Reference	Version	Application date	Expiry date
QUAL-0001	**04**	31/12/2020	31/12/2022

Quality Manual

Signatories of the document:

Role	First Name NAME	Date
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QA Approval	Stephan DIETRICH	28/12/2020

1. QUALITY POLICY

ABL Europe's general Quality policy

ABL Europe is a Contract Manufacturing Organization focused on the manufacturing of products derived from recombinant viral vectors.

Our Quality commitment to our customers leads us to make available safe and effective products that are manufactured and distributed observing both regulatory requirements and our company values.
Our well-established Quality System, built by the Quality Organization, is described in a Quality Manual.
The effectiveness of the implementation of the latter is verified in particular by Quality audits, and a continuous improvement approach is practiced by all entities.

Quality fundamentals are experienced by the whole workforce, from senior management to each and every employee, substantiating a strong Quality Culture, a necessary condition for the Quality System to be fully implemented. All associates must continuously qualify for their job and deploy a constant learning attitude.

Thanks to the commitment of each individual to this Quality mindset, at all levels of the company, we will be able to meet our customers' expectations.

Patrick MAHIEUX
CEO
February 2016

2. PURPOSE AND MANAGEMENT OF THE QUALITY MANUAL

2.1 Purpose

- The purpose of the Quality Manual is to describe the company's established organization system, the Quality system and the strategic documents related to the applicable Quality standards, pursuant to ICH Q10 requirements.
- It is used to present the company's Quality systems and Quality principles to ABL Europe employees aiming to provide an overall, cross-functional vision of how the Quality system is applied companywide.
- It is also used to present ABL Europe's Quality systems to our customers and partners, as well as to the regulatory authorities, with the aim of informing them about our Quality policy.

2.2 Writing, approval and storage location

- The Quality Manual is drafted by the Quality Direction
- It is approved by the Quality director, the Qualified Person, and the CEO.

2.3 System of revision

- Those in charge of drafting and approving the Quality Manual are also in charge of updating it.
- Updating is done every year.
- A special update may be requested, following:
  - an audit or inspection,
  - a change in organization and related resources,
  - an internal or external request.

2.4 Distribution of the Quality Manual

- The Quality Direction is responsible for distributing and updating the Quality Manual. The entire staff is concerned by the application of this manual.
- It is made available to all ABL Europe's new employees, for them to have a comprehensive understanding of the company business.
- It may be distributed outside the company to partners, customers, and health authorities, with the Quality Directors' authorization.

3. ABOUT THE COMPANY

3.1 Main activities

ABL Europe is a Contract Manufacturing Organization focused on the manufacturing of products derived from recombinant viral vectors.

ABL Europe has manufacturing capacities for clinical batches, which operate in compliance with international Good Manufacturing Practices for medicinal products. These units give ABL Europe the capacity to produce and control products for their customers.

Workforce, sites and equipment, and the manufacture of therapeutic products, are subject to very thorough regulations drawn up by numerous governmental authorities in France, Europe, the United States and other countries.

The European Medicines Agency (EMA), the Agence Nationale de Sécurité du Médicament et des produits de santé (ANSM), the Food and Drug Administration (FDA) in the United States and other bodies, impose compliance with strict conditions for the manufacture, development and commercialization of products like those developed by ABL Europe, in particular their preclinical and clinical assessment.

As pharmaceutical facilities, manufacture and control sites are regulated by the French Health Code of Regulations. In accordance, a Qualified Person is named by the Chairman of the company.

ABL Europe is part of ABL, Inc. a global contract research and manufacturing biomedical organization dedicated to advancing vaccines, therapeutics, and other biologic products. ABL, Inc. is located in Rockville, MD, U.S.

3.2 Our team

The achievement of our goals is largely driven by the quality and the skill base of the people employed at ABL Europe. The expertise, professional experience and commitment of our employees, are what lie at the heart of our business. It is through the dedicated work of ABL Europe employees that products are manufactured and delivered to our customers.

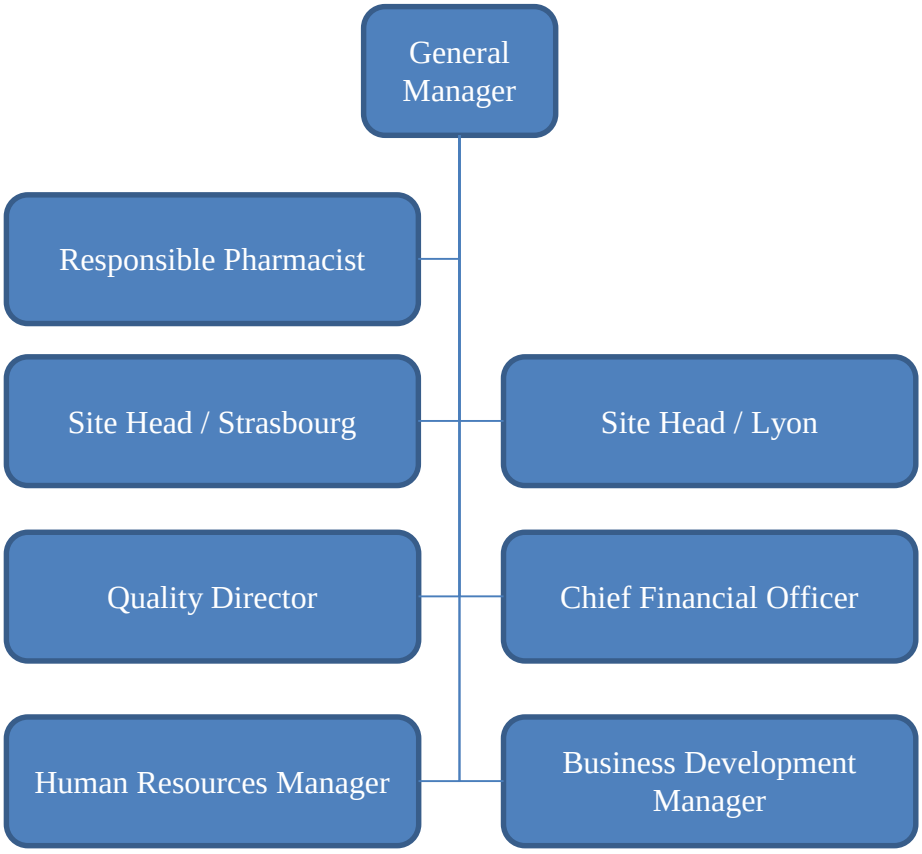
3.3 Locations

- ABL Europe _ Headquarters & Manufacturing
  4 rue Laurent Fries 67400 ILLKIRCH GRAFFENSTADEN

- ABL Europe _ Quality Control
  400 boulevard Gonthier d'Andernach 67400 ILLKIRCH GRAFFENSTADEN

- ABL Europe _ Manufacturing
  317 Avenue Jean Jaurès, 69007 LYON

4. ORGANIZATION CHARTS

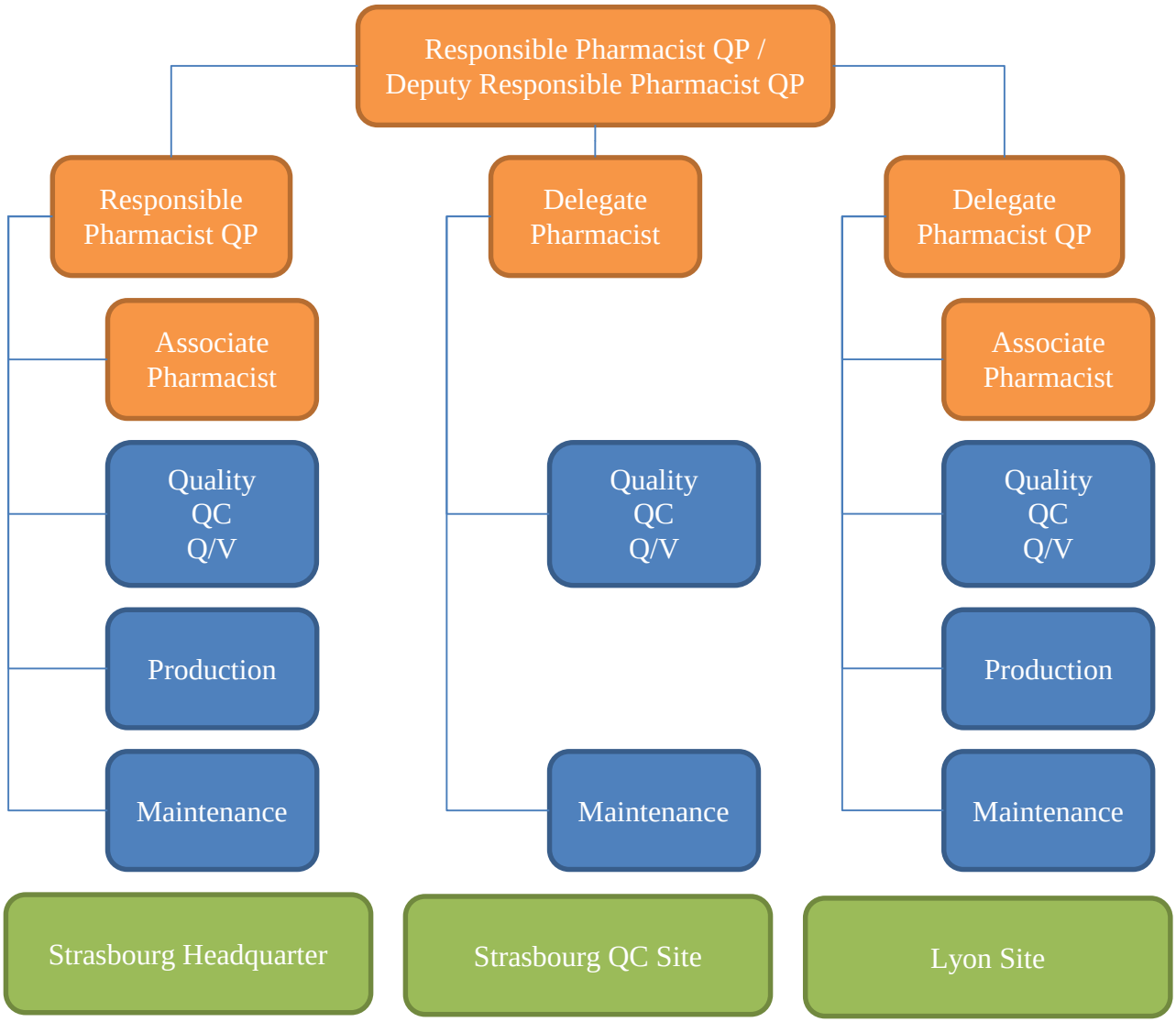


4.1 Quality Direction organization

The Company has set up a Quality Direction, for which the objective is to satisfy regulatory requirements relating to the quality and safety of pharmaceutical products for human use.
The Quality Direction ensures the quality systems are implemented (described in **§ 8**) throughout the company and is supported by the senior leadership team of the organization.

4.2 Pharmaceutical responsibilities

The following organization chart shows supervision relationships between the Responsible Pharmacist, Qualified Person and other registered pharmacists, as Associate Pharmacists or Deputy Responsible Pharmacists or delegated Qualified Persons.



5. APPLICABLE QUALITY STANDARDS

All ABL Europe activities are managed in compliance with Quality Manual directives.

Quality System requirements are based on the following standards or recommendations:

A. French Public Health Code.

B. European and US pharmacopoeias

C. EU GMP – Good Manufacturing Practices

D. ICH guidelines as applicable to ABL Europe business (i.e. ICH Q10)

E. Directive 2009/41/CE on the contained use of genetically modified micro-organisms

F. EU GMP specific to Advanced Therapy Medicinal Products

6. GENERAL REQUIREMENTS

- ABL Europe's Quality System is based on the standards cited in **§ 5**.
- The Quality System also demonstrates the ABL Europe management team's will to standardize the company's practices and to optimize their organization.

7. ORGANISATION AND RESPONSIBILITIES

- The organization chart allows each employee to locate his/her role within the organization. More concisely, Quality management-related responsibilities are described in the table below:

Organization	Quality management responsibility
General Management	– Designates a Head Pharmacist/Qualified Person in charge of endorsing the responsibility of the Pharmaceutical Operations as defined into the French Health Code (Art. R.5124-36). – Establishes and oversees the enforcement of the Quality policy defined by the company and/or by the health authorities of the different countries to which products may be distributed. – Orders Quality management reviews so as to verify the due application and effectiveness of the Quality system and to promote continuous improvement. – Monitors compliance with Quality, Safety, Environment and Productivity objectives. – Ensures that the company's communication procedures are set up in a manner conducive to efficient Research, Development and Production processes as well as to employees' motivation. – Ensures that the company has sufficient personnel with the correct training to maintain the company's level of Quality. – Must ensure that responsibilities and authorities are defined and made public within ABL Europe. – Is in charge of hygiene, security, and working condition-related issues concerning the company personnel and any outside contributors.

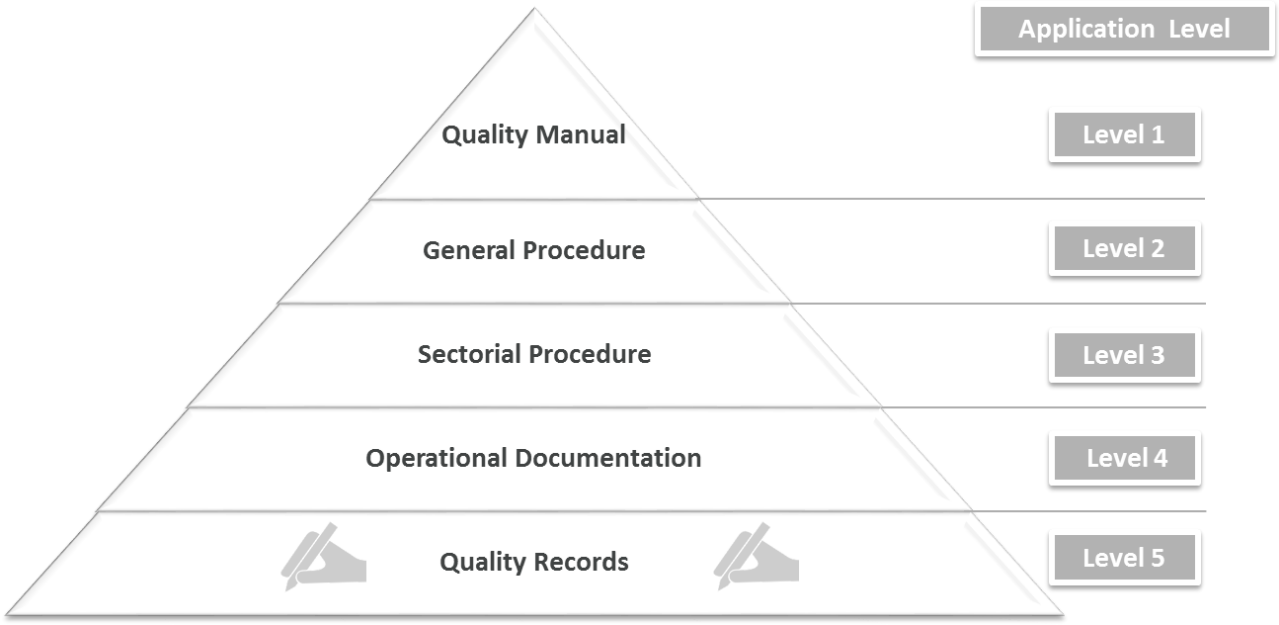
Organization	Quality management responsibility
Head Pharmacist Qualified Person & Quality	– Covers the missions defined into the French Health Code (Art. R.5124-36). – Sustains the Plant licenses & Certifications related to the covered activities and interacts with competent authorities. – Establishes, evaluates and contributes to the implementation of the Quality System (See chapter 8), including the management of deviations, complaints, change control, OOS and CAPAs & related activities. – Reports on the smooth running and update of the Quality system during periodic Quality management reviews, supported by a documented tracking report as well as effectiveness checks of remediation actions if any. – Ensures compliance with regulatory pharmaceutical standards. – Monitors and approves the quality-related documentation system. – Coordinates the Quality documents archiving system. – Responsible of the product certification. – Organizes and contributes to employee training. – Establishes the Pharmaceutical organization to cover pharmaceutical operations in the manufacturing building. – Authorizes and guarantees the monitoring of modifications affecting pharmaceutical operations. – Sets a robust Supplier Quality Assurance process and participates in suppliers' selection and monitoring. – Manages internal and external audits. – Guarantees equipment and systems qualification. – Process and testing methods validation. – Participates in products projects meetings. – Establishes Validation Master Plan. – Control the raw materials within the allocated time. – Plans testing operations in order to fulfil requirements in terms of quantities and lead times, in addition to Quality requirements. – In charge of production and testing specifications. – Tests intermediate and finished products within the allotted time. – Provides stability lots management. – Guarantees the completion and the follow up of corrective and preventive actions. – Coordinates the product recall.
Production	– Produces intermediate and finished products within the allocated time. – Stores intermediate and finished products. – Ships finished product. – Develops new products and processes – Manages necessary investments linked to the site development – Participates in products projects meetings.
Administrative Direction	– Ensures the follow up of financial activities. – Ensures the company's compliance with its legal, social and regulatory obligations. – Ensures the follow-up of legal activities. – Defines purchasing strategy. – Ensures the smooth running of purchasing operations. – Participates in supplier selection and monitoring. – Resource management (recruiting, training and qualification, wage, legal obligation). – Coordinates job description management. – Monitors outside training programs defined in the annual training plan.

8. ABL EUROPE'S QUALITY ASSURANCE SYSTEM

- ABL Europe's Quality Assurance system is built in compliance with the standard requirements listed in **§ 5**.
- A continuous Inspection & Audit readiness objective is pursued.
- The 10 basic elements of this system are:
  - The documentation system,
  - The management of self-inspection and audits,
  - Change management,
  - Deviation management,
  - OOS Management
  - Quality training management,
  - The corrective and preventive action management system,
  - Quality Risk Management,
  - The batch review and Release process.
  - Management review.
- All these systems are managed by Quality indicators grouped in a tracking report. This tracking report is updated monthly and communicated periodically to the Management in order to inform and take decisions on axes of improvement which need to be focused on. Critical gaps are communicated regularly to the Management without necessarily waiting for the next quality review report.
- As having multiple sites, the quality organization chases simplification & synergy across its network, fostering best practices and sharing them whenever possible.

8.1 The documentation System

The documentation system is organized into a 5-level pyramid structure.



These different levels contain the following documents:

Level I (Strategic)
Describes the company's strategy (general policy) in terms of Quality. This level is composed of this Quality Manual.
Level II (General Process)
Describes a process that applies to the whole company. These are the General Procedures; the documents define operation and organization rules and describe associated responsibilities. This level is made up of procedures only.
Level III (Sectorial Process)
Describes a process that applies to part of the company. These are the Sectorial Procedures; the documents define operation and organization rules and describe associated responsibilities. This level is made up of procedures only.
Level IV (Operational)
Describes the operational level; these documents lay out the "who, when, how, where." This level is composed of Instructions, Specifications and Lists.
Level V (Quality Records)
This level is composed of slips, analysis and production batch reports. These records document traceability and serve as proof of the smooth running of operations.

8.2 Management of self-inspection and audits

- ABL Europe has implemented an auditing system with self-inspection and external audits (suppliers/ subcontractors). The objective is to take a picture at a given time, so as to generate progress and, if necessary, to correct a practice or a failure.
- The Quality audits schedule is determined every year and validated by the Quality Director & Qualified Person.
- It is monitored through the use of Quality indicators.
- Audits are performed by trained, authorized employees.
- Each audit is drawn up in a report presenting its findings. The departments audited are responsible for undertaking the necessary corrective actions, which are then monitored by the Quality Assurance.
- Alongside with the managers of the audited units, the quality management is checking the implementation and efficacy of the corrective actions; if necessary, this is also done by the auditing team during subsequent audits.
- An auditing report is drawn up each year. It is presented to the General Management during the Quality reviews.

8.3 Change management

ABL Europe has implemented a change management system. Its objective is to describe, justify, identify and evaluate the direct (re-qualifications, validations, etc.) or indirect, immediate or delayed consequences of the implementation of any change made to an activity, an operating method, a use, a technique, a flow, a responsibility, the implementation or validation of a procedure related to Pharmaceutical activities.

8.4 Deviations management

- ABL Europe has implemented a deviation and planned deviation management system. Its objective is to evaluate the potential impact of the occurrence of a problem or of a planned deviation on the products or systems.
- Any non-forecasted deviation is the subject of an investigation.
- In the event a problem is identified, the corrective and preventive action plans are determined and implemented, according to the causes, in order to avoid any reoccurrence of the problem.
- The services affected are in charge of determining the Quality impact on the product(s) affected and to undertake the necessary corrective actions. These corrective actions are monitored by Quality Assurance.

8.5 OOS management

- ABL Europe has implemented a system to record and investigate Out Of Specification (OOS) results.
- Quality Control laboratory is responsible for the laboratory investigation of OOS.
- If laboratory error cannot be identified, a formal investigation is initiated in the Manufacturing or others related areas.
- Quality Unit is responsible for batch related decisions when an OOS result is confirmed and to assure that CAPA are taken to prevent reoccurrence.

8.6 The corrective and preventive action monitoring system

- ABL Europe has implemented a corrective and preventive action (CAPA) management system for actions related to deviations, internal audits, inspections by regulatory authorities and partner audits.
- Actions are headed by Quality Assurance and each department head has to set up the actions connected to his/her area of activity.
- The efficacy of these actions is checked during self-inspection and by the deviations recurrence analysis.
- A monthly tracking report is presented in the Quality tracking report.

8.7 The quality risk management

ABL Europe has implemented a Quality risk management process.
It applies to the company's activities subject to GMP regulations and to all stages of the product lifecycle. Whenever a situation is encountered where decisions must be taken without clear references or guidance's this process should apply to demonstrate ABL's positioning.
Different methods of risk analysis are in place at ABL Europe to cover these areas.

Quality risk management can be useful for identifying and prioritizing areas for continuous improvement.

8.8 Quality training management

- ABL Europe has implemented an initial and on-going pharmaceutical-related training and certification system for their employees.
- All new employees are provided with an "initial training and certification" for their position.
- Every ABL Europe employee, performing an activity at least directly or indirectly related to an operation pertaining to Good Manufacturing Practices has an Individual Training and Certification File, containing their resume, job description, and an overview of the internal/external training and certification they have received or are yet to receive.
- Training programs and certification are recorded, and their efficacy evaluated.
- A GMP training session is provided annually to the personnel connected to the company's pharmaceutical activities.
- The areas in which each employee must be trained and entitled, and the frequency of re-training or re-certification are defined by the appropriate Department Head, in agreement with Human Resources and Quality department.

8.9 The batch file and pharmaceutical certification file review system

- ABL Europe has implemented a Quality Assurance batch record review system in compliance with the GMP.
- All batches go through a pharmaceutical release.
- Those in charge of this activity are trained and entitled to.

8.10 Management review

ABL Europe has implemented quality reviews to ensure the relevance and effectiveness of its quality system.

Quality reviews are organized as follows:

Committees	Frequency	Main Goals
General Management Review: - Steering committee - COS Illkirch and Lyon - Quality managers Illkirch and Lyon - QPs Illkirch and Lyon	Annually	- Evaluation of the quality matrices monitoring results from previous year, through a review of quality indicators, - Definition of quality objectives and action plan if needed for the new year, - Results of regulatory inspections and client audits, - Follow up of actions raised from previous management reviews - General review of quality management system and organization and quality policy.
Quality Management Review: - Quality managers Illkirch and Lyon	Quarterly	- Follow-up of quality indicators, - Follow-up of action plans and remediation from previous General management review and quality management reviews, - Definition of new actions if needed, allocation of resources, - Adjustments of the QMS and the organization.
Quality Meeting: - Quality managers Illkirch and Lyon	Monthly	- Best practices and quality topics to share between sites - Sites performance review - Systems alignment

9. KEY SOP'S APPLIED AT ABL EUROPE

This listing represents the key SOP's applied at ABL Europe according to a standard Pharmaceutical organization. The main objective of this listing is to give a global and synthetic view on the SOP's system applied in the company.

This listing has been built according to the following topics:
- Quality Management,
- Personnel,
- Premises and Equipment,
- Documentation,
- Production,
- Quality Control,
- Outsourced activities,
- Inspection.

Field	Thematic	Procedures
Quality Management	Change Management	SOP-0004
	Deviation Management	SOP-0005
	CAPA Management	SOP-0008
	OOS Management	SOP-0038
	Regulatory monitoring	SOP-0059
	Quality risk Management	INS-0290
Personnel	Training of Personnel	SOP-0006
Premises and Equipment	Calibration Management	INS-0274
	Maintenance Management	SOP-0022
	Pest Control	SOP-0019
	Cleaning and Sanitization	SOP-0035
	Facility, Utility and Equipment identification	INS-0296
	Prevention of Cross Contamination	SOP-0011
	Waste Disposal	INS-0270
Documentation	Standard Operating Procedures	SOP-0001
	Documents archiving	SOP-0058
	Management of Visa and Signatures	INS-0300
	Electronic Document Management System	INS-0186
Production	Technology Transfer of new API and new DP	SOP-0026
	Flows and access in Manufacturing Areas	SOP-0016
	Manufacturing by campaign	SOP-0010
Quality Control	Management of Laboratory Operations	SOP-0012
	Transfer of analytical methods	SOP-0037
	Stability Programs	INS-0282
	Sampling operations	INS-0381
Outsourced activities	Vendor qualification and follow-up	INS-0280
Inspection	Self-Inspection	SOP-0002

10. GLOSSARY

Definitions of the main terminology and abbreviations	
GMP	Good Manufacturing Practices
FDA	Food and Drug Administration
ICH	International Conference of Harmonisation
GMO	Genetically Modified Organism
CAPA	Corrective and Preventive Action Plan

11. FOLLOW-UP OF THE CHANGES

Version 03	Applicable version	ACT2020-0246: update of quality review topics and frequency Update of key SOPs (§9). Update of revision frequency (§2.3) and applicable quality standards (§5)
Version 02	29AVR19	Document update following new site acquisition
Version 01	24MAR16	Document creation following ABL Europe activities start