Quality Manual

ISO 17025:2017
General requirements for the competence of testing and calibration laboratories

ISO 9001:2015
Quality Management System – Requirements

NF S 96-900:2011
Quality of biological resource centres (BRCs) – Management system of a BRC and quality of biological resources

ISO 20387:2018
Biotechnology – Biobanking – General requirements for biobanking

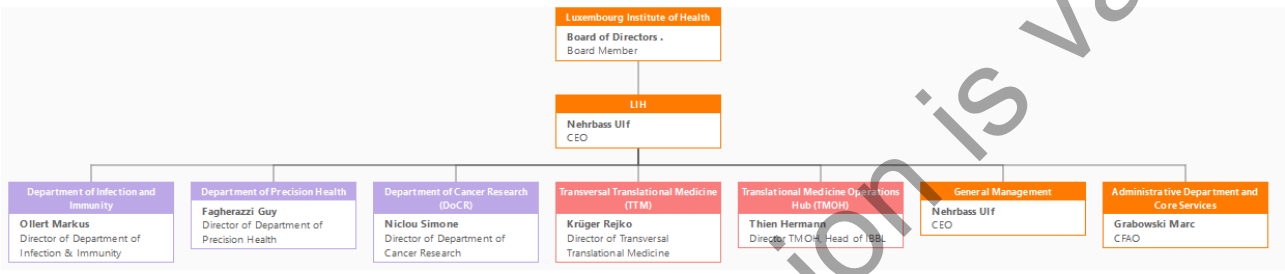
Table of Content

The Organization: IBBL and its place within the LIH

The *Integrated BioBank of Luxembourg (IBBL)* was founded in 2008 as part of the 'Health Sciences and Technology Action Plan' of the Luxembourg government. The premises of IBBL, located in 1, rue Louis Rech, 3555 Dudelange in Luxembourg, were constructed in 2017 and the activities were transferred from its previous location in Luxembourg town to these premises in November 2017.

According to the law of 3rd December 2014 on the organization of public research, the IBBL has been integrated in January 2015 into the new *Luxembourg Institute of Health (L.I.H.),* which was created by fusing the former CRP Santé with the IBBL.

The high-level organizational structure of the LIH is as follows:



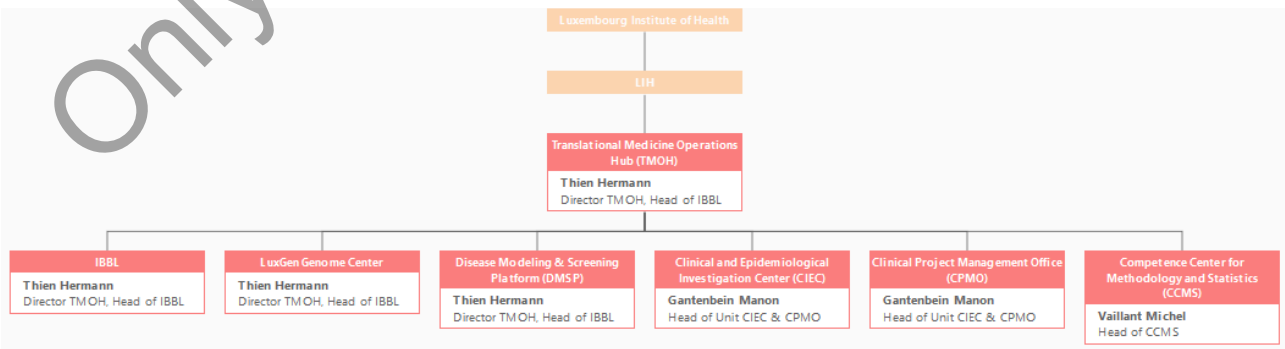
The Board of Directors is legally responsible for the activities of the whole LIH. Its current composition is presented on the LIH website: www.lih.lu

With over 450 staff, the **Luxembourg Institute of Health** performs patient-centric translational research with a focus on cancer and immune-related disorders. Our particular interest lies in the immune system as a shared functional module between health and disease.

Our dedicated teams of multidisciplinary researchers embrace collaboration and disruptive technology to advance the understanding of disease mechanisms. Using technology like Artificial Intelligence on real-world patient-derived data, we create disease relevant knowledge, which can be tangibly translated into clinical applications through a bed-to-bench-to-bed approach.

The IBBL is organizationally placed within the **Translation Medicine Operations Hub (TMOH)**, which provides research services to the internal research departments and to external researchers, partners and customers.

TMOH, with its approx. 100 staff members, is dedicated to improve patients' lives by providing operational excellence using the following resources,



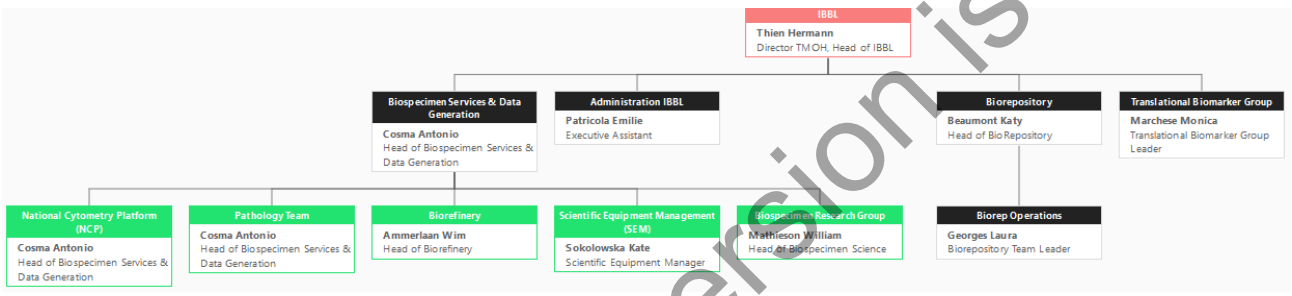
and applying the following principles:

- Single Point of Contact regarding Research Services for internal & external stakeholders
- Consulting for research projects regarding design, operations, regulatory aspects…
- Seamless workflow and high-quality project execution

- Inbuilt collaboration (clear processes, interfaces, roles & responsibilities) and exchange of resources (technologies, SME)
- Transparent information and communication
- Continuous improvement – of methods, technology, science, quality, processes…

The **IBBL** offers biobanking-related services, including the collection, processing, analysis and storage of biological samples and associated data in compliance with international quality standards. This includes activities as Proficiency Testing Provider with a focus on biobank-relevant processes. Biospecimen Research is also performed to optimize sample processing and endorse biospecimen quality.

The institute has invested in laboratory facilities, technology platforms and highly qualified and experienced staff (approx. 45 at IBBL), organized in the shown structure:



Commitment of Management

Mission & Vision

Mission

The mission of LIH is to leverage knowledge and technology arising from research on patient derived data, with the aim of having a direct and meaningful impact on people's health.

As integral part of LIH, IBBL's internal mission is to provide accredited biospecimen-related services and a biobanking infrastructure for applied medical research.

Vision

The vision of LIH is to become a leading European institute for precision medicine and precision health, transforming research excellence into tangible benefits for patients, with the long-term goal of preventing diseases.

Quality Policy

The quality policy aims to build the framework for achieving IBBL's contribution to LIH's mission and vision, the strategic activities and related quality objectives.

- The Board of Directors, the LIH & IBBL Management and Staff commit to implement and maintain a working environment to constantly provide service quality that meets the expectations of our customers, partners and other interested parties.
- The LIH & IBBL Management lives this commitment by the implementation and maintenance of a Quality Management System and its certification/accreditation by external bodies. Ensuring compliance with the requirements of the certification and accreditation standards in the certification/accreditation scope and the applicable legal and statutory requirements is our aim. Changes in the organization are managed to preserve the consistency and integrity of the QMS.
- IBBL strives for continuous improvement of the organization and the optimization of its services by careful planning of its activites with a focus on customer satisfaction, legal compliance and effectiveness & efficiency of its operations. Through regular monitoring and measuring of the performance level and the follow-up of scientific advances in the area of biospecimen science and biobanking practices IBBL is able to identify and implement adequate measures in case of quality problems or opportunities identified for improvement.
- All IBBL staff members are committed to familiarize themselves with the provisions of the QMS and to apply the defined procedures at their level of responsibility.
- LIH & IBBL foster communication of its mission, vision and objectives internally and externally.

Quality Objectives

IBBL utilizes different means to continuously determine the performance levels of its processes. Wherever possible, this takes place by the definition and monitoring of Key Performance Indicators (KPI) and Quality Indicators (QI) as measurable quality objectives. *WI QM-004 Performance Evaluation & Continuous Improvement* summarizes all applicable tools.

Interested Parties

As an infrastructure dedicated to support biomedical and translational research, IBBL seeks to satisfy the requirements of its interested parties. A specific organization can fall into one or more of the categories listed below.

Interested Party Category	Interested Parties (Explanations and Examples)	Requirements relevant to the quality of IBBL's service provision
LIH	Research Departments, TMOH units	Fulfillment of vision and mission (see page 5) Optimized inter-departmental collaboration and mutualization of internal resources for the support of transversal translational medicine (TTM) projects
Funding Bodies	Ministry of Higher Education and Research (MESR)	A multi-year performance contract 2022-2025 contains the obligations of LIH and IBBL; this includes the definition of key performance indicators as well as the mechanisms for measuring performance.
	National and International Competitive Funding Bodies, e.g. those funding H2020, IMI, FNR, JNPD…	Project-specific contracts define the obligations of IBBL. They include deliverables and performance indicators as applicable as well as the mechanisms for measuring project performance.
	Humanitarian funders of research, e.g. Patient organizations, Rotary Club…	Infrastructure and operations that demonstrate an innovative and/or effective contribution to biomedical research
Clients	Public or private organizations to whom IBBL provides services, without sharing a common (research) goal, e.g. BIG, EORTC…	Flexibility, scientific and operational excellence paired with customer focus and embedded in a well-established QMS. This encompasses for example: ✓ Responding to customers' needs and expectations and the ability to understand and forecast such needs ✓ Providing samples and services in compliance with customers' needs and expectations ✓ Assuring the quality of our services and support ✓ Having competent and available and staff, able to provide information and advice on samples and services
Research Partners	National and international partners for the establishment or management of sample collections and/or transversal, translational medicine (TTM) projects with shared (research) goals, e.g. Personalized Medicine Consortium, Luxembourg Clinical Researchers (from Hospitals and/or Public Institutions), Consortium partners…	Availability of reliable, standardized, state-of-the-art biobanking infrastructure and operations for: ✓ Reception, storage and re-distribution of biological resources under controlled, optimal conditions ✓ Provision of "fit-for-purpose" biological resources ✓ Provision of (accredited) test and characterization data of biological material ✓ Support in project management for complex research projects Contribution of IBBL to innovation by performing biospecimen research activities
Biospecimen Research Collaborators	Biospecimen research activities in collaboration with national and international academic, public and private research collaborators, e.g. Suppliers of consumables, suppliers of equipment, other biobanks, universities…	Set-up and execution of research studies to establish evidence-based procedures for the collection, processing, testing and handling of biological resources. Communication of research outcome for the benefit of the scientific community. Integration of research outcome into the operational activities of IBBL, so that interested parties benefit from IBBL's research.
Healthy Donors & Patients	IBBL does not have direct contact with donors, but keeps indirect contact via relevant patient organizations.	Strict application of ethical, regulatory and quality standards in the scope of sample collection, transport, processing, storage and re-distribution as sign of respect and valorization of the donor's voluntary contribution to research.

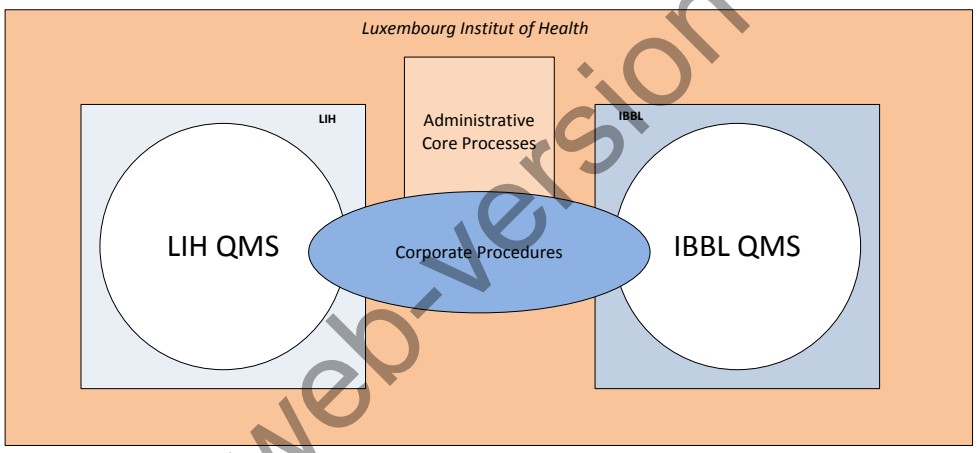
Interested Party Category	Interested Parties (Explanations and Examples)	Requirements relevant to the quality of IBBL's service provision
Governmental Bodies	CNPD – Commission Nationale pour la Protection des Données	Internal processes and provision of services to customers in line with national and international data protection and privacy rules
	CNER – Comité National d'Ethique de Recherche	Services in line with national and international ethical rules with respect to human biological resources
	ITM – Inspection du Travail et des Mines	Infrastructure and operational processes in line with rules with respect to health and safety at the workplace
	Ministry of Health	Meaningful and high-quality contribution to activities focusing on public health, e.g. in sanitary crisis situations, by providing infrastructures and logistics for related biological materials and data management
Proficiency Testing (PT) Partners & Participants	Biobanks and other laboratories processing and testing biological samples Consortia ISBER	Contribution to the overall improvement of comparability of biological resources by: ✓ Providing a general, open proficiency testing program that serves the biobanking community to benchmark the performance of their processing and testing methods ✓ Providing case-by-case, customized PT programs
Suppliers	Supplier of equipment and consumables; Supplier of services; Subcontractors	Establishment of contractually based (long-term) relationships for supplying goods and services to IBBL Acknowledgement of suppliers as collaboration partners in the provision of IBBL's services
General Public of Luxembourg and the "Grand Region"	Citizens of Luxembourg and the "Grand Region" are tax payers and thus indirectly contributing to the funding of IBBL They are also potential donors of biological resources	Information in formats and words understandable by laymen about: ✓ Personalized medicine and the role of biobanks in transversal, translational medical research at Luxembourg and abroad ✓ IBBL's contribution to achievements for the benefit of Luxembourg's population ✓ Information about possibilities how to support medical research Communication channels to IBBL (e.g. via Twitter, Facebook, Website, meetings, press conferences)
Personnel	Staff of IBBL Staff of LIH	A working environment which ✓ has defined roles and responsibilities ✓ promotes the valorization of individual contributions to the objectives of the organization ✓ provides motivating elements in compliance with labor laws and other related agreements
Students	National and international students (at LIH)	Training by competent staff covering all themes relevant for biobanking operations with actionable information
Neighbors	Co-tenants in IBBL's premises: LNS – Laboratoire National de Santé LMVE – Laboratoire de Médicine Vétérinaire de l'Etat	Collaborative relationships linked to the use of the same building and infrastructures

Quality Management System (QMS)

Rationale of the QMS

Different activities within the LIH require different levels of a (formalized) quality management system. Therefore, the institute decided to develop and maintain a quality management system according to the requirements of ISO 9001 as basis for the management and support processes of the institute. The research service activities of the TMOH require in addition focused quality approaches to the different steps of the life cycle of biospecimen, especially by elimination of pre-analytical variations of samples and by providing reliable data. Therefore, related processes are submitted to additional quality requirements as expressed in sector-specific standards or regulations as ISO 17025, ISO 17043, ISO 20387 or GCP as examples.

The structure of the QMS has its roots in the independent development of two QMS at the former CRP Santé and the IBBL. During its journey to a unique system, the current set-up can be depicted as follows:



The overall responsibility for the design, implementation and maintenance of the QMS of LIH and IBBL lies with the Head of the Quality & Safety Management Office (QSMO), reporting to the CEO of LIH.

Scope of the QMS of IBBL

The QMS for IBBL has been conceived and is maintained by considering the requirements of the following laws, norms, guidelines and “Best Practices” (non-exhaustive list):

- Loi du 3 décembre 2014 – Organisation des centres de recherche
- ISO 17025:2017 General requirements for the competence of testing and calibration laboratories
- ISO 9001:2015 Quality Management Systems – Requirements
- NF S 96-900:2011 Quality of biological resource centres (BRCs) – Management system of a BRC and quality of biological resources
- ISO 20387:2018 Biotechnology – Biobanking – General requirements for biobanking
- ISO 21899:2020 Biotechnology – Biobanking – General requirements for the validation and verification of processing methods for biological material in biobanks
- ISO/IEC 17043:2010 Conformity assessment – General requirements for proficiency testing

- Best Practices for Repositories: Collection, Storage, Retrieval and Distribution of Biological Materials for Research – International Society for Biological and Environmental Repositories (ISBER), Forth Edition 2018
- NCI Best Practices for Biospecimen Resources – US National Cancer Institute, 2016
- OECD Best Practice Guideline for Biological Resource Centres – General Practices for all BRC's, 2007
- Council of Europe, Recommendation Rec(2006)4 on Research on Biological Materials of Human Origin
- Good Clinical Laboratory Practice (GCLP) – World Health Organization (WHO), 2008
- ICH GCP – Guidelines for good clinical practice (ICH E6(R2)), Nov. 2016
- ISO 31000: 2018 – Risk Management – Guidelines
- ISO 45001: 2018 – Occupational health and safety management systems – Requirements with guidance for use
- ISO 19011:2018 Guidelines for auditing management systems
- ISO 10012:2003 Measurement management systems – Requirements for measurement processes and measuring equipment
- EU 2016/679 Regulation on the protection of natural persons with regard to the processing of personal data and on the free movement of such data (General Data Protection Regulation) – GDPR
- Clinical Trial Regulation on medicinal products for human use (Regulation (EU) No. 536/2014)

The present Quality Manual summarizes the QMS implemented for the accreditation of IBBL according to:

- **ISO/IEC 17025:2017** General requirements for the competence of testing and calibration laboratories,

and for the certification of IBBL according to:

- **ISO EN DIN 9001:2015** Quality Management Systems – Requirements

The activities in the accreditation scope are:

- **Acquisition, validation, processing, storage, administration and distribution of biological material and associated data on which tests are done:**
  - **M007**: Nucleic acid quantification by Spectrophotometry (in-house developed)
  - **M005**: DNA quantification by Spectrofluorometry (in-house developed)
  - **M008**: RNA Integrity Measurement (in-house developed)
  - **M053**: 16S rRNA Gene Sequencing

The activities in the certification scope are:

- **Acquisition, validation, processing, storage, administration and distribution of biological material and associated data to public or private end-users / researchers**

The biospecimen research and biomarker validation activities as well as the activities of the National Cytometry Platform (NCP) of IBBL are excluded from the accreditation scope.

The activities of the NCP are currently included in the certification scope of the LIH.

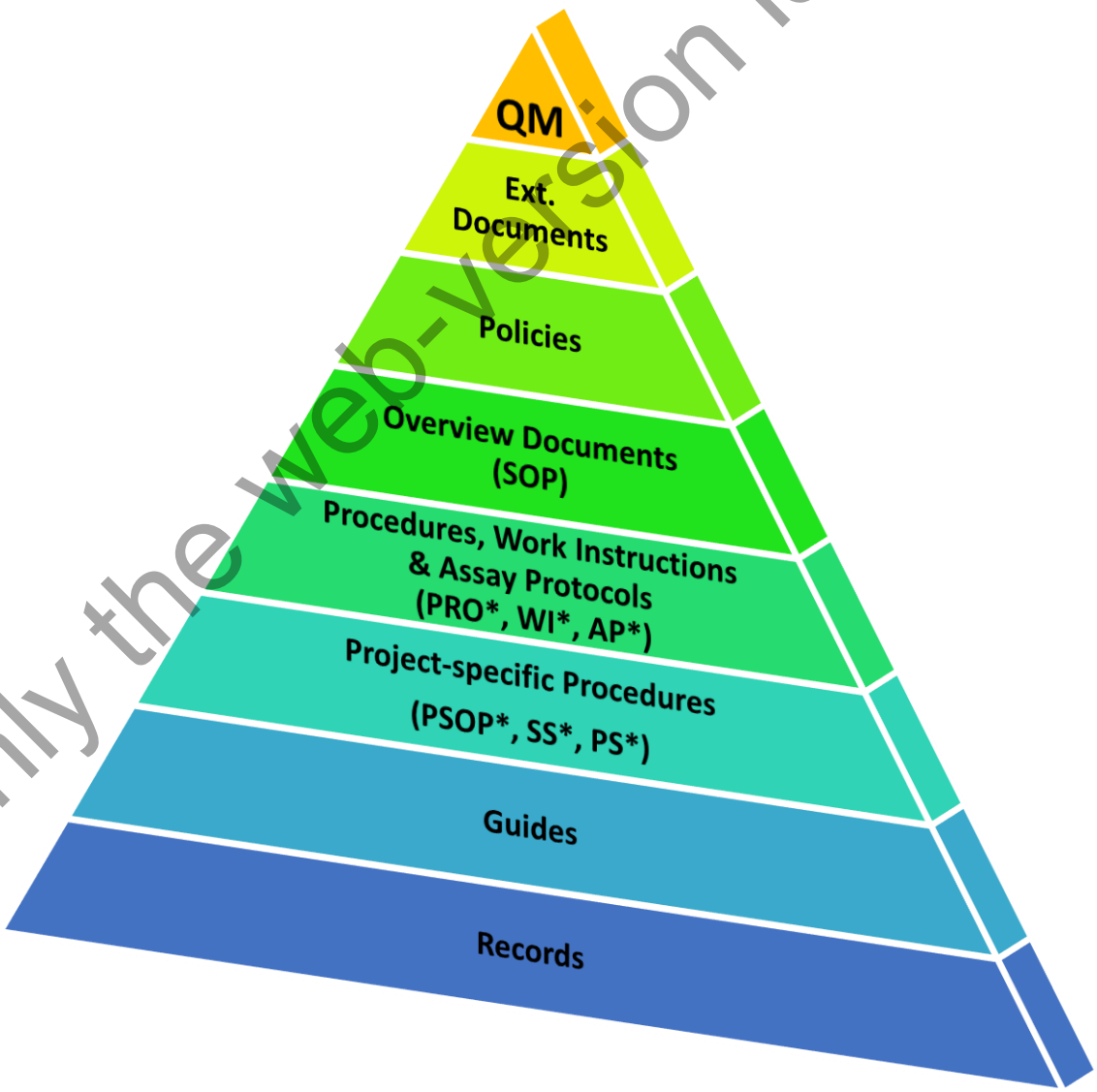
The quality processes apply to activities executed by IBBL at its premises in 1, rue Louis Rech, 3555 Dudelange, Luxembourg.

The IBBL Quality Manual is an integral part of the documented QMS of IBBL. Internal publication follows the rules of *SOP QM-DC Document Control*.

IBBL promotes the accessibility of the Quality Manual to its partners, clients and other interested parties by providing the current version on its website. However, this version of the IBBL Quality Manual is an authorized, but uncontrolled copy. Only the electronic version available on the website at its day of access is deemed valid and current.

Document Hierarchy

The QMS is planned and maintained via quality documents, which include:



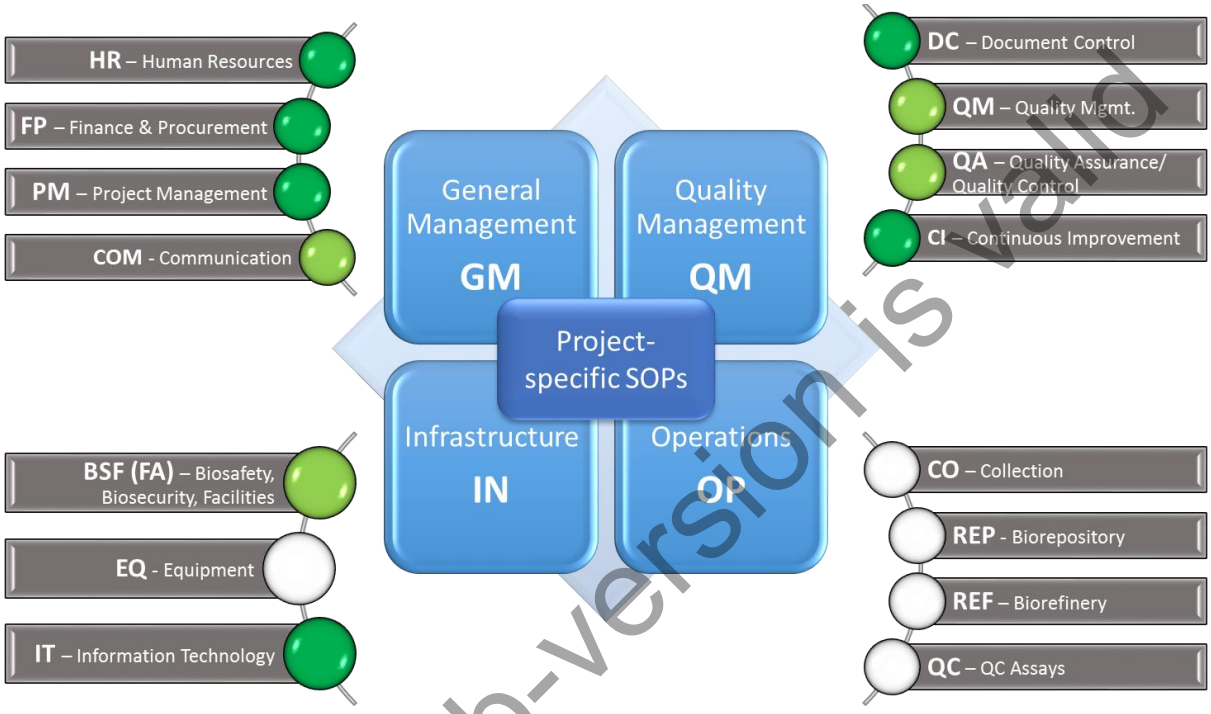
* can have A, AS, F, T and S associated

- **Quality Manual**
- **External Documents**
  - Regulatory texts, guidelines, publications…
- **Policies**
  - Intentions and directions of the organization, formally expressed by the top management
- **Overview Documents (SOP)**
  - High-level process descriptions, including related process flowcharts (SOPs – IBBL only)
- **Procedures (PRO) and Work Instructions (WI) and Assay Protocols (AP) with associated forms (F), assay sheets (AS), templates (T), spreadsheets (S) and annexes (A)**
  - Detailed instructions for the execution of standard tasks including corporate procedures (PRO) and work instructions (WI) (for administrative core services)
  - Protocols for Test Methods (APs – IBBL only)
  - Related annexes, forms, templates and spreadsheets for standardized record keeping
- **Project-specific Procedures with associated annexes, forms, templates and spreadsheets**
  - Detailed instructions for the execution of project-specific tasks with the associated annexes, forms, templates and spreadsheets
  - Examples: Project-specific Standard Operating Procedures (PSOPs), Project Specifications (PS) and Study Summaries (SS)
- **Guides**
  - Guidelines to describe specific tasks and not requiring the creation of any records
- **Records**
  - All types of quality records, resulting from the execution of tasks covered by the documents above.
  - Examples: completed forms, tables, lists, databases, reports, logbooks, job descriptions, control charts, analytical raw data…

The principles of document and record control are summarized in *SOP QM-DC Document Control*.

QMS Structure

The documented QMS is structured in four chapters with related sub-chapters, constituting the four pillars on which the execution of IBBL's services is based:



The procedures defined in the QMS chapters "GM – General Management" and "IN – Infrastructure" are the backbone of the "**support processes**", while the "**management processes**" are covered in the QMS chapter "QM – Quality Management"; both process types are essential to fulfill the services to the customers. The "**service or operational processes**" are described in the QMS chapter "OP". A supplementary layer of "project-specific procedures" ensures the fulfillment of customer-specific needs, where needed. *SOP QM-DC Document Control* provides more details about the structure.

One Standard Operating Procedure (SOP) is established for each sub-chapter, summarizing IBBL's policies and processes relevant to this part of the QMS and their interactions with other QMS parts. The section below provides a snapshot of items covered in each subchapter.

Depending on the processes, activities may fall under the "IBBL QMS" or the "LIH QMS" or be "Corporate Procedures". Sub-chapters indicated in light or dark green are those, where corporate procedures have been (dark green) or may be (light green) implemented.

Related procedures are documented in "Corporate Quality Documents" (refer to *WI DC-901 Corporate Quality Documents Administration*), which are fully integrated into the above-mentioned QMS structure of IBBL.

Core Processes

General Management

- *Human Resources (SOP GM-HR)*

  This sub-chapter covers the principles and provisions for the administration of human resources at IBBL:

  IBBL and LIH Management define its human resource forecast in order to provide competent staff in sufficient number to execute all tasks within its mission. A formal recruitment process is applied.

  IBBL and LIH ensure that management and staff are free from any undue internal and external commercial, financial or other pressures that may adversely affect the quality of their work. IBBL and LIH adhere to stringent confidentiality rules in order to protect the privacy of employees, donors and partners, but also the intellectual property of LIH and its collaboration partners, where needed.

  Job Descriptions are used to define the job holders' responsibilities in relation to required skills, competencies and experience and hierarchical structures within LIH. LIH has processes in place, which ensure that hired staff is continuously trained in job-specific, regulatory, safety & health and quality matters. The appraisal process serves to determine the performance level of staff, identifying individual objectives and related development needs, and the effectiveness of training measures.

- *Finance & Procurement (SOP GM-FP)*

  The "FP" section of the QMS contains the processes for purchasing of goods & services and includes provisions for the selection and evaluation of suppliers and subcontractors.

- *Project Management (SOP GM-PM)*

  This subchapter addresses all phases of project management of a project, such as lead, design, setup, initiation, operation and closure. It includes specific procedures for the structure and execution of IBBL's Proficiency Testing Services.

  In addition, provisions for sample and data access (such as governance, policies and procedures) are covered in this part of the QMS. This includes policies and procedures for sample and data distribution and destruction.

  The Clinical Project Management Office (CPMO) within TMOH is the owner of all these processes and accompanies IBBL in the execution of its services as coordinating body between the researchers or customers and the internal organization.

Quality Management

- *Document Control (SOP QM-DC)*

  This subchapter covers Document Management and Records Management processes applied at IBBL.

  A Document Hierarchy has been established to manage documents and records within the Quality Management System (QMS) of IBBL and those overlapping with the quality management system of LIH. Naming and coding systems, including version numbering, ensure unique identification of each internal and external document.

  For internal documents, formalized review and approval processes are in place, related to the type of document. Controlled distribution and retraction of internal and external documents takes place and, where needed, access to obsolete versions is granted under controlled conditions. Listings of current documents and the documents themselves are easily accessible to the employees of IBBL.

  The principles for archiving documents are defined. Rules related to periodic revisions are specified as well as processes for annotations, corrections or deviations, when needed.

  This chapter also contains corporate processes and procedures for ensuring compliance with current data protection regulations.

- *Quality Management (SOP QM-QM)*

  The "QM" subchapter covers the key Quality Management processes within the QMS of IBBL such as management of nonconformities, administration of corrective and preventive actions, customer complaints management and continuous improvement, including customer satisfaction surveys and management review.

- *Quality Assurance / Quality Control (SOP QM-QA)*

  This subchapter contains the general principles for Quality Assurance (QA) and Quality Control (QC) at IBBL. QA and QC are vital monitoring methods, in addition to processes such as control of nonconforming work, customer complaints management and continuous improvement.

  IBBL maintains a process for internal and external audits, performs quality control checks and quality assessments to verify process or product quality, and ensures that related findings are used to continuously improve the system.

- *Continuous Improvement (CI)*

  This subchapter contains the corporate risk management processes of LIH. Other processes at IBBL contributing to continuous improvement are – for historical reasons – covered in the sub-chapter "Quality Management" (see above).

Infrastructure

- *Biosafety, Biosecurity, Facilities (SOP IN-FA)*

  This subchapter covers the general provisions related to the IBBL facilities including biosafety and biosecurity aspects. Biobanking facilities are important to ensure biospecimen, sample and data integrity throughout the whole life cycle of samples, from reception until distribution, including processing and testing methods.

  Therefore, IBBL ensures that the premises conform to legal and security requirements and are appropriately arranged for different process steps. IBBL controls access, maintains procedures for operational safety & hygiene (biosafety/biosecurity) and performs environmental monitoring.

- *Equipment (SOP IN-EQ)*

  The "EQ" chapter consists of processes for the management of laboratory and storage equipment used for IBBL's services.

  The laboratory is furnished with all equipment, necessary for the correct performance of its services. A life cycle approach for equipment administration is applied to ensure that equipment is fit for purpose within the scope of IBBL's services. This includes the execution of pre-defined qualifications or checks before an instrument is put into operation, a controlled phase of use as well as an organized retirement.

  IBBL has defined responsibilities for the metrological function in job descriptions and procedures as applicable. IBBL has chosen to distribute responsibilities throughout the organization. Activities and requirements related to metrology (measurement processes and measuring equipment) are seamlessly integrated into the QMS, thus ensuring the establishment, documentation, maintenance and continuous improvement of the underlying measurement management system. Where required, related personnel at IBBL has the adequate competence; alternatively activities are outsourced.

- *Information Technology (SOP IN-IT)*

  Here are summarized processes related to the information & communication technology (ICT) infrastructure on a corporate level and IBBL-specific processes of the Business Information Solutions (BIS) unit for the benefit of the whole organization.

  Data management during the life-cycle of a biospecimen is increasingly performed using computerized systems. Therefore, the administration of these data must ensure data integrity throughout collection, processing storage and transmission. IBBL puts specific emphasis on data protection, including the privacy of donor and sample-related data.

Operations

- *Collection (SOP OP-CO)*

  The "CO" subchapter of the QMS contains general principles for specimen collection and data collection & management performed – including the administration of informed consent of the donors – under the responsibility of, or with support of IBBL.

  The respect of legal and ethical principles for collecting biospecimens and related data is of utmost importance to ensure the rights, safety and well-being of the donors.

  Biospecimen science has demonstrated that the pre-analytical conditions of biological samples are relevant for the "fitness-for-purpose" of biospecimens and samples. In addition, the type and quality of associated data – sample and donor related – is important for providing useful and reliable input to biomedical research.

  The implemented processes are intended to ensure these goals are achieved.

- *Biorepository (SOP OP-REP)*

  This subchapter defines the general principles for reception, storage, internal and external distribution as well as destruction of biological material by the "Biorepository" team of IBBL. The collection kit production and administration process is also included in this QMS section.

- *Biorefinery (SOP OP-REF)*

  Here are covered the general principles applied to "Sample Processing" performed at IBBL.

  "Sample Processing" is defined as manual and/or automated manipulation of specimens or samples to produce derivatives.

  Sample Processing is a crucial step in the life cycle of biological samples. Therefore, IBBL maintains Work Instructions to describe risk-based specifications and requirements of Sample Processing Methods, validates critical methods, executes Sample Processing Methods under controlled environmental conditions, using suitable equipment and software, and adequately trained personnel, and ensures traceability of the Sample Processing steps by relevant records.

- *QC Assays (SOP OP-QC)*

  The "Quality Control (QC) Assays" section of the QMS covers the processes related to sample testing performed at IBBL.

  "Sample Testing" is defined as manual and/or automated testing of specimens or samples to determine characteristics of specimens and samples. Output of a testing process is a result. Results can be quantitative or qualitative. Depending on needs, test results may be complemented with a statement of conformity.

  Sample Testing is an important step in the life cycle of biological samples, especially when samples have been produced by "critical" methods (see *SOP OP-REF Biorefinery*) and in the scope of the "fitness-for-purpose" for any downstream use of the samples.

  IBBL maintains Assay Protocols to describe risk-based specifications and requirements of Sample Testing Methods, validates important testing methods, executes Sample Testing under controlled environmental conditions, using suitable equipment and software, and adequately trained personnel, ensures traceability of the Sample Testing steps by relevant records, and communicates results to collaboration partners/clients only after formal approval and by official reporting means.

  The submission of selected analytical methods for accreditation according to ISO 17025 demonstrates IBBL's commitment to reliable test and characterization data for biospecimens and samples.

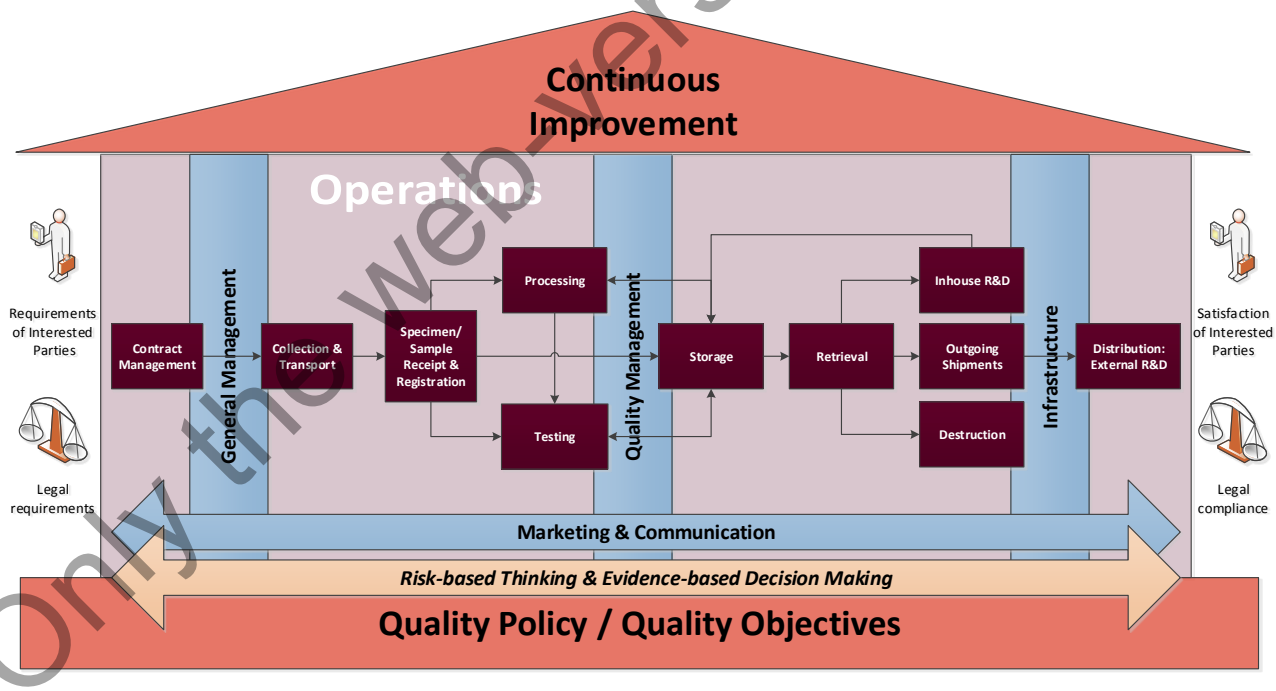
Services Types

LIH/IBBL distinguishes between the following service types in which IBBL performs one or more of the typical biobanking activities such as collection, acquisition, processing, testing, storage and distribution:

- **Research Projects**
  - LIH and national and/or international partner(s) collaborate in (translational) research projects, potentially including the establishment and maintenance of biological material and data collections. An example workflow – based upon the use of collection kits provided by IBBL – is presented in Exhibit A.
- **Service Contracts**
  - IBBL performs selected services such as processing and/or testing and storage of samples, e.g. in the scope of clinical trials.
  - The activities of IBBL as PT provider are managed by Service Contracts as well as IBBL's biomarker validation services.

Biobanking Process Overview

The following scheme provides a schematic overview of the way the Quality Management System interacts with the major components of IBBL's service processes.



The focus of providing services is put on the fulfillment of requirements of interested parties in compliance with applicable laws and regulations. The quality policy and the related quality objectives form the foundation of IBBL's service quality. These, in combination with the organization-wide application of the support processes "General Management", "Quality Management" and "Infrastructure" (as described before) are the measures implemented to ensure customer-oriented "Operations", i.e. the execution of services to the customers. Risk-based thinking and continuous monitoring of performance levels with respect to efficiency, compliance and customer satisfaction via the "QM" processes guarantees evidence-based decision making and the continuous improvement of the organization.

Furthermore, the Marketing & Communications Unit of LIH ensures that LIH's/IBBL's vision, mission, strategic plans and concrete projects are regularly and adequately communicated within the

organization and to our interested parties including the general public. Examples are the annual report, internal and external newsletters, press releases and the website: www.lih.lu.

The key business process of IBBL is composed of the milestones of **acquisition, receipt, processing, testing, storage, administration and distribution** of biological material and associated data. These milestones are broken down into sub-processes (e.g. contract management, collection & transport…) depicted above, which in turn are composed of one or more procedures.

The specifications for a sub-process may be adapted for each project, collection or fee-for-service contract, based upon the client needs. These needs are documented in contracts and communicated to the organization by the documented quality system. Consequently, a customer service can include all process steps or only a part of them.

Sub-process	Input	Actions	Output
Contract Management	Customer requirements Legal requirements IBBL/LIH standard procedures	Definition and documentation of the project scope (e.g. specifications, responsibilities, timelines, budget)	Project-related Contract(s) and related operational documents (e.g. WIs/APs, PSOPs)
Collection & Transport	Project-specific requirements (e.g. consenting, type of biospecimens, conditions of collection, transport…)	Collection & Transport of Biospecimens and Samples according to project specifications	Biospecimens & Samples collected and transported to IBBL
Biospecimen/Sample Receipt & Registration	Biospecimens/Samples collected and transported to IBBL	Verification of received biospecimens/samples and associated data against the project specifications; registration in the LIMS; verification of consent.	Received biospecimens/samples are registered and identified with unique identifier at IBBL; any discrepancies from specifications are documented
Processing	Received & Registered Biospecimens/Samples	Processing of samples according to project specifications	Samples as specified in the project scope are produced; related records are available; nonconformities are documented and followed-up
Testing	Received & Registered Biospecimens/Samples or Samples produced at IBBL (see “Processing”)	Testing of samples according to project specifications	Characteristics/annotations of biospecimens/samples have been established according to project specifications; nonconformities are documented and followed-up
Storage	Received & Registered Biospecimens/Samples or Samples produced at IBBL (see “Processing”) or Samples tested at IBBL (see “Testing”)	Storage and registration of biospecimens/samples in defined storage locations following the project-specific requirements Management of sample movements maintaining integrity and traceability. Continuous control of environmental conditions related to storage.	Samples are physically stored in defined storage locations under controlled environmental conditions; sample information and sample location are recorded in the LIMS; sample movements are performed maintaining integrity and traceability of the samples; nonconformities are documented and followed-up
Retrieval	Internal or External Distribution Request for Samples and/or Data Stored Biospecimens/Samples	Preparation of sample picklist and picking of samples; Preparation of related data – both according to the provisions of the project scope and in accordance with the Distribution Request	Samples ready for shipment; Data ready for transfer
In-house R&D (outside the certification scope)	Samples retrieved from stock	Execution of Biospecimen Research projects	Evidence-based information about the impact of pre-analytical conditions on the “fitness-for-purpose” of samples

Sub-process	Input	Actions	Output
Outgoing Shipment	Samples ready for Shipment; Data ready for transfer	Packing and organization of shipment of samples according to project-specifications, the Distribution Request and legal requirements; Transfer of Data to the Recipient ensuring data privacy, data security and data integrity.	Samples are shipped to the Customer or a Third Party (according to project scope); receipt of samples has been confirmed; data are transferred to the Customer or a Third Party (according to the project scope); data are received in integrity and securely by the recipient, respecting data privacy requirements; nonconformities are documented and followed-up.
Destruction	Client Request Withdrawal of consent Quality issue	Samples and data (when applicable) are safely destroyed	Destruction records
Distribution: External R&D	Samples are shipped to the Customer or a Third Party (according to project scope); receipt of samples has been confirmed	Customer or Third Party perform research using the provided biospecimens & samples	Research output such as publications, diagnostic or prognostics markers/tools, personalized medicine…

Exhibit C provides an overview of the main actors for each of these sub-processes.

Exhibit D shows the schematic workflow of a typical testing process.

Exhibit A: Example Workflow for a Research Project

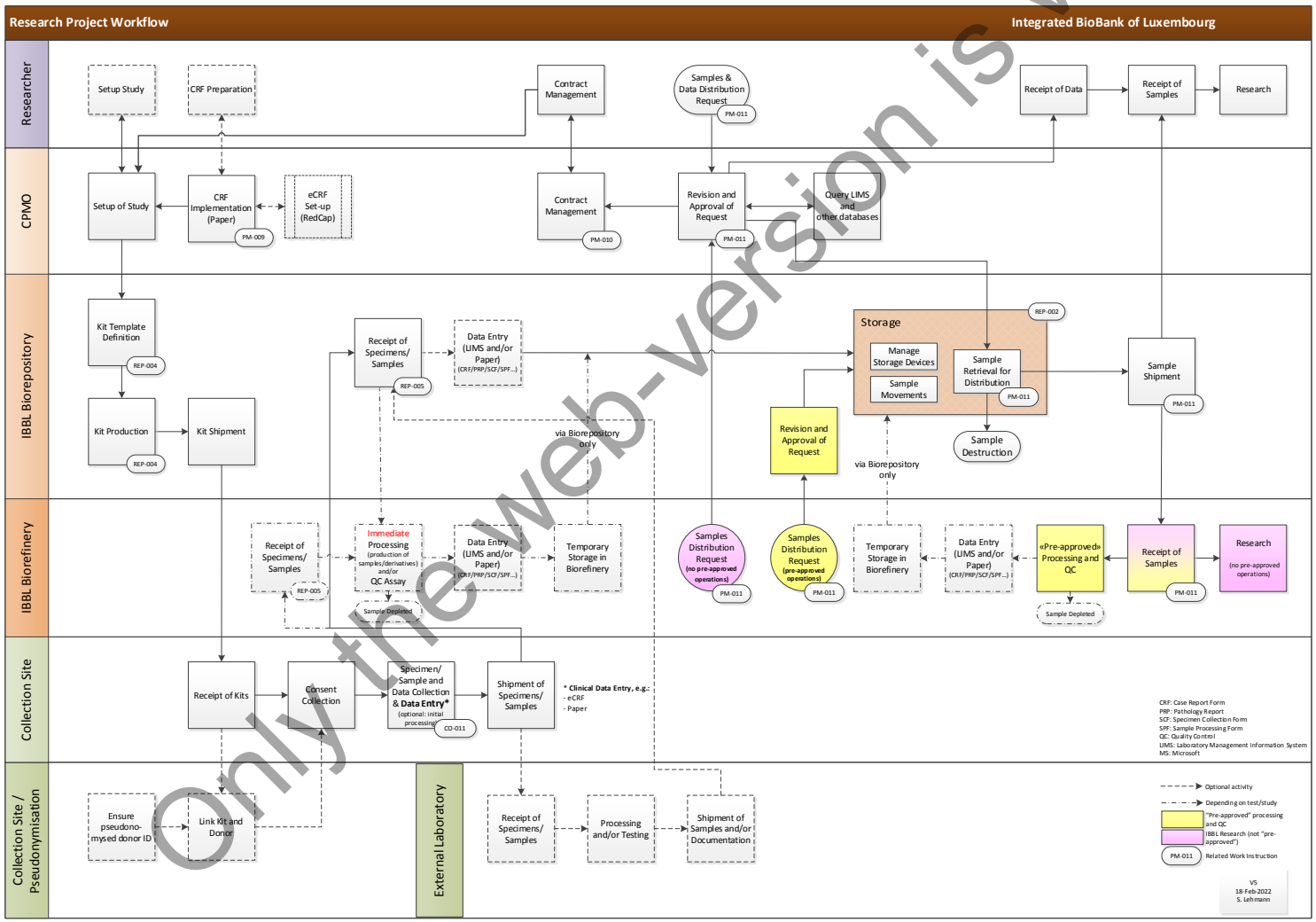


Exhibit B: Example Workflow for a Client Collection Project

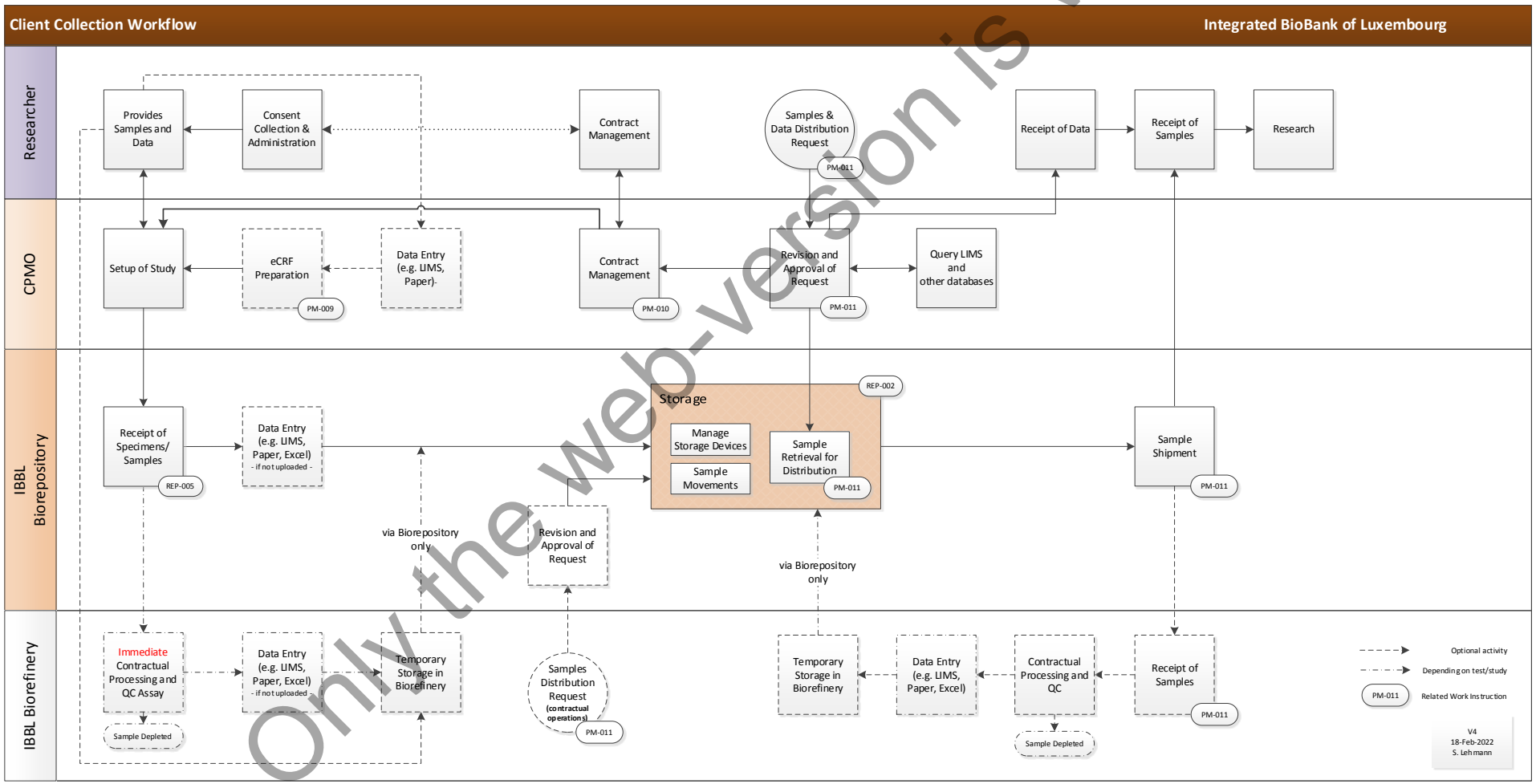


Exhibit C: Actors in standard sub-processes

The table below provides an overview of the involvement of IBBL's operational departments in the different operational sub-processes.

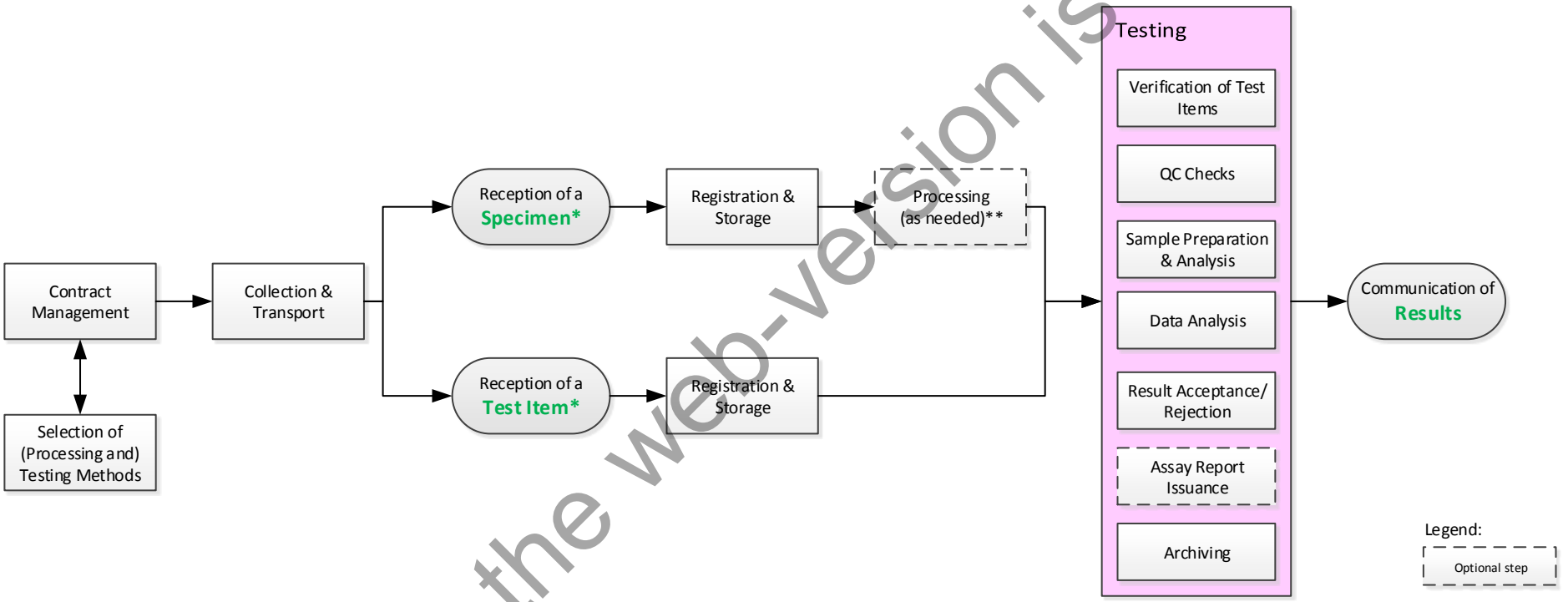
	Contract Manage-ment	Collection & Transport S = Samples D = Data	Specimen/ Sample Receipt & Registration S = Samples D = Data	Processing S = Samples D = Data	Testing S = Samples D = Data	Storage S = Samples D = Data	Retrieval S = Samples D = Data	In-house R&D*	Outgoing Shipment S = Samples D = Data	Destruction S = Samples D = Data	Distribution: External R&D S = Samples D = Data
CPMO	X	●		●	●		X (S)		● (S,D)	X (S)	X (S)
Admin	X										
Pathology	●	X (S)	●	X (S)	X (S)	●	●	X		●	
Biorefinery	●		●	X (S)	X (S)	●	●	X		●	
Biorepository	●	X (S)	X (S)			X (S)	X (S)		X (S)	X (S)	X (S)
BIS	●	X (D)	X (D)	X (D)	X (D)	X (D)	X (D)		X (D)	X (D)	X (D)
QMS Sub-chapter	PM	CO/REP	REP	REF	QC	REF/REP	REP/PM	--	REP/PM	PM/REP	PM/REP

* outside the certification/accreditation scope

X Responsible / Accountable

● Contributor

Exhibit D: Schematic Workflow for a Testing Process



* **Specimen** = primary biological material received in the scope of a research/collaboration/fee-for-service project, typically requiring "processing" before being submitted to a test
Test Item = biological material received from a customer, in most cases "ready for testing", i.e. not requiring "processing" before being submitted to a test.

** **Processing** = production of the item to be submitted for testing, when the provided specimen cannot be directly submitted to the test method
(e.g. The specimen "PAXgene stabilized blood" is provided to IBBL for the determination of quantity and integrity of RNA [extracted (i.e. "processed") by IBBL from the delivered specimen]); this processing shall not be confused with any "sample preparation", specifically required for the execution of the test method.

Exhibit E: List of Referenced Documents

Document Code	Title
SOP GM-HR	Human Resources
SOP GM-FP	Finance & Procurement
SOP GM-PM	Project Management
SOP QM-DC	Document Control
SOP QM-QM	Quality Management
SOP QM-QA	Quality Assurance / Quality Control
SOP IN-FA	Facilities
SOP IN-EQ	Management of Equipment
SOP IN-IT	Information Technology
SOP OP-CO	Collection
SOP OP-REP	Biorepository
SOP OP-REF	Biorefinery
SOP OP-QC	Quality Control Assays
WI QM-004	Performance Evaluation & Continuous Improvement
WI DC-901	Corporate Quality Document Administration

Exhibit F: Abbreviations, Acronyms, Definitions

A	Annex
AP	Assay Protocol
AS	Assay Sheet
BIS	Business Information Solutions
BRC	Biological Resource Centre
CEO	Chief Executive Officer
CI	Continuous Improvement
CO	Collection
CPMO	Clinical Project Management Office
CRP	Centre de Recherche Publique
DC	Document Control
DNA	Deoxyribonucleic acid
EQ	Equipment
F	Form
FA	Facilities
FP	Finance & Procurement
GCP/GCLP	Good Clinical (Laboratory) Practice
GDPR	General Data Protection Regulation
GM	General Management
HR	Human Resources
IBBL	Integrated BioBank of Luxembourg
ICH	International Conference on Harmonization
ICT	Information & Communication Technology
IEC	International Electrotechnical Commission
IN	Infrastructure
ISBER	International Society for Biological and Environmental Repositories
ISO	International Organization for Standardization
IT	Information Technology
KPI	Key Performance Indicators
LIH	Luxembourg Institute of Health
MESR	Ministère de l'enseignement supérieur et de la recherche (Ministry of higher education and research) (Luxembourg)
NCI	National Cancer Institute (USA)
NCP	National Cytometry Platform
NF	Norme française (French norm)
OECD	Organization for Economic Co-operation and Development
OP	Operations
PM	Project Management
PRO	(Corporate) Procedure
PS	Project Specification
PSOP	Project-specific Standard Operating Procedure
PT	Proficiency Testing
QA	Quality Assurance
QC	Quality Control; Quality Control Assays
QI	Quality Indicators
QM	Quality Management, Quality Manual
QMS	Quality Management System
QSMO	Quality &Safety Management Office
R&D	Research & Development
REF	Biorefinery
REP	Biorepository
RNA	Ribonucleic acid
S	Spreadsheet
SME	Subject Matter Experts
SOP	Standard Operating Procedure
SS	Study Summary
T	Template
TMOH	Translational Medicine Operations Hub
TTM	Transversal Translational Medicine
WHO	World Health Organization
WI	Work Instruction

DOCUMENT METADATA

Document Information			
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Authorship & Approval	**Names**	**Functions**	**Approval Date(s)**
Author(s):	Sabine LEHMANN	Head of Quality & Safety Management	21/02/2022
Approver(s):	Hermann THIEN	Director TMOH, Head of IBBL	21/02/2022
QM Approver(s):	Thérèse BAURITH, Alessandra ROSSATO	Quality Officer, Quality Officer	22/02/2022, 22/02/2022
Changes Compared to Previous Version	**Revision History** (see separate section for history of changes for documents updated before the implementation of eQMS)		
General review to accommodate the organizational changes within LIH with an impact on IBBL, update the interested parties section, expand the rationale of the QMS in the scope of the overall LIH QMS, update the overviews of some Core Processes, update of Exhibit A and B to accommodate new unit names (e.g. CPMO instead of IBBL PM) and Exhibit F with new abbreviations; re-organization of the order of sections and deletion of the service offers section; editorial updates.	01 - 15/09/2014 - Legacy Document import., 02 - 09/06/2015 - Legacy Document import., 03 - 19/07/2016 - Legacy Document import., 04 - 17/10/2016 - Legacy Document import., 05 - 25/09/2017 - Regular update; update of members of Board of Directors; clarification of "Core Administrative Services" and their role in IBBL QMs; clarification of "Corporate Quality Documents" in the role of IBBL QMS., 06 - 19/01/2018 - Change of address after move; indication of voluntary interruption of accreditation due to move; addition of "neighbors" as interested parties after move., 07 - 28/06/2018 - Updates to cover ISO 9001:2015 requirements; removing certification for NF S96-900 and removing suspension of accreditation; update of some charts; editorial updates., 08 - 31/10/2019 - Update to ISO 17025:2017, Addition of ISO 20387 as reference, Update of PT schemes, Update of LIH overall org chart, Update of ISO 17025 accreditation scope (removal of 4 methods: M004, M006, M017, M046), Update of Document Hierarchy to add new document types (PS and G), Update of QMS structure drawing to highlight areas with (potentially) corporate procedures, addition of LIH as interested party, minor editorial updates across the whole document., 09 - 26/05/2020 - General review; editorial updates; Removal of details related to board of directors composition replaced byreference to website; Integration of LIH's mission and vision and embedding of IBBL's specific contributions to them; Editorial updates in the Quality Policy without changing the policy core; Update of the Interested Parties table, e.g. by focusing on TTM partners and by adding the Ministry of Health as explicit interested party in the view of LIH/IBBL roles in the COVID-19 pandemic contributions.		

REVISION HISTORY

Version	Effective Date	Author	Summary of changes
.01	15/SEP/2014	Sabine LEHMANN	New document
.02	09/JUN/2015	Sabine LEHMANN	Changes related to the merger with CRP-Santé (e.g. "The organization", "Management Structure"); update of section "Service offers"; update of section "Quality Manual" to integrate requirements for ISO 17025 accreditation; update of "Process Overview" flowchart; update of "Interested Parties" section to include the 'General Public of Luxembourg' and the 'Grand Region'; two Exhibits added (C, D); renumbering of all Exhibits; minor editorial changes throughout the whole document.
.03	19/JUL/2016	Sabine LEHMANN	Revision of section "Service Offers" to align it with the updated marketing strategy of IBBL; section "Management Structure": update of board members; section "Quality Manual": inclusion of methods for extension of the accreditation scope; section "Document Hierarchy": inclusion of "Corporate Documents"; update of the "Mission & Vision" section; minor editorial changes throughout the whole document.
.04	17/OCT/2016	Sabine LEHMANN	Clarification of certification & accreditation scope; addition of the law of 3rd December 2014 as reference; elucidation on the roles & responsibilities of technical management and quality manager; clarification of terminology used in Annex D.

*** End of document ***