to clinics from the Medical University of Graz to donate blood and saliva samples, as well as nasopharyngeal swabs. All participants sign a study-specific informed consent and fill out a detailed questionnaire. The cohort is jointly set up by a consortium including the Department of Internal Medicine, Section of Infectious Diseases and Tropical Medicine ([Universitätsklinik für Innere Medizin, Sektion für Infektiologie und Tropenmedizin](#)), the Department of Blood Group Serology and Transfusion Medicine ([Universitätsklinik für Blutgruppenserologie und Transfusionsmedizin](#)), the Diagnostic & Research Institute of Hygiene, Microbiology and Environmental Medicine ([Diagnostik & Forschungsinstitut für Hygiene, Mikrobiologie und Umweltmedizin](#)) and the Institute of Medical Informatics, Statistics and Documentation ([Institut für Medizinische Informatik, Statistik und Dokumentation](#)). Blood samples are collected in various types of primary tubes (i.e. serum with clot activator, lithium heparin, sodium citrate, EDTA) and transported to the Central Laboratory for processing and storage. Nasopharyngeal swabs and saliva samples are transported to the Diagnostic & Research Institute of Hygiene, Microbiology and Environmental Medicine, where PCR and neutralization tests are performed.

It should be noted that this cohort recently received the quality label CEN/TS 16945:2015 of BBRMI-ERIC.

Automated sample processing and storage of blood samples from COVID-19 patients

The majority of the steps for the processing and storage of the COVID-19 coalescent cohort samples are automated on the Microlab® STAR™ and the BiOS® L9 (Figure 2). Dr Perz describes the workflow:

“Once the blood samples arrive at the Central Laboratory, they are scanned and assigned to the respective workflow. Depending on the sample type, primary tubes are centrifuged before loading into the Hamilton Microlab® STAR™. During loading, the system scans the barcodes and generates a sample list that is sent to the Laboratory Information System (LIS). The LIS sends back the sample description, which contains the information that the Hamilton software needs to calculate the number of aliquots to be made from each sample after the automated fraction analysis. The modules on the Hamilton deck allow the detection of the different phases in the primary sample tubes, the aliquoting of the samples into target tubes and the subsequent freezing at -20 °C.”

The Hamilton Microlab® STAR™ at Biobank Graz is equipped with an easyBlood unit, a 2D barcode reader, two freezing carriers, four pipetting channels and two tube handler channels (see Figure 3 for a description of the deck). The easyBlood unit is composed of a mirror system, a high-resolution industrial camera and processing software that allows the detection of the layers in the centrifuged blood sample. Hamilton currently offers a standardized platform or Assay Ready Workstation for customers interested in this type of solution. The freezing carriers and the tube handler channels are customized modules that allow on-deck freezing of tubes and racks in SBS format and opening/closing of biobanking tubes, respectively.

Dr Perz continues with the description of the workflow: “As soon as the processing of the last samples finishes, the system generates a report file of the sample run which includes (i) the barcodes of the tubes and the storage plate, (ii) the position of each tube within the storage plate, (iii) the volume of the aliquot and (iv) the timestamps of each automated step. All report files are imported into the Biobank Graz database. During the same day, the plates are temporarily stored at -20°C in manual freezers and at the end of each day, samples are transported on dry ice to the Hamilton BiOS® L9 for storage at -80°C until needed for further analysis.”

The Hamilton BiOS® L9 is equipped with nine chest freezers and has a storage capacity of up to 4.23 million 1.0 mL 2D coded tubes. Currently, only four of the nine chest freezers are filled with storage cassettes. Additional cassettes will be added to the remaining freezers when the need for storage capacity increases. Figure 4 describes the main features of a BiOS® system.

Benefits

From automated sample processing

Biobank Graz has been processing liquid samples on Hamilton automated liquid handling systems since 2012. The methods for the processing of serum, plasma, buffy coat and urine is well established and is routinely used in the day-to-day activities. Thanks to the robustness of the methods, it

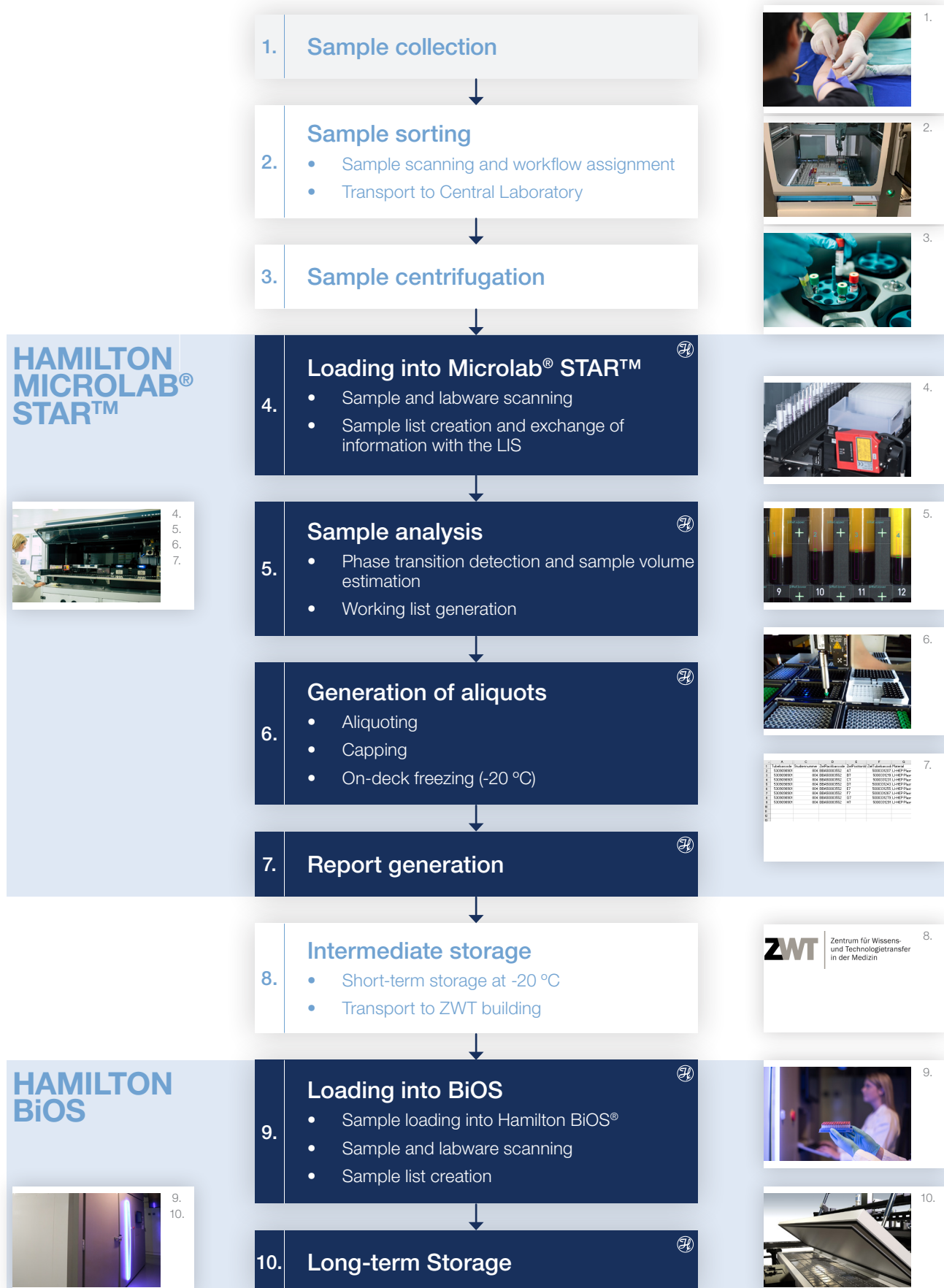


Figure 2: Workflow for the processing and storage of liquid samples from patients recovered from COVID-19

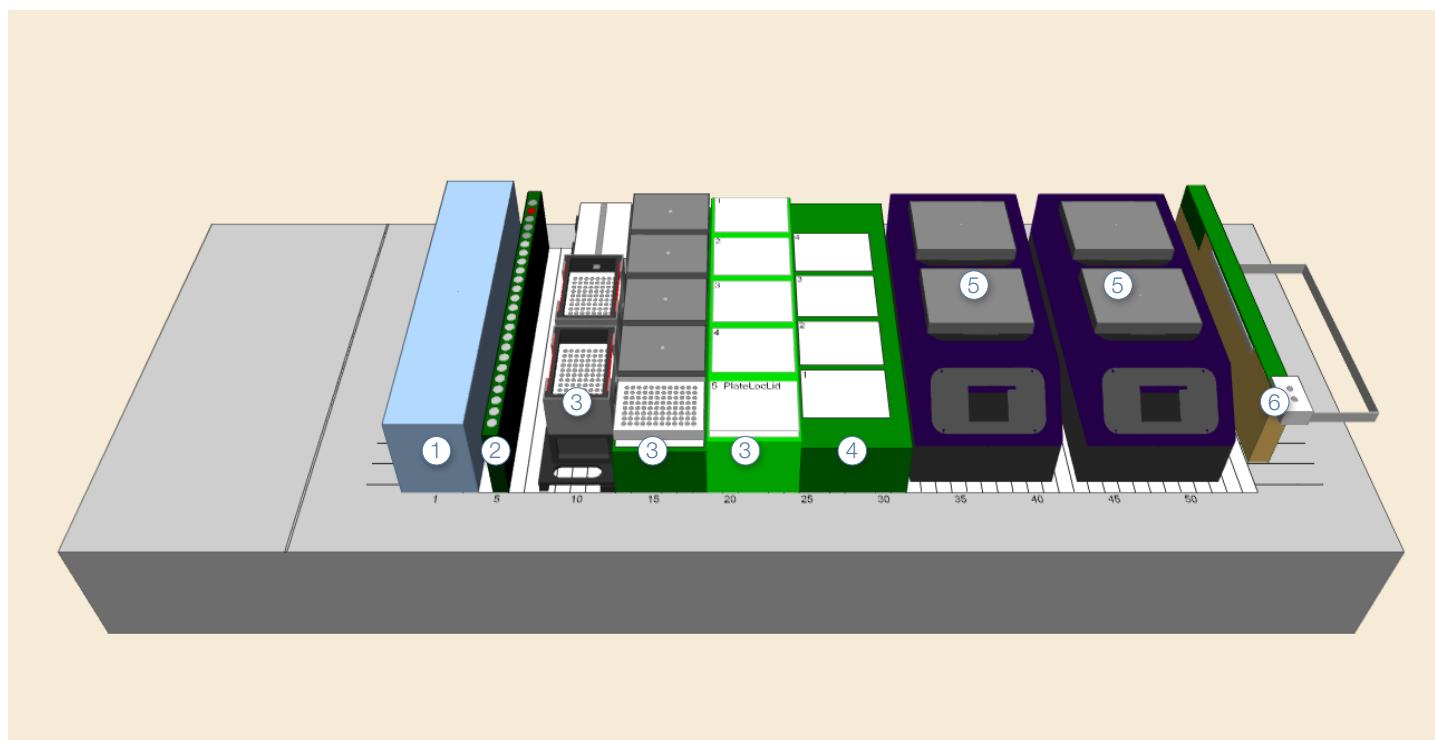


Figure 3: Deck-layout of Customized Hamilton Microlab® STAR™ platform at the Central Laboratory of Biobank Graz. (1) Mirror Carrier, (2) Sample Carriers, (3) Target Containers and Tips (4) 2D Barcode Reader, (5) Freezing Carriers, (6) CO-RE® Gripper



Figure 4: Main Features of the BIOS® automated storage system. (1) Graphical User Interface, (2) User Access, (3) System Enclosure, (4) Internal Robotics at -20°C, (5) -80°C Tube Picker, (6) -80°C Storage Compartments, (7) Refrigeration Systems (freezers), (8) Service Access. The figure at the bottom left offers a perspective of the size of the system in comparison to the size of an average adult.

was very straightforward to implement the protocol for the new COVID-19 convalescent cohort. “All in all, it took about one hour to implement the new protocol. The majority of the work went into inputting the necessary information into the LIS, which includes parameters such as volume and number of aliquots. The calculation of the number of tips and labware required by the system was generated by the Hamilton software”, says Dr Perz.

As of November 19th 2020, Biobank Graz had collected 9’649 aliquots from 140 patients on the COVID-19 convalescent cohort. Furthermore, during the year 2019, Biobank Graz collected, processed and stored more than 130,000 vials (aliquots) of liquid samples.

For Biobank Graz, the most valuable benefit of the Hamilton automated liquid handling systems is the ability to trace samples according to standards such as CEN/TS 16945:2016 and ISO 9001:2015. “Thanks to the capabilities to read barcodes and communicate with the LIS, the Hamilton platforms can produce reports that include key information such as timestamps of the pipetting steps, freezing time, and location of the sample within the rack. The report also includes data recorded in the LIS, such as the timestamp of the blood sampling and the arrival time of the sample in the laboratory”. The traceability of the samples using this automated method (automated documentation) significantly increases the efficiency of the process by eliminating error-prone manual reporting and decreasing the overall processing time.

From automated sample storage

The Hamilton BiOS® L9 automated storage system has been active in Biobank Graz since 2019. As of November 19th 2020, the system stored more than 650,000 aliquots, including the aliquots from the COVID-19 convalescent cohort. Similar to the case of the Hamilton liquid handling systems, the most valuable benefit of the Hamilton automated storage system for Biobank Graz is its ability to allow for full traceability of samples, including (i) timestamps for the different handling steps, (ii) movement history of single tubes and (iii) temperature recordings. In addition to this, the BiOS® system significantly reduces the handling time of the tubes compared to manual storage system, and it allows for seamless defragmentation. However, Dr Perz highlights, some challenges “There are limitations in the type of labware that can be used. Moreover, putting in operation an automated system like this requires much more time than using a conventional freezer and if the system has a major problem, it is not possible to simply open a door and take all samples out. Nevertheless, the BiOS has built-in redundancy systems that make sure samples are kept at -80 °C at all times, and once the system is well established, the benefits largely prevail”.



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Web: www.hamiltoncompany.com/robotics

United States
Tel: +1 775 858 3000

United Kingdom & Ireland
Tel: +44 121 272 92 80

Spain, Portugal
Tel: +34 930 186 262

China
Tel: +86 21 6164 6567

France
Tel: +33 184 008 420

Italy
Tel: +39 039 689 33 93

**Sweden, Norway,
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Tel: +46 8410 273 73

**Germany, Switzerland,
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Europe, Middle East, Africa & Asia
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