Quality Manual / Site Master File

Combined document

Name of the Company:	Nelson Labs NV
Address:	Romeinse Straat 12 3001 Leuven, Belgium
Phone:	+32 16 400484
Fax:	+32 16 401304
24h contact:	Dr. Bart Boerjan (+32 472 533307)
	(Back-up) Dr. Lise Vanderkelen (+32 499 340128)
Location:	Lat / Lng: 50°50'40.8"N 4°44'10.5"E
DUNS:	766951479

Revision History:

Rev. No.	Date Revised	Revision Summary	Author
13	18 APR 2019	- Addition of revision history - Complete rearrangement of the quality manual in line with the requirements of ISO 17025:2017 - Update of organizational structure - Change of procedural references to new MasterControl references - Upgrade to multi-use document Quality Manual / Site Master File (incorporation of site master file). - General upgrade of outdated information - Including definition of GxP criticality	BB
14	10 JUL 2020	- Replacement of Jos Bollen by Bart Boerjan as 24-hour contact. - Addition of cleaning, disinfection and steam sterilization validation of reusable devices to scope of services. - Clarification on mutual acceptance of data (MAD) for GLP studies and mutual recognition agreement between US FDA and EU GMP for GMP studies - Introduction of HCM for direct reporting lines and responsibilities. - Split of Health, Safety and Environment management and maintenance of facility. - Replacement IT Manager by IT Director EMEAA - Clarifying note on replacement QP and end responsibility Qualified Person. - Alignment of processes and referenced procedures - Clarifying note added on job aids - Use of Kaizen cards for bottom-up continuous improvement - Use of LIMS for equipment status introduced - Involvement of QP in management review process clarified. - Included new GLP website of Sciensano	BB
15	31 MAY 2021	- Incorporation of MAN0017: User Access Management Policy - Update organizational chart GLP for transition and split of TFM responsibilities - Update of Top Management transition of VP EMEAA Operations and Managing Director to Managing Director (management responsibility and org charts). - List of procedures updated - Rephrased verbiage of Validation Master Plan to Validation Policy - Addition of silver fish monitoring to the pest control program	BB

		- Describing reference standards as second source to check calibration standards rather than exclusive use as reference standard. - Added requirement for e-signatures on final reports - Monthly dashboarding of global quality objectives added - Addition of Frank De Smedt's and Lise Vanderkelen's approval as Test Facility Management - Addition yearly review of risk assessments during management review - Addition of effectiveness checks as a built-in part of the CAPA process - Link added to the website of the Belgian official journal for records on Nelson Labs NV.	
16	31 AUG 2022	- Update of OECD reference documentation (incl. n° 23 and 24 published in 2022). - Addition of insider trading policy training in impartiality clause. - Introduction of "teamleader" as a responsibility throughout the management structure. - Introduction of Back-office management responsibility. - Update of organizational charts - Introduction of MAN0018 – Change Policy - Clarification on first line controls added (second source standard) - Change remedial action into immediate corrective action - Inclusion of OECD 22 as Data Integrity reference - Clarification on quality critical job Aids in MasterControl. - Update GMP certificate reference to 2022 inspection	BB
17	See mastercontrol for effective date	- Change of back-up 24hour contact to Lise Vanderkelen. - Addition of additional regulatory requirements imposed by ISO17025 accreditor. - Update to change department supervisor to (Sr.) Lab Operations Manager or Team Manager (whichever applicable). - Description of function and job description in a more general way to anticipate archival of AUX1815. - Introduction of scientific project manager and scientific expert to describe the project management responsibilities for E&L (previously Study Director) - Update Organizational charts with new function titles - Addition of detailed chart of lab organization	BB

		- Addition of SOP0922 for global IT system change control. - Omittance of SOP0384 which is integrated into SOP0377. - Addition of SOP0888 to introduce good practices for manual integration - Addition of corporate context information for Nelson head quarters and Sotera IT organisation - Clarification added for sampling	
18		- Typo corrections for FAMHP abbreviation - Addition of list of critical software and applications - Addition of list of critical suppliers - Addition of Personnel overview - Update of GMP org chart (initials)	BB

TABLE OF CONTENTS

1 Scope 10

1.1 BRIEF HISTORY OF THE LABORATORY 10
1.2 TESTING SERVICES IN SCOPE 11
1.3 PREDICATE RULES AND APPLICABLE REGULATIONS FOR THE QUALITY SYSTEM 12
1.3.1 Licensing, certification and accreditation by notified bodies 12
1.3.2 Integration into a global or corporate organization 13

2 Regulatory QMS References 13

2.1 ADDITIONAL REGULATION IMPOSED BY ACCREDITORS 14

3 Terms and definitions 14

4 General requirements 15

4.1 IMPARTIALITY 15
4.2 CONFIDENTIALITY 15

5 Structural requirements 15

5.1 LEGAL ENTITY 15
5.2 RESPONSIBLE MANAGEMENT 16
5.3 ORGANIZATIONAL CHARTS 18
5.3.1 Organizational chart ISO 17025 19
5.3.2 Organizational chart GLP 21
5.3.3 Organizational chart GMP 23
5.4 RELATED DOCUMENTATION 25

6 Resource requirements 25

6.1 GENERAL 25
6.2 PERSONNEL 25
6.2.1 Related Documentation 25
6.2.2 Personnel Evolution and current state 26
6.3 FACILITIES AND ENVIRONMENTAL CONDITIONS 27
6.3.1 Related Documentation 27
6.4 EQUIPMENT 27
6.4.1 Related Documentation 28

6.5 METROLOGICAL TRACEABILITY 28
6.5.1 General 28
6.5.2 Specific Requirements 28
6.5.3 Reference Standards and Reference Materials 28
6.5.4 Related Documentation 29
6.6 EXTERNALLY PROVIDED PRODUCTS AND SERVICES 29
6.6.1 Externally provided Products 29
6.6.2 Externally provided Services 29
6.6.3 Related Documentation 30

7 Process requirements 30

7.1 REVIEW OF REQUESTS, TENDERS AND CONTRACTS 30
7.1.1 Related Documentation 30
7.2 SELECTION, VERIFICATION AND VALIDATION OF METHODS 31
7.2.1 Selection of Methods 31
7.2.2 Laboratory Developed Methods 31
7.2.3 Non-Standard Methods 31
7.2.4 Validation of Methods 31
7.2.5 Related Documentation 32
7.3 SAMPLING 32
7.4 HANDLING OF TEST OR CALIBRATION ITEMS 32
7.4.1 Related Documentation 33
7.5 TECHNICAL RECORDS 33
7.5.1 Related Documentation 33
7.6 EVALUATION OF MEASUREMENT UNCERTAINTY 33
7.6.1 Related Documentation 33
7.7 ENSURING THE VALIDITY OF RESULTS 34
7.7.1 Related Documentation 34
7.8 REPORTING OF RESULTS 34
7.8.1 General 34
7.8.2 Test Report 34
7.8.3 Test Result Report 35
7.8.4 Study Report 35
7.8.5 Calibration Reports 35
7.8.6 Certificate of Analysis 35

7.8.7 Conclusions, Statement of Conformity, Opinions, and Interpretations 35
7.8.8 Test and Calibration Results Obtained from Subcontractors 35
7.8.9 Electronic Transmission of Results 35
7.8.10 Amendments 35
7.8.11 Related Documentation 36
7.9 COMPLAINTS 36
7.9.1 Related Documents 36
7.10 NON-CONFORMING WORK 36
7.10.1 Related Documentation 37
7.11 CONTROL OF DATA AND INFORMATION MANAGEMENT 37
7.11.1 Related documentation 37
8 Management system requirements 37
8.1 MANAGEMENT SYSTEM OPTION ACCORDING TO ISO/IEC 17025:2017 37
8.2 MANAGEMENT SYSTEM (MS) DOCUMENTATION 37
8.2.1 Quality Manual / Site Master File 38
8.2.2 Quality Policy Statement 38
8.2.3 Quality Objectives 38
8.2.4 Nelson Labs Values 38
8.2.5 Nelson Labs Goals and Management Commitment 39
8.3 CONTROL OF MANAGEMENT SYSTEM DOCUMENTS 42
8.3.1 General 42
8.3.2 Internal Documents 42
8.3.3 External Documents 43
8.3.4 Related Documentation 43
8.4 CONTROL OF RECORDS 43
8.4.1 General 43
8.4.2 Technical Records 43
8.4.3 Quality Records 44
8.4.4 Related Documentation 44
8.5 ACTIONS TO ADDRESS RISKS AND OPPORTUNITIES 44
8.5.1 Related Documentation 44
8.6 IMPROVEMENT 44
8.6.1 Related Documentation 45
8.7 CORRECTIVE ACTIONS 45

8.7.1 General 45
8.7.2 Related Documentation 45
8.8 INTERNAL AUDITS 45
8.8.1 Related Documentation 46
8.9 MANAGEMENT REVIEW 46
8.9.1 Related Documentation 46

9 Appendix A: Quality Assurance at Nelson Labs NV, overview of Roles and Responsibilities 47

9.1 QUALITY ASSURANCE 47
9.2 RELATED DOCUMENTATION 47

10 Appendix B: Scope of accreditation and certification 48

11 Appendix C: Nelson Labs SOP Matrix 49

11.1 MANAGEMENT SOPS 49
11.2 QUALITY MANAGEMENT SOPS 50
OPERATIONS SOPS 52
11.2.1 Conduct of a study 52
11.2.2 Conduct of a study performing the test: microbiology and toxicological procedures 53
11.2.3 Conduct of a study performing the test: analytical procedures 54
11.2.4 Conduct of a study: Use and maintenance and reagentia & standards 55
11.2.4 Conduct of a study: Use and maintenance (Continued) 56
11.2.5 Global Nelson Policies 56
11.2.6 Sotera Health IT Policies 57

12 Appendix D: GMP justification for this document as Site Master file 58

12.1 AUTHORIZED PHARMACEUTICAL MANUFACTURING ACTIVITIES OF THE SITE 58
12.2 QUALITY MANAGEMENT SYSTEM OF NELSON LABS 58
12.3 RELEASE PROCEDURE OF FINISHED PRODUCTS 59
12.4 MANAGEMENT OF SUPPLIERS AND CONTRACTORS 59
12.5 QUALITY RISK MANAGEMENT (QRM) 59
12.6 PRODUCT QUALITY REVIEWS 59
12.7 PERSONNEL 59
12.8 PREMISES AND EQUIPMENT 59

12.8.1 Premises 59
12.8.2 Equipment 60
12.9 DOCUMENTATION 60
12.10 PRODUCTION 60
12.10.1 Type of products, Process validation, Material management and warehousing 60
12.10.2 Quality Control 60
12.11 DISTRIBUTION, COMPLAINTS, PRODUCT DEFECTS AND RECALLS 61
12.11.1 Distribution 61
12.11.2 Complaints 61
12.11.3 Product defects 61
12.11.4 Recalls 61
12.12 SELF-INSPECTION 61
12.13 QUALIFIED PERSON APPROVAL OF SMF JUSTIFICATION 62

13 Appendix E: list of GxP critical Software and applications 63

13.1 NON-EQUIPMENT RELATED COMPUTERIZED SYSTEMS 63
13.2 EQUIPMENT RELATED COMPUTERIZED SYSTEMS (ACQUISITION/PROCESSING SOFTWARE) 65

14 Appendix F: List of GxP Critical suppliers 66

14.1 RAW MATERIAL SUPPLIERS 66
14.2 PACKAGING MATERIAL SUPPLIERS 66
14.3 EQUIPMENT SUPPLIERS 66
14.3.1 Calibration service suppliers 66
14.3.2 Maintenance service suppliers 67
14.4 LABORATORY SUPPLIERS 67
14.5 TRANSPORTATION AND LOGISTICS PROVIDERS 69
14.6 CLEANING AND SANITIZATION SUPPLIERS 69
14.7 UTILITIES SUPPLIERS 69
14.8 MISCELLANEOUS SERVICES 70
14.8.1 Waste Management and Disposal Services 70
14.8.2 Pest Control 70
14.8.3 Off-site Archiving 70

1 SCOPE

This document and related Standard Operating Procedures (SOPs) are applicable to the ISO 17025, GLP and GMP requirements needed for our third party laboratory participation services (§1.2).
Throughout this document, paragraph 4, 5, 6, 7 and 8 are aligned with the ISO 17025:2017 requirements.

This document is reviewed yearly. Illustrations from underlying documents are to be evaluated on the latest revision of the respective documents.

1.1 BRIEF HISTORY OF THE LABORATORY

The European Laboratory was started in 1991 with the opening of a new facility in Leuven, Belgium. The laboratory was named Toxikon Europe NV and was part of the Toxikon Corporation with headquarters in Boston, US. This laboratory was initially specialized in environmental chemistry and pollutant testing, for which it was officially accredited. Toxikon Europe gradually expanded into a contract laboratory specializing in Analytical Chemistry Studies, *in vitro* Toxicology, and Microbiology Studies, servicing the Life Science Industry.

In 2007, Toxikon Europe moved into a brand-new state of the art facility at the research park in Leuven. During the past 10 years, the laboratory has constantly developed its business by becoming a world-leading lab in the field of container-closure interaction studies (Extractables and Leachables).

Toxikon Europe was acquired by Sotera Health (formerly Sterigenics International LLC) on October 31, 2017. Following the acquisition, the name of the company changed to Nelson Labs NV and became part of the business unit of Nelson Laboratories within Sotera Health. Sotera Health goes to market through its three companies: Nelson Labs®, Nordion® and Sterigenics®:

Figure 1: Illustration of Nelson Labs as one of the 3 business units under the Sotera Health umbrella

Nelson Labs is a global provider of laboratory testing and consulting services and performs over 400 microbiological and analytical laboratory tests across the medical device, pharmaceutical and tissue industries.

Nordion is a global provider of mission-critical radioisotopes used for the prevention, diagnosis and treatment of disease. Nordion ensures the reliable supply of Cobalt-60, the primary input to the gamma sterilization process, to the leaders in healthcare, including sister company Sterigenics.

Sterigenics is a global provider of comprehensive sterilization solutions that eliminate potential health threats, using the most advanced and reliable medical sterilization techniques available. Sterigenics has deep expertise across Gamma, Ethylene Oxide (EO), Electron Beam (E-beam) and X-ray sterilization.

In November 2017, the parent company name changed from Sterigenics International LLC to Sotera Health LLC. Its three operating companies – Nelson Labs®, Nordion® and Sterigenics® – continue to maintain their current names.

The business activities of Toxikon Europe are from November 2017 embedded in the laboratory services of Nelson Labs. As from April 24th, 2018 the laboratory is branded as Nelson Labs and no longer uses the Toxikon reference. Legally "Nelson Labs NV" and commercially "Nelson Labs Europe" are used.

Further references to Nelson Labs in this document apply to the Leuven laboratory facility only.

1.2 TESTING SERVICES IN SCOPE

Nelson Labs is a service-based company and its success in the contract testing area has been through a demonstrated ability to provide testing services of high scientific quality, in a cost-effective manner, and in conformance with projected schedules. Nelson Labs mainly serves the medical device, pharmaceutical and biotechnology industries.

Testing services provided by Nelson Labs include:

- General Analytical Chemistry – Extractables/Leachables – Compendial testing
- Product/Special Chemistry/Impurities
- *In Vitro* Toxicology Testing
- Microbiology Testing
- Drug Release and Stability Testing
- Cleaning, disinfection and steam sterilization validation of reusable devices

This document is designed to register the Quality Management System and Technical Competencies of Nelson Labs' facility.

1.3 PREDICATE RULES AND APPLICABLE REGULATIONS FOR THE QUALITY SYSTEM

The laboratory has the ability to develop, validate and conduct methodologies in a wide variety of scientific disciplines and support research and development efforts in compliance with different regulations (see §10).

Depending on the predicate regulation to which the test should comply, three regulations are incorporated into the laboratory quality system.
The ISO/IEC 17025 for testing laboratories is used as a backbone to which requirements of EudraLex Good Manufacturing Practices (GMP) and OECD Good Laboratory Practices (GLP) are added where applicable.

It remains the responsibility of our sponsors to request and qualify Nelson Labs NV as supplier for the appropriate regulation in relation to the testing service (§1.2) requested.

Nelson Labs continues to monitor all regulatory changes for appropriate updates to all of its quality and regulatory programs.

Nelson Labs maintains its quality system and management procedures compliant with the requirements of the above regulations. As a consequence, most quality and management procedures are covered by all three regulations. For the technical procedures, the applicable regulation is indicated in section 11.

1.3.1 Licensing, certification and accreditation by notified bodies

All SOPs are prone to inspection by competent authorities (§1.3.1.1, 1.3.1.2, 0 and 1.3.1.4).

1.3.1.1 ISO/IEC 17025 accreditation of the laboratory by BELAC

ISO/IEC 17025 compliance is monitored by BELAC, a Belgian government institution. BELAC is a signatory of all existing MLAs (multilateral agreements) and MRAs (multilateral recognition agreements) of EA (European co-operation for Accreditation), ILAC (International Laboratory Accreditation Cooperation) and FALB (Forum of Accreditation and Licensing Bodies).

In this way, reports and certificates issued by BELAC accredited bodies are internationally recognized.

1.3.1.2 GLP compliance monitoring of the laboratory by Sciensano

Sciensano represents Belgium in various international networks and assures compliance of good laboratory practices for activities on behalf of international clients such as the Organization for Economic Cooperation and Development (OECD).

Nelson Labs NV and its national GLP authority Sciensano fulfil the requirements defined in the Mutual Acceptance of Data (MAD) system which allows OECD member countries to mutually accept Study Data generated according to Good Laboratory Practice regulations. These data can thus be accepted in regulatory filing requiring compliance to 21CFR58.
Reference: http://www.oecd.org/env/ehs/mutualacceptanceofdatamad.htm

1.3.1.3 GMP compliance monitoring of the laboratory by FAMHP

The FAMHP is the Belgian competent authority which grants authorizations and checks that medicines and health products conform to current regulations concerning manufacture, distribution, delivery and import. Only QC-testing on medicinal products as manufacturing activity is applicable for Nelson Labs.
Nelson Labs NV holds a valid EU GMP manufacturing and import authorization for QC testing and hence Study Data generated by Nelson Labs NV in accordance with Good Manufacturing Practice regulations can be accepted in regulatory filing requiring compliance to 21CFR210 and 21CFR211.
Reference: https://www.ema.europa.eu/en/human-regulatory/research-development/compliance/good-manufacturing-practice/mutual-recognition-agreements-mra

1.3.1.4 FDA registration and compliance with 21 CFR Part 11, 210 & 211

Next to the official European certification, the laboratory is also FDA registered and prone to inspection by this US Authority. As stated in §0, the Belgian FAMHP is allowed to conduct inspections on behalf of FDA under the mutual recognition agreement concluded on 16 November 2018 between the European Union (EU) and the United States (USA).
Principles from 21 CFR part 11 on e-records and e-signatures are implemented where applicable.

1.3.2 Integration into a global or corporate organization

1.3.2.1 Nelson Laboratories LLC

Although Nelson Labs NV operates with an independent QMS from Nelson Laboratories LLC, there are ongoing harmonization efforts which lead to the introduction of global policy documents. These are integrated in this document where applicable. The Leuven site operates in accordance with the global quality policy (POL0001).

1.3.2.2 Sotera Health Information Technology

Although Nelson Labs NV operates with an independent QMS form the Sotera Health Organization, the IT Department, operates at the Sotera level as a one company service department. Nelson Labs maintains IT compliance procedures within the boundaries of its QMS wherever required, but also leverages IT services established through service level agreements (SLA). The Sotera Health IT Department operates under its own policies and procedures which are available upon request depending on the confidential content of the respective policy or procedure (11.2.6).**Error! Not a valid link.**

2 REGULATORY QMS REFERENCES

- ISO/IEC 17025, General Requirements for the Competence of Testing and Calibration Laboratories, with respect to the technical and quality system requirements applying to test laboratories
- EudraLex Volume 4, EU Guidelines to Good Manufacturing Practice (Medicinal Products for Human and Veterinary Use) and Annexes
- OECD Principles of Good Laboratory Practice N° 1 to 24
- 21 CFR Guidance for Industry Part 11, Electronic Records; Electronic Signatures

Note: guidelines are referenced throughout this document where applicable (e.g. ICH Q2(R2))

2.1 ADDITIONAL REGULATION IMPOSED BY ACCREDITORS

The following documents are considered regulation and are monitored to maintain compliance with the requirements therein:

- BELAC 2-001 current revision - Rules governing the reference to BELAC accreditation and BELAC signatory status of international multilateral agreements/recognitions
- BELAC 2-002 current revision - Accreditation certificate and corresponding scope of accreditation: general guidelines for the formulation and the evaluation
- BELAC 2-003 current revision - Policy and provisions on traceability of measurement results
- BELAC 2-004 current revision - Rules for the notification to BELAC and the management by BELAC of significant changes by the accredited bodies
- BELAC 2-101 current revision - Schedule of accreditation of a testing laboratory: guidelines for formulation and evaluation
- BELAC 2-106 current revision - Proficiency testing: guidelines on the level of participation and evaluation of performances in proficiency testing activities in the context of accreditation assessments
- BELAC 2-108 current revision - Expression of the uncertainty in quantitative testing
- BELAC 3-11 current revision - The Accreditation Procedure: Provisions for Implementation
- BELAC 6-101 current revision - Checklist for assessment of compliance with the requirements of EN ISO/IEC 17025: 2017
- BELAC 1-03 current revision - BELAC activities: description and criteria for selection

3 TERMS AND DEFINITIONS

For the purpose of Nelson Labs' quality management system, general definitions are provided in ISO 9000. ISO/IEC 17000 is preferred, when related to certification and laboratory accreditation.

Depending on the predicate regulation, terminology used, especially for roles and responsibilities, can be different and is based on:

1. ISO/IEC 17000 Conformity Assessment – Vocabulary and General Principles
2. ISO 9000 Quality management systems - Fundamentals and vocabulary
3. VIM, International Vocabulary of Metrology, issued by BIPM, IEC, IFCC, ILAC, ISO, IUPAC, IUPAP, and OIML
4. OECD Principles of Good Laboratory Practice N°1 to 24
5. EudraLex The Rules Governing Medicinal Products in the European Union, Volume 4, EU Guidelines to Good Manufacturing Practice Medicinal Products for Human and Veterinary Use

4 GENERAL REQUIREMENTS

4.1 IMPARTIALITY

Nelson Labs' personnel are free from any commercial, financial or other pressures, which might influence their technical judgment. Influence on the results of examinations and tests by external persons are excluded. The remuneration of analysts is independent of the number of tests carried out and of the results of the tests. All employees sign agreements related to their independence.

Given the nature of the testing services which Nelson Labs provides, the risk of personal benefit and impartiality is considered low. For release testing on medicinal products, release of testing results is the sole responsibility of the qualified person (EudraLex Vol 4 Annex 16).

Being embedded in a Sotera Health corporate organization, every employee of the laboratory has to follow courses on anti-bribery and corruption and Insider Trading policy, and sign approval with the Sotera Health Ethics and code of conduct.

4.2 CONFIDENTIALITY

Nelson Labs has policies and procedures in place to ensure the protection of its clients' confidential information and proprietary rights, including procedures for protecting the electronic storage and transmission of results.

If required by the sponsor, confidentiality and non-disclosure agreements are put in place.

5 STRUCTURAL REQUIREMENTS

5.1 LEGAL ENTITY

Nelson Labs is a Limited Liability Company (Société Anonyme – Naamloze Vennootschap), according to Belgian Company Law since 28th December 1990 (founded as Toxikon Europe), with a capital of 125.000 €, fully subscribed and paid up. Nelson Labs is located at Romeinsestraat 12, 3001 Leuven, Belgium and delivers analytical and microbiological laboratory services to support the medical device, biotech and pharmaceutical industry. The company number (Ondernemingsnummer) is 0442.395.719.

When required during regulatory inspection, more information can be requested from management and is to be found in the coordinated statutes (Document in Dutch) dated on April 24th, 2018 and signed by Isabelle Mostaert (associated notary).

The statutes, Board of Directors and published financial statements can be consulted on the website of the Belgian Federal Government linking also to other official publications in the Belgian official journal:
https://kbopub.economie.fgov.be/kbopub/toonondernemingps.html?ondernemingsnummer=442395719

5.2 RESPONSIBLE MANAGEMENT

This section describes the responsibility, authority, and management structure of the facility in view of quality critical activities. Top Management is responsible for the laboratory testing services and quality programs. Together with the Quality Manager Top Management is also responsible for setting the laboratory quality policy and meeting the expectations and needs of clients and Regulatory-Monitoring authorities. The Managing Director ensures that all staff are trained to understand, implement and maintain the quality objectives outlined in this document, at all levels.

Study Directors, Team Managers and Directors are responsible for implementing the quality programs described in this document. They, together with technicians and all designated staff members, are responsible for the quality of services under their control.

The organization of Nelson Labs is described as follows: the hierarchical structure is defined through the organizational charts (§5.3) Responsibilities are departmentalized by functional area (technical areas). The responsibilities of the different functions are described in detail within a function or job description as well as the authority and interrelationships of all personnel who manage, perform or verify work. Named organizational charts and direct reporting lines can be found in an oracle cloud Human Capital Management system (HCM).

Top Management: The Managing Director has the final responsibility for the European Operations and reports to the business unit president of Nelson Laboratories.

The Managing Director acts as Top Management and is supported by the following Key Managerial structure:

Technical Management: The Director of Lab Operations (DLO) to which the responsible (Sr.) Lab Operations Managers ((S)LOM; analytical and microbiological labs) report to, holds final accountabilities for all commercial laboratory related activities and corresponding technical release of results under ISO 17025, and commercial R&D. The Head of QC (HoQC) holds the final technical responsibility related to QC testing activities on medicinal products, under GMP. Lab Management is used as a general management responsibility combining lab responsibilities from the DLO and (S)LOM.

Project Management: Depending on the type of service and the governing regulation the customer project responsibility resides at different functions. Scientific project managers or experts for E&L testing, under coordination of the Sr. Manager E&L Services. Study Directors are responsible to manage GLP and GMP projects. The project responsible is responsible for interfacing with clients and coordinating the reporting process, which contain results released by Technical Management. Project managers and Study Directors are the internal clients who order a specific analysis (under the scope of the laboratory) from the lab.

Note: Scientific responsibility
Next to technical responsibilities, scientific and regulatory responsibility is managed as a collaboration between the Director of Science and Technology, the DLO , the Director of Business Development and Regulatory Affairs and the responsible project managers or study directors.

Quality Assurance Management: The Sr. Quality Manager is ensuring compliance with the applicable international standards, functioning independently from laboratory operations and reporting directly to Top Management.

Health, Safety and Environmental Management: The EH&S Manager is responsible for activities and processes related to Health, Safety and Environment.

Facility Maintenance: The Facility Engineer acts as the responsible for all infrastructural related activities.

Back-office Management: The Back-office Manager is responsible for activities and processes related to customer support, outsourcing of biocompatibility studies and the coordination of certain activities (e.g. Procurement, archiving, HR Payroll, reception, events).

The following Key Managerial personnel reports directly into the corporate Sotera Health structure but has a "dotted" reporting line to the Managing Director:

Support Management: Holding overall responsibilities:
- with respect to all IT related activities (IT Director, EMEAA)
- related to the Sales services of the company (Head Sales & Business Development)
- related to Marketing (Marketing Manager)
- related to Finance (FP&A manager)
- related to HR (HR Business partner)

The Qualified Person operates in close collaboration with the Quality Assurance unit but holds final responsibility as per EudraLex volume 4 Annex 16:

Qualified Person: Holding final responsibility for all quality decisions (GMP) related to the QC testing of medicinal products and holding final responsibility to issue Certificates of Analysis and GMP study reports. Nelson Labs QP never holds the final certifying responsibility but supports the sponsor's certifying QP with a confirmation statement indicating that Nelson Labs testing is performed according to GMP.

There is substitute arrangement for the key management tasks and responsibilities to maintain continuity of the management system.

The only exception is the Qualified Person, who can only be replaced by another Qualified Person, entitled as registered industrial pharmacist after formal cumul acceptance by the Belgian Federal Agency for Health and Medicinal Products.

According to GMP, the overall organizational procedure is initiated by the project responsible, who, after Sponsor communication, orders a study from the lab. According to ISO, the latter organizes the planning and follow-up of the study, and based on the obtained results, releases a test report (containing results). The raw data is passed to the project responsible, who, based on the test report and raw data, writes either a test result report or a study report, which is communicated to the Sponsor after QA approval. For the QC testing of medicinal products, the only difference implicates the final responsibility of the Qualified Person for the release of a certificate of analysis.

For GLP studies, the overall organizational procedure is initiated, conducted and reported by the Study Director GLP, in collaboration with QAU.

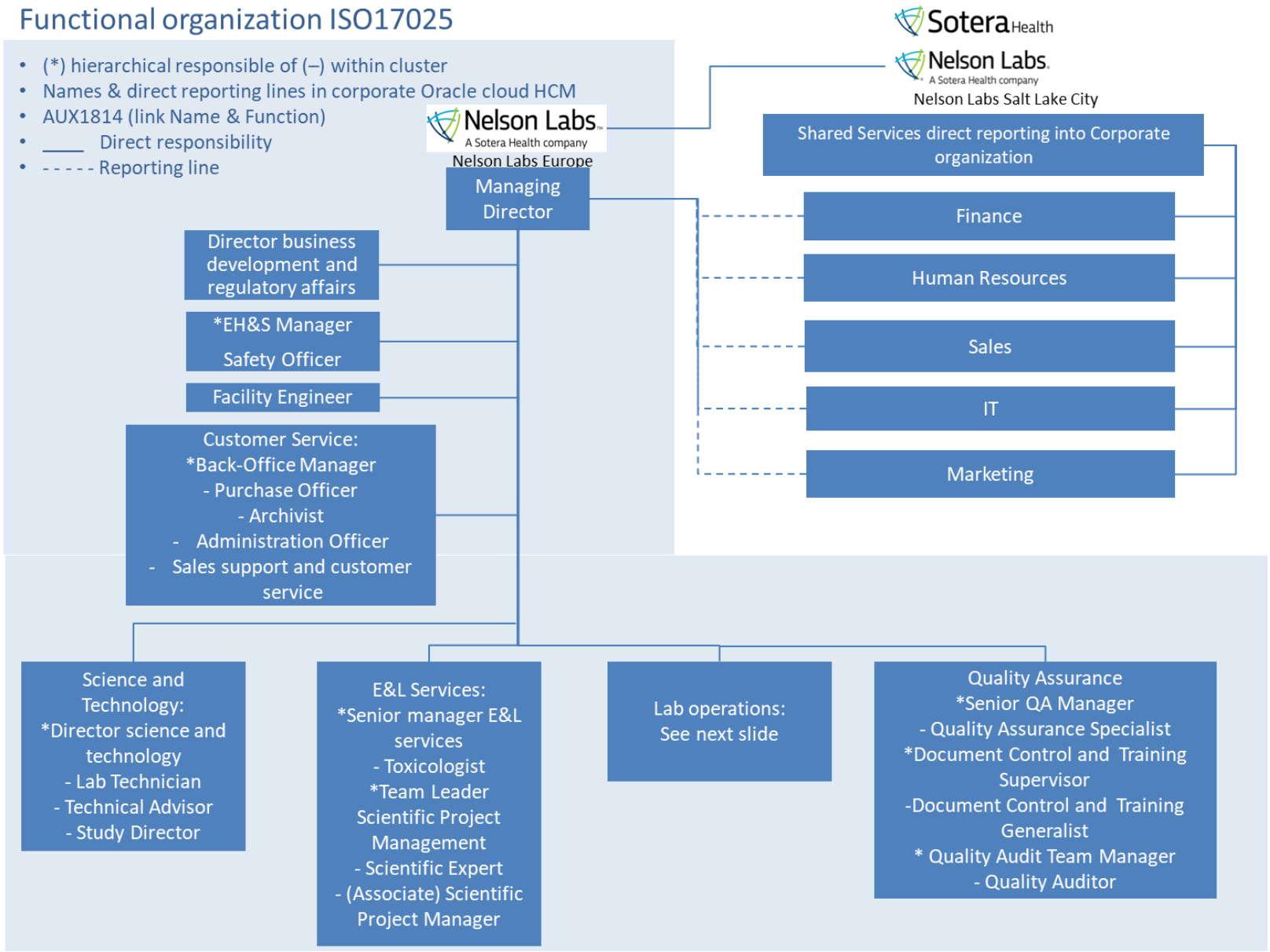
Team meetings on the different levels of the managerial structure are held on a regular basis to discuss operational matters and monitor the effectiveness of the general operation and quality system within Nelson Labs.

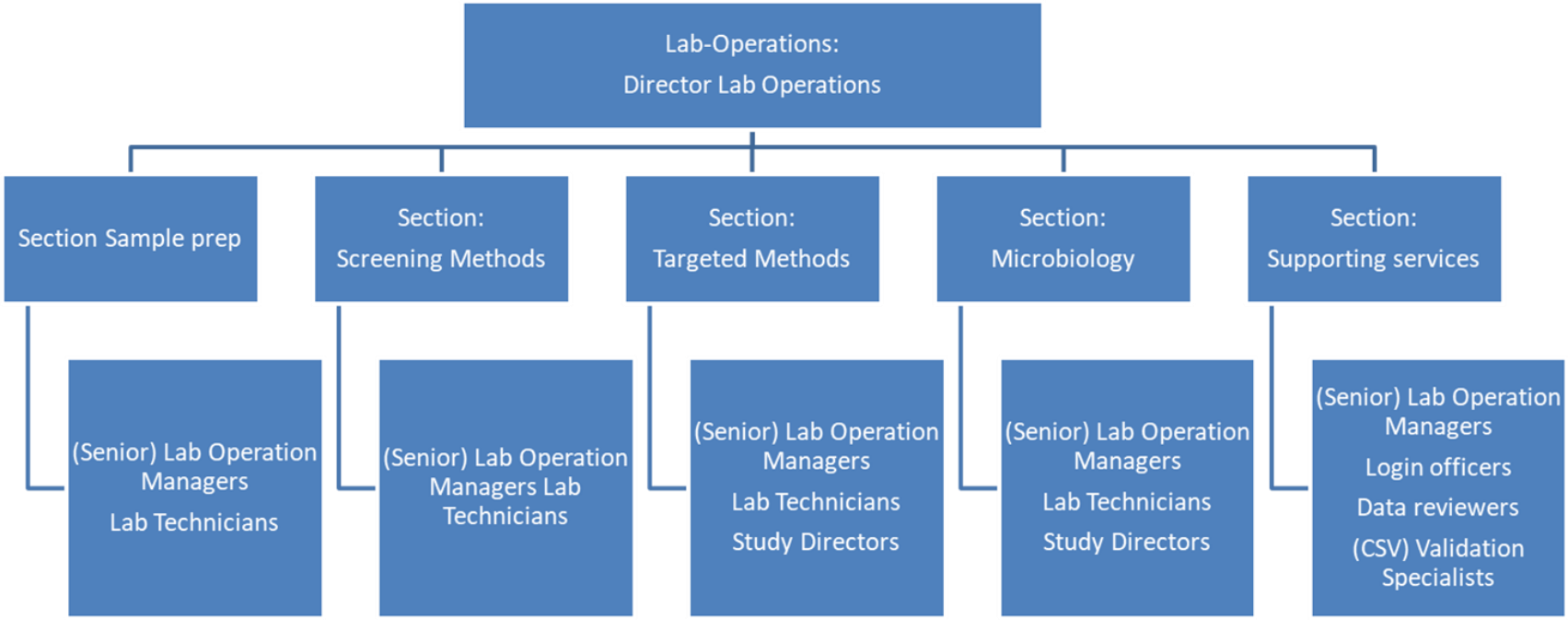
Quarterly (during Site Leadership Team meetings) the status of yearly management review imperatives is evaluated. Monthly, during Site Leadership Team meetings, a dashboard containing Quality Performance Indicators is discussed to track the implementation of goals, continuous improvement, objectives and specific actions.

5.3 ORGANIZATIONAL CHARTS

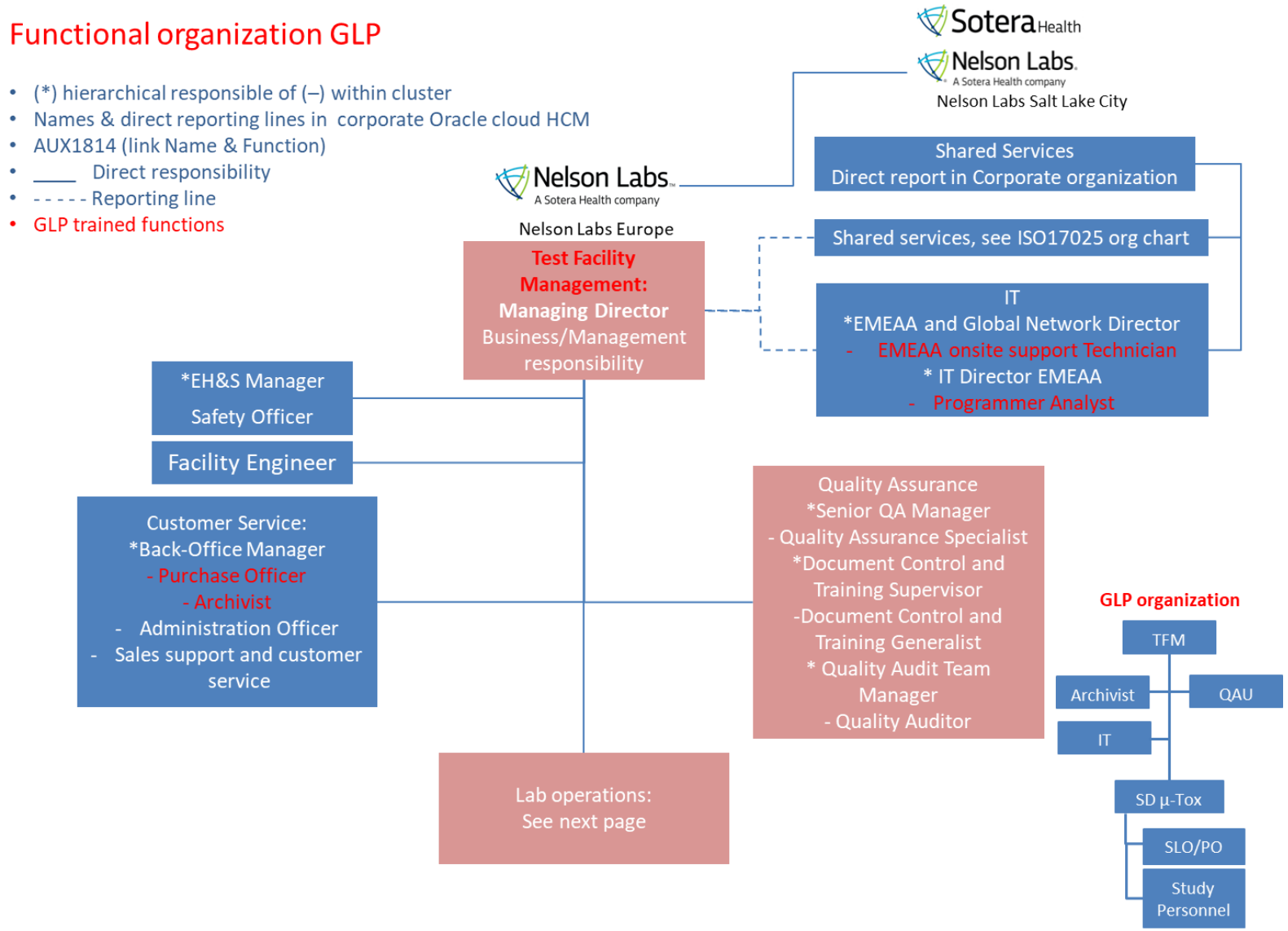
In the following sections the hierarchical relationships for every predicate regulation are indicated thereby using the nomenclature from those regulations (ISO 17025: AUX1800; GMP: AUX1801 and GLP: AUX1803, current revisions).

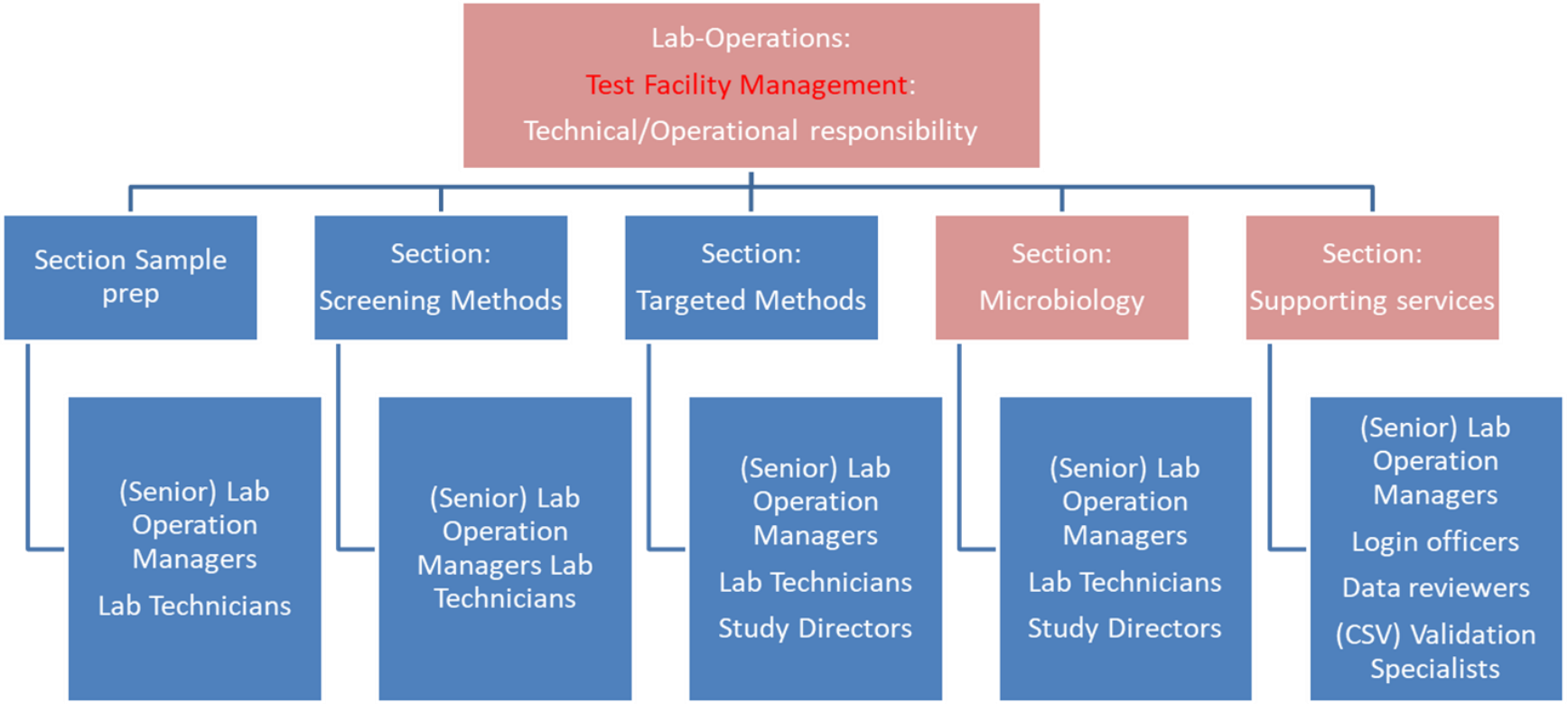
5.3.1 Organizational chart ISO 17025



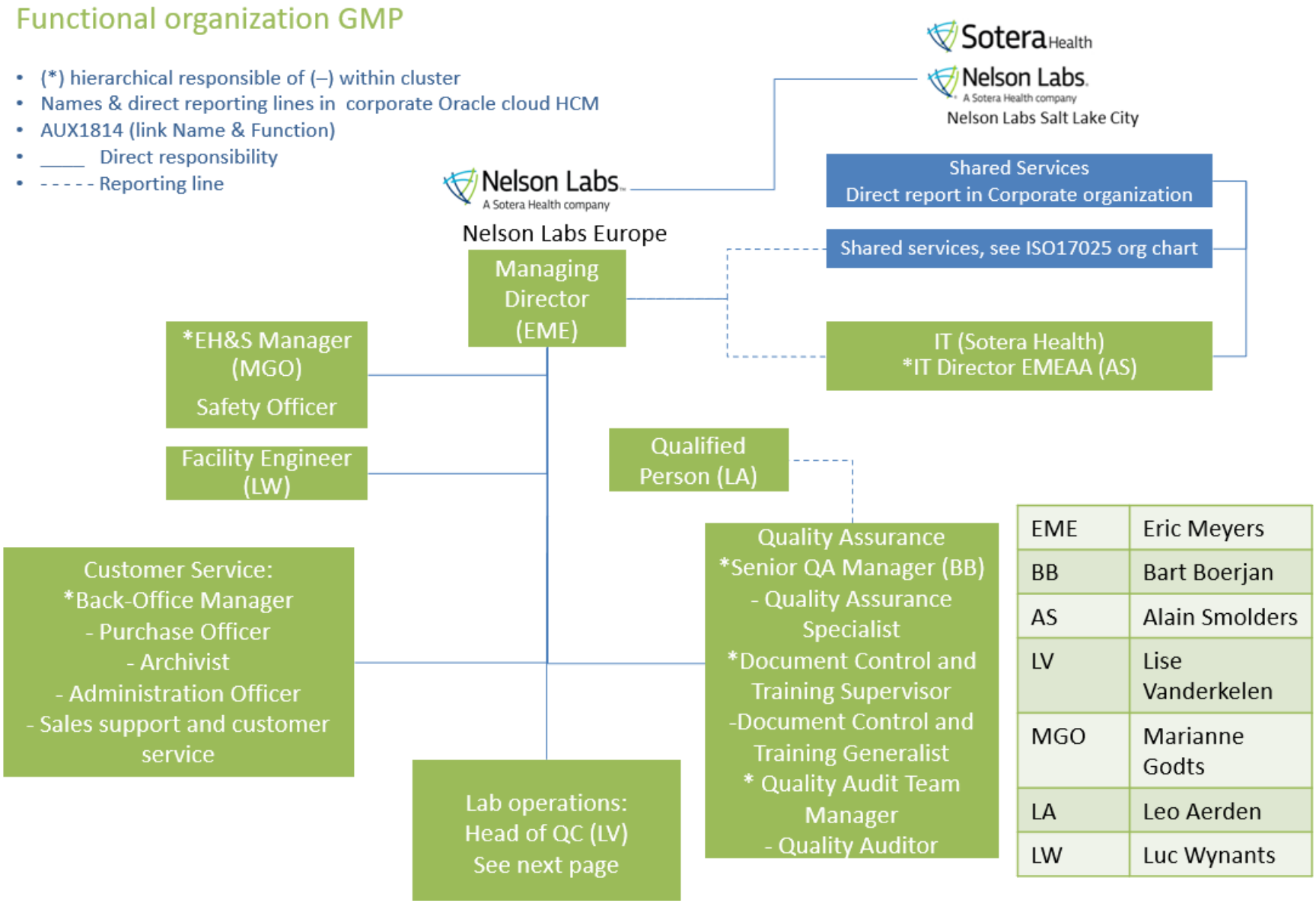

Lab-Operations:
Director Lab Operations
Section Sample prep
Section:
Screening Methods
Section:
Targeted Methods
Section:
Microbiology
Section:
Supporting services
(Senior) Lab Operation Managers
Lab Technicians
(Senior) Lab Operation Managers Lab Technicians
(Senior) Lab Operation Managers
Lab Technicians
Study Directors
(Senior) Lab Operation Managers
Lab Technicians
Study Directors
(Senior) Lab Operation Managers
Login officers
Data reviewers
(CSV) Validation Specialists

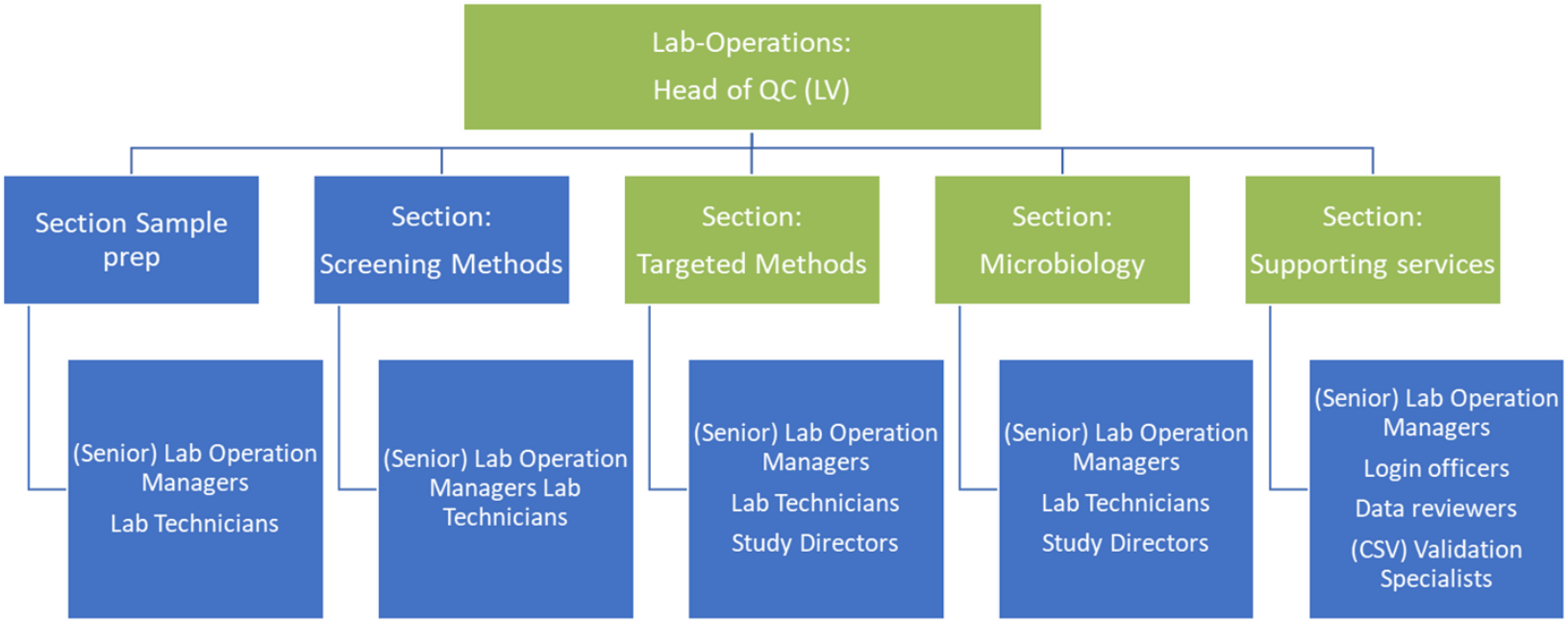
5.3.2 Organizational chart GLP




Lab-Operations:
Test Facility Management:
Technical/Operational responsibility
Section Sample prep
Section: Screening Methods
Section: Targeted Methods
Section: Microbiology
Section: Supporting services
(Senior) Lab Operation Managers
Lab Technicians
(Senior) Lab Operation Managers Lab Technicians
(Senior) Lab Operation Managers
Lab Technicians
Study Directors
(Senior) Lab Operation Managers
Lab Technicians
Study Directors
(Senior) Lab Operation Managers
Login officers
Data reviewers
(CSV) Validation Specialists

5.3.3 Organizational chart GMP




Lab-Operations:
Head of QC (LV)
Section Sample prep
Section: Screening Methods
Section: Targeted Methods
Section: Microbiology
Section: Supporting services
(Senior) Lab Operation Managers
Lab Technicians
(Senior) Lab Operation Managers Lab Technicians
(Senior) Lab Operation Managers
Lab Technicians
Study Directors
(Senior) Lab Operation Managers
Lab Technicians
Study Directors
(Senior) Lab Operation Managers
Login officers
Data reviewers
(CSV) Validation Specialists

5.4 RELATED DOCUMENTATION

These procedures are fully documented in the following Standard Operating Procedures (SOPs):

SOP0448	Company Organization Table
SOP0420	Job descriptions
SOP0440	Personnel and Organization
SOP0445	Conduct of Site Leadership Team, Quality, Lab and SD Meetings
SOP0199	Matrix of (Technical) Competence

6 RESOURCE REQUIREMENTS

6.1 GENERAL

Nelson Labs' strategy for resource management always returns to "fit for purpose" or "suited for intended use" and "maintaining the validated state".

6.2 PERSONNEL

Nelson Labs' Management ensures the competency of all who operate specific equipment, who perform tests, evaluate results, and sign test reports.

Nelson Labs' Management formulates the goals with respect to the education and the skills of the laboratory personnel. Nelson Labs has a policy and procedures for identifying training needs and providing initial and ongoing training of personnel. The training program is relevant to present and anticipated tasks of the laboratory, on a retrospective, ongoing, and prospective basis.

Nelson Labs Management authorizes specific personnel to perform particular types of tests, to issue test reports, to give opinions and interpretations, and to operate particular types of equipment. The laboratory ensures that such personnel work in accordance with the laboratory's quality management system. Job descriptions are maintained for managerial, technical, and all support personnel involved in testing, the generation of data, and any other support role related to the testing services provided. The laboratory maintains records of the relevant competence, educational and professional qualifications, training, skills, and experience of all technical personnel.

6.2.1 Related Documentation

These procedures are fully documented in the following SOPs:

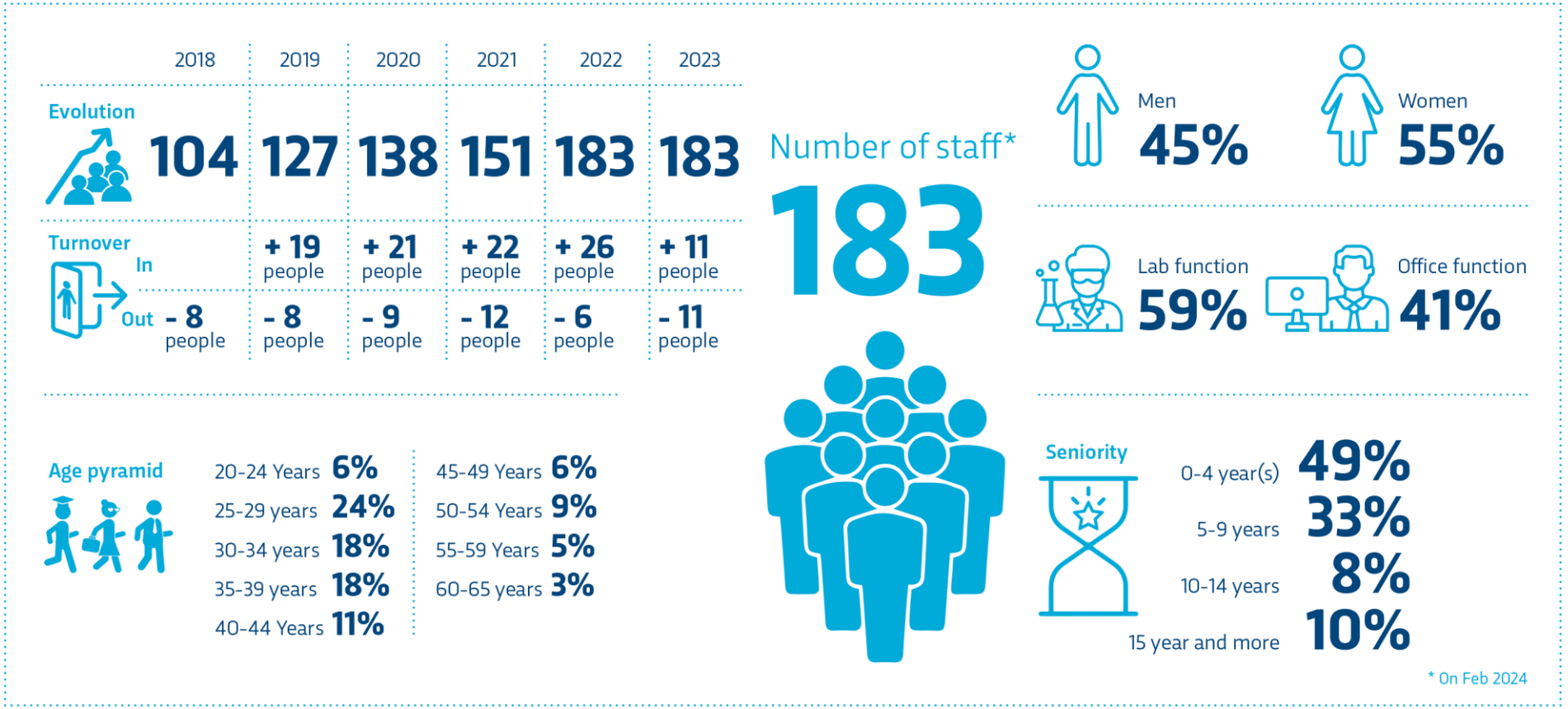
SOP0441	Personnel, Recruitment and Evaluations
SOP0432	Occupational health and health assessments
SOP0419	Personnel and Training
SOP0420	Job Descriptions
SOP0199	Matrix of (Technical) Competence
SOP0475	Training in MasterControl - User guide for Document Management team

Global Nelson Policy Document

POL0004	Training Policy

6.2.2 Personnel Evolution and current state

Nelson Labs values and invests in people including additions of staff. Of the approximate 180 headcounts, 13 belong to the QA unit and 9 to QC.



6.3 FACILITIES AND ENVIRONMENTAL CONDITIONS

Nelson Labs Management ensures that the physical laboratory and non-laboratory environment of the building do not invalidate the results or adversely affect the required quality of any measurement. Contamination is prevented by effective separation of adjacent areas with incompatible activities. Good housekeeping rules and standard laboratory hygiene and safety procedures are employed by all personnel.
To avoid the presence and development of pests in the laboratories and offices, a pest prevention and control program has been developed in collaboration with a specialized company. The pest control and prevention program will focus on rodents (rats and mice), cockroaches, flying insects and silverfish.

Nelson Labs monitors critical environmental conditions as required by relevant specifications or where they may influence the quality of the results. Tests are suspended when the environmental conditions, which may affect the tests, are in question. Specialized test areas are monitored and maintained to specific technical/condition requirements specific to the type of work. Examples include cell and tissue culture and sterility rooms and other conditioned environments. Nelson Labs has a Thermoguard monitoring system in place for controlled storage rooms, such as refrigerators and climatic chambers, which generates alarm messages to Nelson Labs personnel, in case an Out-Of-Specification signal occurred.

6.3.1 Related Documentation

These procedures are fully documented in the following SOPs:

MAN0013	Risk assessment for “mixed use” of premises, resources and systems
MAN0017	User Access Management Policy
MAN0018	Change Policy
SOP0442	Facilities Description
SOP0443	Visitor Registration at Nelson Labs Premises
SOP0224	Use and Maintenance of cell and tissue culture room
SOP0278	Monitoring of controlled storage for temperature and humidity
SOP0198	Use and Maintenance of sterility room
SOP0444	Use and Maintenance of emergency generator

6.4 EQUIPMENT

Nelson Labs is equipped with appropriate instrumentation for conducting the tests within its scope of application. The equipment is operated by authorized/trained personnel. All instruments are qualified by means of calibration wherever applicable. Nelson Labs has a Validation Policy, which provides a framework and practices for validation and qualification of equipment, computer systems and networked systems for Nelson Labs’ laboratory processes based on GAMP 5 (Good Automated Manufacturing Practices published by ISPE). It is also applicable to the validation of Macros and Spreadsheet applications. The Validation Policy aims to ensure that validations, qualifications and calibrations are done efficiently and consistently throughout the organization and meet regulatory, quality and business requirements. The policy should ensure that the company's validation procedures are followed. The company Validation Policy is the basis of individual project Validation Plans.
The process of new equipment to be qualified (based on EudraLex Volume 4, Annex 15) is initiated by an assessment for criticality. Hereby, GxP-critical systems are established and

monitored through an IQ (initial qualification), OQ (operational qualification) and PQ (performance qualification) program. DQ (design qualification) procedures are also utilized as required for appropriate selection procedure for acquisition of equipment. All changes to qualified equipment shall be made traceable to a risk assessment and are validated accordingly in order to "Maintain a Validated and Calibrated State". In addition, an Event and Error Log is kept, and formal change control applies when critical changes are made to a GxP-controlled system.

6.4.1 Related Documentation

These procedures are fully documented in the following SOPs:

MAN0012	Validation Policy
MAN0018	Change Policy
SOP0383	General procedures including use and maintenance for laboratory systems
SOP0386	System Validation
SOP0387	Operational Change Control for Lab- and IT Systems

Global procedure, applicable to LOMS/LIMS application only:

SOP0922	IT Computer System Change Control

6.5 METROLOGICAL TRACEABILITY

6.5.1 General

All equipment used for tests, having a potential or significant effect on the accuracy or validity of the test result, are calibrated (and/or qualified) before being put into service, and recalibrated (and/or requalified) on a routinely basis. The equipment is labelled to indicate its status with a physical label either indicating the qualified state directly or a scannable label for the LIMS system.

6.5.2 Specific Requirements

Nelson Labs has full traceability for all related standards/materials in use to the International System of Units (SI). Nelson Labs also employs the use of certified reference materials to provide reliable chemical characterization and utilizes consensus standards wherever applicable. Nelson Labs performs interlaboratory and/or proficiency testing wherever required and available.

6.5.3 Reference Standards and Reference Materials

Nelson Labs has procedures for safe handling, transport, storage and use of reference standards and materials in order to prevent contamination or deterioration, and in order to protect their integrity.

Reference standards and materials are purchased with certificates, to facilitate tracking to international standards. Certified weights and thermometers are available for internal verification purposes and are periodically calibrated by an external ISO17025 calibration service supplier. These materials are used for no other purpose within the laboratory.

Internal reference standards are to be used as a second source to evaluate the correct preparation of calibration standards. Reference materials can be used for quality control purposes. Checks needed to maintain confidence in the calibration status of reference standards materials may be carried out according to defined procedures and schedules, as required. All materials are tracked and their proper storage and integrity maintained.

6.5.4 Related Documentation

These procedures are fully documented in the following SOPs:

SOP0391	Calibration Weights for Balances
SOP0367	Use and Calibration of Thermometers
SOP0390	Control of Reference Standards and Materials
SOP0377	Management of Inventories (Chemicals and Consumables) at Nelson Labs
SOP0378	Determination of the purity of qualitative and quantitative standards
SOP0215	Characterization of test, control and reference items
SOP0227	Culture and maintenance of reference micro-organisms

6.6 EXTERNALLY PROVIDED PRODUCTS AND SERVICES

Nelson Labs has procedures for selecting suppliers of materials and services, and to assure the conformance of purchased items. The Director Lab Operations is accountable for providing specific order information and release of materials from designated vendors in case of absence of a certificate of analysis. They select and manage contract service providers from a qualified supplier list. Criteria for supplier acceptability include providing acceptable levels of performance in terms of quality, cost, delivery, and service.

6.6.1 Externally provided Products

Requests for the purchase of routine materials or services are processed through the Back-office. For non-routine purchases, responsible management appoints specifications, which should be purchased by using qualified suppliers.

After arrival of the materials, the product is logged in using Nelson Labs' LIMS system and calibration or reference standards are verified before release into the laboratory.

6.6.2 Externally provided Services

Nelson Labs uses subcontractors in a limited way. Nelson Labs' business strategy is to only work in areas where Nelson Labs has the expertise and control over the scientific test data, and does not have to rely on outside sources to provide this information. In the event Nelson Labs does require subcontracting of tests, all subcontractors must be qualified through vendor qualification procedures under ISO 17025. Only qualified, accredited and licensed subcontractors who comply with the ISO standard may be utilized as per the contract requirements between Nelson Labs and the Sponsor, and for the work in question, within the testing scope of Nelson Labs.

Concerning QC testing of medicinal products, intended for the generation of a certificate of analysis, subcontracting laboratories should be certified according the GMP in the European

Union, and in Belgium according to the accreditation by the Belgian authorities, represented by the Federal Agency for Medicines and Health Products (FAMHP).

6.6.3 Related Documentation

These procedures are fully documented in the following SOPs:

SOP0381	Vendor and subcontractor Qualification and Monitoring Procedures
SOP0380	Purchasing Services, Equipment and Supplies
SOP0208	Conduct of a GMP study
SOP0382	Communication and sample flow between Nelson Labs NV/Qualified Contractor and Nelson LLC

7 PROCESS REQUIREMENTS

Many factors collectively determine the correctness and reliability of tests and/or calibrations as performed by the laboratory. The extent to which these factors contribute to total uncertainty may differ from test to test, and in the calibration performed. Nelson Labs takes all relevant factors like human factors; accommodation and environmental conditions; test and calibration methods and method validation; equipment; metrological traceability; sampling; the handling of test and calibration items; into account in developing test and/or calibration methods.

7.1 REVIEW OF REQUESTS, TENDERS AND CONTRACTS

Nelson Labs has procedures for contract or project review available to ensure that project requirements (incl. applicable quality level) are clearly and adequately defined and understood; the laboratory has the capability and resources to meet the requirements; and the appropriate test methodology is selected and capable of meeting the Sponsors' requirements. To facilitate the project review, the author of a quotation (and/or protocol) stipulates which methodology is applicable on the samples by means of a reference to the SOP, Sponsor Specified Procedure (SSP) and/or by specifying additional project specific requirements in a protocol (if applicable). Any differences between the test request forms, purchase orders (POs), or any other contract review documentation and instructions are resolved prior to beginning any work, and the project is logged as “non-conforming”. Each contract must be acceptable both to the laboratory and the Sponsor.

The same contract review process is repeated whenever amendments or other post-delivery requests are made or required after work has started, and any requested procedural changes or deviations are communicated to the Sponsor and finally approved and documented.

7.1.1 Related Documentation

These procedures are fully documented in the following SOPs:

SOP0200	Study Logging Procedures, Sample Receipt, Storage and Contamination Control Practices Using LOMS System
SOP0446	Quotation Procedures
SOP0202	Communication with Sponsors
SOP0211	Assignment of Study Responsibles – GLP
SOP0213	Study Plan for a GLP Study

7.2 SELECTION, VERIFICATION AND VALIDATION OF METHODS

Nelson Labs has Standard Operating Procedures (SOPs) for all tests within its scope, as well as for the use and operation of all relevant equipment, and on the handling and preparation of items for testing. All instructions, standards, manuals and reference data relevant to the work of the laboratory is maintained in an updated and current status and is made readily available to all personnel through the laboratory computer network, MasterControl, or through certified hard copies.

7.2.1 Selection of Methods

Nelson Labs uses test methods that meet the needs of the Customer and which are appropriate for the tests it performs, preferably those published as international, national, or regional standards. Nelson Labs ensures that it uses the latest edition of a standard unless it is not appropriate or possible to do so. When necessary, the standard is supplemented with additional details to ensure consistent application, and incorporated into company SOPs and protocols, wherever required and applicable.

When the Customer does not specify the method to be used, the laboratory selects appropriate methods that have been published either in international, national, or regional standards, by reputable technical organizations, or in relevant scientific texts or journals, compendia methods, or as specified by the manufacturer. Laboratory-developed methods or methods adopted by the laboratory are also used if they are appropriate for the intended use and if they are appropriately validated. The Customer is informed as to the method chosen and works collaboratively with the laboratory to reach consensus on method selection. The laboratory first confirms that it can properly perform the new methods before introducing the tests. If the standardized method changes, the confirmation/validation is repeated. Nelson Labs will inform the Customer when the method proposed by the Customer is considered to be inappropriate or out of date.

7.2.2 Laboratory Developed Methods

When it is necessary to employ methods not covered by standardized methods, these are subject to agreement with the Customer and include a clear specification of the Customer's requirements and the purpose of the test. Laboratory developed methods are planned activities and assigned to qualified individuals equipped with adequate resources to develop the method. Effective communication among all related departments is conducted for proper implementation.

7.2.3 Non-Standard Methods

Deviations from approved test methods have to be documented, technically justified, authorized and when having potential impact, accepted by the Customer. For new test methods, procedures are developed prior to the tests and calibrations being performed and must include all applicable technical SOP/SSP required content.

7.2.4 Validation of Methods

Nelson Labs validates all non-standardized methods, laboratory designed methods, methods used outside their original scope, and modifications to methods to confirm that they are fit for the intended use. The validation is as extensive as necessary to meet the needs in the given

application or field of application. Extensive validations of analytical methods are performed based on the ICH Q2(R2) guideline.

When validated methods are transferred between laboratories and sites, their validated state should be maintained to ensure the same reliable results in the receiving laboratory.
Nelson Labs uses an 'analytical method transfer' process that establishes documented evidence that the analytical method works as well in the receiving laboratory as in the originator's laboratory, or the transferring laboratory.

7.2.5 Related Documentation

These procedures are fully documented in the following SOPs:

MAN0018	Change Policy
SOP0204	Method Validation
SOP0216	Reporting and Rounding off Results
SOP0205	Measurement of Uncertainty and Validation for Microbiological Methods
SOP0426	Non-conformances/Deviations (including retest)
SOP0202	Communication with Sponsors
SOP0206	Estimation for Measurement of Uncertainty
SOP0429	Out-Of-Specification Procedure

7.3 SAMPLING

Nelson Labs has material selection procedures in place as required by each specific test preparation standard or test method. Nelson Labs is provided test material by the customer and does not implement sampling plans or statistical sampling techniques based on its scope of business. The customer provides to Nelson Labs the appropriate sample or subsection of a sample for testing purpose. In certain cases special instructions from the sponsor are required to empty or sample a complex device or container closure system in order to obtain a representative sampling or extraction process. These instruction need to be provided by the sponsor and included in quotes or protocols where appropriate.

The laboratory records describe, or make traceable, the sample condition, amounts received, amounts utilized, and sample preparation procedures for testing. No other specific sampling plans are part of the scope of services provided by Nelson Labs, or its management system.

7.4 HANDLING OF TEST OR CALIBRATION ITEMS

Nelson Labs has procedures for the receipt, handling, protection, retention and/or disposal of test items, including all provisions necessary to protect the integrity of the test item. Upon receipt, the test item is uniquely identified. Any non-conforming samples or projects are logged and testing will not be initiated until all requirements, based on stated paper work or other specified conditions, as described in the relevant test method, are met. When there is any doubt as to the suitability of a test item, or when an item does not conform to the description provided, or the test requirements are not specified in sufficient details, the Study Director consults the Sponsor for further instructions before proceeding. In this case, samples are indicated as "non-conforming", and are put on hold. All relevant discussions between Study Directors and Sponsor are recorded.

Nelson Labs has procedures and appropriate facilities for avoiding deterioration, loss or damage to the test item during storage, handling and preparation; instructions provided with the item shall be followed.

7.4.1 Related Documentation

These procedures are fully documented in the following SOPs:

SOP0200	Study Logging Procedures, Sample Receipt, Storage and Contamination Control Practices using LOMS System
SOP0278	Monitoring of controlled storage for temperature and humidity
SOP0203	Subsampling of aqueous and organic solvent-based extracts/test solutions for extractables and leachables studies
SOP0221	Sample Return and Sample Destruction procedures
SOP0207	Conduct of a leachable study
SOP0201	Management of specially regulated substances
SOP0454	Aseptic Techniques

7.5 TECHNICAL RECORDS

Nelson Labs retains original observations, derived data, calibration records, and a copy of each test report for a defined period. The records for each study contain sufficient information

- to establish an audit trail,
- to facilitate, if possible, identification of factors affecting the uncertainty and
- to enable the study to be repeated under conditions as close as possible to the original.

The records include the identity of personnel responsible for performance of each test, and data auditing personnel involved.

Nelson Labs has no control over sampling uncertainty, as test materials and products are sampled by the Sponsor and provided to Nelson Labs (see also §7.3).

7.5.1 Related Documentation

These procedures are fully documented in the following SOPs:

SOP0417	Development, review, reconciliation and archiving of forms and raw data
SOP0430	Good Documentation Practice (GDP) and Signature policy
SOP0220	Contents and Final Review of a Completed Project File

7.6 EVALUATION OF MEASUREMENT UNCERTAINTY

Nelson Labs has procedures in place for estimating uncertainty for all calibrations and types of calibrations. Nelson Labs validates its methods taking predefined criteria for accuracy and precision, and as a consequence maximum uncertainty, into account. By doing so Nelson Labs guarantees appropriate accuracy in reporting and interpretation of uncertainty upon Sponsor's request.

7.6.1 Related Documentation

These procedures are fully documented in the following SOPs:

SOP0204	Method Validation
SOP0216	Reporting and Rounding off Results

SOP0205	Measurement of Uncertainty and Validation for Microbiological Methods
SOP0202	Communication with Sponsors
SOP0206	Estimation for Measurement of Uncertainty
SOP0888	Good Practices for Manual Integration

7.7 ENSURING THE VALIDITY OF RESULTS

Nelson Labs ensures the quality of its test results by QC verification prior to issuing results. All reported results are double checked by reviewing raw data sheets, instrument printouts, draft reports, and all other relevant documentation to guarantee the traceability of the reported results. Finally, QAU reviews all projects.

The controls can be divided in three categories: first line controls (e.g. QC verification with second source standards or appropriate controls (where applicable)), second line controls (e.g. blind sample analysis) and third line controls (e.g. participation in interlaboratory comparison and/or proficiency testing programs).

7.7.1 Related Documentation

These procedures are fully documented in the following SOPs:

SOP0220	Contents and Final Review of a Completed Project File
SOP0425	Quality Assurance and Quality Control
SOP0210	Assuring the Quality of test results
SOP0208	Conduct of a GMP study
SOP0214	Conduct of a GLP Study
SOP0424	QA program GLP
SOP0209	Conduct of a commercial R&D study

7.8 REPORTING OF RESULTS

7.8.1 General

Results for all studies carried out by Nelson Labs are reported in a Test Report. This report includes all the information requested by the Customer and necessary for the interpretation of the test results and all information required by the method used.

Depending upon the type of study and in agreement with the Customer, results are represented in the form of a Test Result Report, Study Report or Certificate of Analysis. The applicable quality level (ISO17025, GLP, GMP or R&D) is agreed upon during the quoting stage (7.1). For reporting of testing solely covered by our BELAC approved scope of ISO17025 accreditation, a clear link to ISO17025 and scope (certificate) should be present in the reports to allow or sponsors to unambiguously link our test data to the accreditation certificate (where applicable). For GLP and GMP tests or studies, appropriate statements are included in the respective reports as well.

7.8.2 Test Report

This type of report is released per Nelson Procedure SOP0425 under ISO 17025 and typically contains the raw data package released from the lab to internal customers (project responsibles).

7.8.3 Test Result Report

This is a short report form, with summarized procedures and results. The results may be presented in tabular form.

7.8.4 Study Report

A test result report may be expanded into a full study report if required by the Customer to provide a detailed description of the applied procedures and of the obtained results, per ISO 17025; GMP and / or GLP requirements (whichever applicable).

7.8.5 Calibration Reports

Nelson Labs can provide certificates and calibration information with respect to instrumentation utilized during study conduct, either internal or external certificates, upon Sponsor's request. Nelson Labs does not provide independent calibration certification services for customers. It is an internal program for Nelson Labs' equipment only.

7.8.6 Certificate of Analysis

Under GMP, a Certificate of Analysis is issued by the Qualified Person in case of QC testing on medicinal products.

7.8.7 Conclusions, Statement of Conformity, Opinions, and Interpretations

Conclusions and statements of conformity can only be made based on a predetermined and on the report documented decision rule (e.g. specification). Opinions and interpretations shall be clearly marked and may include recommendations, guidance, or other statements interpreted to be subjective.

7.8.8 Test and Calibration Results Obtained from Subcontractors

Results for tests/calibrations performed by subcontractors are clearly identified in the test report. Only qualified subcontractors through appropriate supplier qualification procedures are utilized. A list of approved subcontractors can be included in sponsor specific quality agreements. Subcontracting of testing should always be notified to and approved by the sponsor in advance.

7.8.9 Electronic Transmission of Results

In the case of transmission of test and calibration results by phone or other electronic means, copies of these transmissions are retained by the laboratory to document delivery. PDF files are typically utilized. In case final reports are approved electronically, the e-record and its approval must comply with the data integrity requirements of e-signatures as per 21CFR part 11 at all times.

7.8.10 Amendments

Any corrections and/or additions to the signed final report are in the form of an amended report. An amended report is clearly identified as such on the cover page and the header of each subsequent page. All changes made to the amended report are listed within a section

"Amendments" together with the reason (and a rationale whenever applicable) for changes and signed and dated by the project responsible and QAU (where applicable).

7.8.11 Related Documentation

These procedures are fully documented in the following SOPs:

SOP0217	Reporting of a GLP study
SOP0218	Test Report, Test Result Report and Study Report Generating Procedures
SOP0219	Certificate of Analysis Generating Procedures
SOP0425	Quality Assurance and Quality Control

7.9 COMPLAINTS

Nelson Labs has procedures for the resolution of complaints received from Sponsors or other parties, and to file complaints towards her suppliers.

Considering customer complaints, three categories are attributed: Level 1, Level 2, and Level 3, depending on the gravity of the issue.

Records are maintained of all complaints, investigations and corrective and preventive actions taken by the laboratory.

7.9.1 Related Documents

SOP0428	Dealing with Complaints

7.10 NON-CONFORMING WORK

Nelson Labs has procedures in place to monitor for actual or potential non-conformances to the Management System or Sponsor contracts, including all testing and/or related calibration work. The following procedures are in place:

- responsibilities and authorities for the management of non-conforming work are designated and actions (including halting of work and withholding of test reports as necessary) are defined and taken when non-conforming work is identified;
- an evaluation of the significance of the non-conforming work is made, including a full technical and quality review;
- immediate corrective actions are taken together with any decision about the acceptability of the non-conforming work;
- the responsibility for authorizing the resumption or retesting of work is defined prior to data release;
- Customers are notified of deviations where potential impact on results of tested products cannot be excluded.
- Customers are contacted for corrective actions and/or retesting when non-conformances are noted after data is reported and potential impact on reported results cannot be excluded (see also §7.8.10).

Deviations from SOPs, protocols, SSPs and quotations might occur during a study, and can lead to immediate corrective actions such as retests. Retests can also originate when Out-of-Specifications (OOS) results were obtained.

Based on the criticality of the non-conformance (grade A (=critical), grade B (=major) or reoccurring grade +* (=minor)) and when a significant risk exists for the integrity of the results or for the effectiveness of the Quality Management System, corrective/preventive actions are to be considered.

7.10.1 Related Documentation

These procedures are fully documented in the following SOPs:

SOP0426	Non-Conformances/Deviations (including Retest)
SOP0429	Out-Of-Specification Procedure

Global Nelson Policy Document

POL0007	Quality Event and CAPA Policy

7.11 CONTROL OF DATA AND INFORMATION MANAGEMENT

Calculations and data transfers are subject to appropriate checks in a systematic manner. Where computers or automated equipment are used for the acquisition, processing, recording, reporting, storage or retrieval of study data, the laboratory ensures that the integrity of the results is protected. For GxP critical systems, requirements from EudraLex Volume 4 annex 11 and/or OECD N°17 and 22 and 21CFR11 are implemented whenever appropriate.

7.11.1 Related documentation

Management system documentation:

MAN0014	Data Integrity Policy
MAN0017	User Access Management Policy
MAN0018	Change Policy
SOP0220	Contents and Final Review of a Completed Project File
SOP0425	Quality Assurance and Quality Control
SOP0481	Audit trail review
SOP0208	Conduct of a GMP Study
SOP0214	Conduct of a GLP Study
SOP0408	Open lab ECM User Procedure
SOP0409	Open lab ECM System Procedure

8 MANAGEMENT SYSTEM REQUIREMENTS

8.1 MANAGEMENT SYSTEM OPTION ACCORDING TO ISO/IEC 17025:2017

Nelson Labs maintains a Management system according to option A of the ISO 17025:2017 standard.

8.2 MANAGEMENT SYSTEM (MS) DOCUMENTATION

Nelson Labs has established, documented and implemented a MS, and maintains and continually improves its suitability and effectiveness in accordance with the requirements of ISO 17025:2017.

The basic elements of Nelson Labs' MS are the Quality Manual / Site Master File, standard operating procedures (SOPs), protocols, sponsor specified procedures (SSPs), instructions, and any other documentation or instructions provided to Nelson Labs by its Customer or study Sponsor.

Note: Job aids can be generated and managed in the same document management system as the documents described above. When considered quality critical, they must be referenced and linked to the respective procedure to be included in training and periodic review processes.

All staff, directly or indirectly, involved in testing services are obligated to work in accordance with the specific requirements of the documented MS. All internal quality-related activities are governed by procedures and written instructions. The document structure consists of a Quality Manual / Site Master File, policies and procedures (management, operations, Quality management system and supporting flows).

Nelson Labs manages these processes in accordance with the requirements of ISO/IEC 17025:2017.

8.2.1 Quality Manual / Site Master File

The Quality Manual / Site Master File includes the scope of the management system. This document outlines and refers to documented procedures established for the MS and their interrelationship to other processes of the MS.

8.2.2 Quality Policy Statement

This statement and the implementation and adherence to the principles of ISO 17025:2017, EudraLex GMP and OECD GLP, reflects management's commitment to provide assurances of the highest level for managing quality and focusing on meeting customer requirements and satisfaction.

8.2.3 Quality Objectives

Nelson Labs' management ensures that quality and management system objectives are established at relevant functions and levels within the company. Nelson Labs demonstrates this through this Mission Statement:

Mission statement: We help the best companies in the world improve the quality of life by providing the highest standard in laboratory testing, partnering to bring life-enhancing innovative products to market.

This commitment of continuous improvement is monitored on a monthly (MMR, monthly management review) and yearly (YMR, yearly management review) basis and decided upon in EMEAA leadership meetings and assured by Nelson Labs training policy, based on Plan-Do-Check-Act cycle. Additionally, the Nelson Labs' global quality unit coordinates monthly input for dashboarding of quality objectives over different Nelson Labs sites.

8.2.4 Nelson Labs Values

SAFETY, PEOPLE, INTEGRITY, CUSTOMER FOCUS and EXCELLENCE

8.2.5 Nelson Labs Goals and Management Commitment

Based on the corporate Sotera Health goals, Nelson Labs employees strive towards achieving the following goals with the highest respect of the company values:

- Expand Global Network
- Deliver Profitable Volume Growth
- Create One Company Capabilities
- Maximize Investment Returns

The entire Nelson Labs staff team must adhere to the spirit and letter of the firm's quality policy as well as the directives outlined in the Quality Manual / Site Master File and its subordinate documents, and maintain impartiality and independence of testing activities. I have continuously supported these objectives and plan to continue to be actively involved through personal commitment, active participation, and financial support in meeting the goals and objectives outlined in this document. I will continually be available to address all management system issues either directly or through directives to Quality Assurance Unit and Laboratory Management.

With regard to our GLP compliance program, the Test Facility Management will provide all necessary means (qualified and sufficient personnel, appropriate infrastructure and dedicated instrumentation) that are indispensable for the proper conduct of a GLP compliant study.
The GLP qualified personnel will be specifically assigned, and will receive appropriate tools and time for the proper conduct of a GLP study.

For Qualified Person approval, see 12.13.

8.2.5.1 Global Quality policy POL0001

Nelson Labs
A Sotera Health company

POL0001 - Global Quality Policy
Rev: 1.0

*We partner with the best companies in the world in **Safeguarding Global Health®** by maintaining the Nelson Labs Standards of Quality, Service, and Science.*

Uncompromised Quality

We act with integrity, impartiality, and independence and can be trusted to do things right. We continually strive to meet our clients' requirements and maintain compliance with all governing regulations. We monitor our quality management systems and performance while fostering a culture of operational excellence and continuous improvement.

Exceptional Service

We actively listen to our clients and strive to understand their needs to provide personalized service, solutions, and timely turnaround. We build long-standing partnerships with our clients that are mutually beneficial. We help our clients deliver timely, safe products to the market to positively impact lives and healthcare outcomes.

Innovative Science

We partner with our clients, industry experts, and business partners to provide solutions. We participate in industry groups and actively lead development of industry standards. We are committed to educating and training our staff, clients, and regulators on best practices and scientific methods that will lead to accurate and reliable results.

Every team member is committed to providing the quality, service, and science that our clients need. To successfully deliver on these high standards, each member of our team lives and upholds our company values of:

- ***SAFETY**: We are uncompromising in our commitment to health and well-being.*
- ***CUSTOMER FOCUS**: We are driven to fulfill our customers' needs with the highest quality and care.*
- ***PEOPLE**: We value our people who are part of a global team that is diverse, respectful, passionate, and collaborative.*
- ***INTEGRITY**: We are honest, reliable, and accountable in everything we do.*
- ***EXCELLENCE**: We exceed the expectations of our stakeholders and continue to improve and innovate in everything we do.*

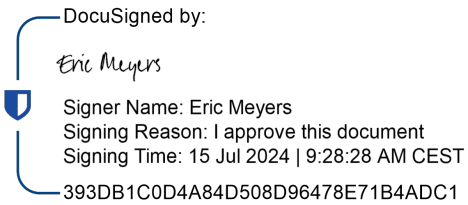
Every test and interaction matter because every person matters – We adhere to the Nelson Labs Standards for our clients, patients, families, friends, healthcare workers, and neighbors.

*Our mission is **Safeguarding Global Health®***

8.2.5.2 Management Commitment approval section

Eric Meyers
Managing Director
Top management and GLP TFM

Sign:

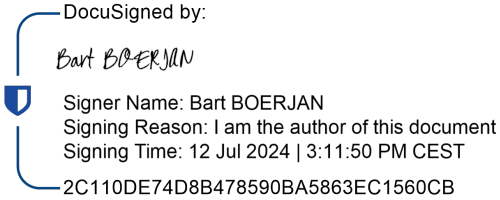


Lise Vanderkelen
Director of Lab Operations
Technical management and GLP TFM
Head of QC GMP

Sign:

Bart Boerjan
Sr. Quality Assurance Manager

Sign:



8.3 CONTROL OF MANAGEMENT SYSTEM DOCUMENTS

8.3.1 General

Nelson Labs has procedures to control all documents that comprise the quality documentation system. Documents are circulated for use by management and technical staff as required. All documents issued to personnel in the laboratory are reviewed and approved prior to issue.

All document management related processes are under control of a document management team which resides at QAU.

The Quality System of Nelson Labs is based on and often refers to 'external' documents, such as regulations, standards, normative documents and guidelines.

Three levels of (internal) documentation define the Quality System of Nelson Labs:

- The first level is the Quality Manual / Site Master File, which include or make reference to established policies and supporting procedures including technical procedures.
- The second level is comprised of SOPs and SSPs (Sponsor Specified Procedures), which are written documents to describe an operation, analysis or action that could influence data quality.
- The third level consists of data recording forms in support of SOPs: documents / templates to record raw data, log equipment activities or to describe the actual organizational / technical situation of Nelson Labs (or a department thereof).

8.3.2 Internal Documents

Internal documents can be of different types: Standard Operating Procedures (SOPs), Sponsor Specific Procedures (SSPs), Protocols, Logs, Instructions, Forms, or other Nelson Labs generated documents.
All internal documents are uniquely identifiable and revisioning and changes thereof are traceable.
Nelson Labs has processes in place which guarantee review, approval and training of internal documents prior to issue.
All documents are accessible to staff by logging into the corporate document management tool called MasterControl. Access is managed in cooperation with document management.

8.3.2.1 SOP, SSP and forms

The respective overview Matrices for Standard Operating Procedures, Sponsor Specific Procedures and forms can be found on the local network and are accessible through MasterControl:
T:\Quality\Quality Public\MasterControl

SOPs are periodically evaluated for their suitability and completeness.

8.3.2.2 Protocols

Study and test specific protocols are, on request of the sponsor, generated and, at least, approved by Study Director, QAU and Sponsor prior to initiation of a test.

An overview can be found on the local network:
T:\Quality\Quality Public\Protocols Nelson Labs (Pdf)

8.3.3 External Documents

External documents, such as books, regulations, standards, reference articles, etc. are indexed and contained in a database of secured Office® documents on the laboratory computer network. The use of external document control ensures that only current external information is utilized and updated on a periodic and/or scheduled basis.

8.3.4 Related Documentation

These procedures are fully documented in the following SOPs:

SOP0416	External Document Control – Library Management
SOP0413	Development, Change Control, Periodic Review and Archiving of a Standard Operating Procedure
SOP0414	Development, Review and Archiving of Sponsor Specified Procedures (SSP)
SOP0151	Document Management using MasterControl
SOP0179	MasterControl Document Management – User guide for general staff
SOP0189	MasterControl Document Management – User guide for Document Owners and Management
SOP0417	Development, review, reconciliation and archiving of forms and raw data
SOP0430	Good Documentation Practice (GDP) and Signature policy
SOP0194	MasterControl Document Management - User guide for Document Management team
SOP0475	Training in MasterControl - User guide for Document Management team

8.4 CONTROL OF RECORDS

8.4.1 General

Nelson Labs has procedures for identification, collection, indexing, access, storage, maintenance and disposal of quality and technical records.

8.4.2 Technical Records

Nelson Labs retains original observations, derived data, calibration records, and a copy of each test report, for a defined period. The records for each study contain sufficient information

- to establish an audit trail,
- to facilitate, if possible, identification of factors affecting the uncertainty and
- to enable the study to be repeated under conditions as close as possible to the original.

The records include the identity of personnel responsible for performance of each test, and data auditing personnel involved.

Nelson Labs has no control over sampling uncertainty, as test materials and products are sampled by the Sponsor and provided to Nelson Labs.

8.4.3 Quality Records

Quality records are generated and maintained by Nelson Labs to demonstrate the successful operation of the facility's quality and management system.

8.4.4 Related Documentation

These procedures are fully documented in the following SOPs:

SOP0417	Development, review, reconciliation and archiving of forms and raw data
SOP0430	Good Documentation Practice (GDP) and Signature policy
SOP0392	Archive Procedures
SOP0220	Contents and Final Review of a Completed Project File
SOP0393	Lab Systems Backup procedure

8.5 ACTIONS TO ADDRESS RISKS AND OPPORTUNITIES

Nelson Labs addresses risks and opportunities by built in impact analysis in the quality management flows of deviation handling, corrective and preventive actions, dealing with complaints, lab and IT system validation, change control and management review.

Periodical trending analysis and KPI evaluations might bring forth new imperatives which are evaluated in a risk-based manner.

Ad hoc risk assessments are preferably done by a failure mode and effects analysis by taking probability, severity and detectability of the risk into account. Established risk assessment are periodically reviewed, typically yearly, as part of management review activities.

8.5.1 Related Documentation

These procedures are fully documented in the following SOPs:

SOP0426	Non-conformances/Deviations (including retest)
SOP0427	Corrective / Preventive Action Procedures
SOP0428	Dealing with Complaints
SOP0386	System Validation
SOP0387	Operational Change Control for Lab- and IT Systems
SOP0449	Management Review Procedures
SOP0431	Quality Risk Management

8.6 IMPROVEMENT

Nelson Labs continually measures goal setting and the effectiveness of its management system through the use of the quality policy, quality objectives, audit results, quality system data analysis, corrective and preventative actions and effectiveness checks, Quality metrics and Quality management review status reports. In addition, a training policy was created, including the qualification of personnel by education, experience and training. An internal training program was designed to adequately train the personnel.
Opportunities for improvement are identified as output from the Quality Management system (see 8.5) or bottom-up using A3 suggestions. There is a central Operational Excellence (OPEX) team and departmental sub teams coordinating these initiatives using A3 problem solving as a structured problem-solving and continuous-improvement approach.

8.6.1 Related Documentation

Management System documentation:

SOP0449	Management Review Procedures
SOP0445	Conduct of Site Leadership Team, Quality, Lab and SD Meetings
MAN0015	Training Policy

8.7 CORRECTIVE ACTIONS

8.7.1 General

Nelson Labs has procedures to implement corrective and/or preventive actions to eliminate the causes of existing non-conformances in order to prevent re-occurrence. Furthermore, Nelson Labs evaluates the need for improvement to prevent occurrence of non-conformances, either technical or within the quality management system.
Corrective/Preventive actions are initiated with a cause analysis, followed by a selection and implementation of corrective/preventive actions and finally monitoring of the planned actions. Additional audits are also possible.

8.7.2 Related Documentation

These procedures are fully documented in the following SOPs:

SOP0426	Non-conformances/Deviations (including retest)
SOP0427	Corrective / Preventive Action Procedures

8.8 INTERNAL AUDITS

Nelson Labs conducts process and facility-based audits to verify the compliance, implementation and suitability of Nelson Labs' quality activities with the requirements of the management system and to gain evidence of full traceability. The internal audit program addresses all elements of the quality system covering both the management system and testing activities with respect to the ISO/IEC 17025, GLP and GMP. The QAU is responsible for planning and organizing audits.

The QAU or an authorized and qualified external auditor carries out all technical audits. Audits of Nelson Labs' QAU are performed on an ongoing basis by Sponsor audits or other external auditors or Nelson Labs' management.

Results of internal quality audits are recorded, agreed upon corrective/preventive actions, individuals responsible, and time schedules for completion are defined.

Process and facility-based inspections are performed at least every 2 years according an Internal Audit Schedule and the results are incorporated in the Management Review.
These internal audits are used for ISO/IEC 17025, GLP and GMP.
Additional auditing activities are required for GMP and GLP:

- for GMP, a periodic review is established on computerized systems
- for GLP, critical phase audits are planned. Audits concerning the archive and computerized system are already part of the internal audit program

8.8.1 Related Documentation

These procedures are fully documented in the following SOPs:

SOP0421	Internal audit: process and facility-based inspections
SOP0422	Sponsor Inspections
SOP0423	Periodic Review of (critical GxP) computerized systems
SOP0424	QA program GLP

8.9 MANAGEMENT REVIEW

Team Meetings are held regularly to discuss operational matters and monitor the effectiveness of the general quality and management system. Also, an evaluation and planning of the personnel and investment is established every year and incorporated in the Management Review.

Yearly, typically near the end of the first quarter of the year, the Management Review is organized in order to assess the effectiveness of the Quality Management System, the suitability of the company Quality policy and testing activities, concluding with decisions regarding necessary process changes or improvements versus the prior year.
The Quality Manager will draft a presentation, including the required elements to be reviewed by ISO 17025, which will be discussed during a dedicated Site Leadership Meeting.
All responsible management will evaluate and discuss the hits and misses of the actionables of prior management review and based on the review of the presentation set forth new imperatives for the year to come.

A Management Review report is generated by the QA Manager and approved by the Managing Director summarizing the review and evaluation of the Quality Management System of the past year and goal setting for the subsequent year, including needed changes or improvements to the Quality Management System.
The findings of the Management Review and objectives for the subsequent year are translated into actionables which are tracked and evaluated quarterly during Site Leadership Team meetings. The qualified person is notified of the report and the status of actionable follow-up.

8.9.1 Related Documentation

This procedure is fully documented in the following SOPs:

SOP0445	Conduct of Site Leadership Team, Quality, Lab and SD Meetings
SOP0449	Management Review Procedures
SOP0428	Dealing with Complaints
SOP0450	Customer Survey
SOP0422	Sponsor inspections
SOP0421	Internal audit: process and facility-based inspections
SOP0423	Periodic Review of (critical GxP) computerized systems
SOP0426	Non-conformances/Deviations (including retest)
SOP0427	Corrective / Preventive Action Procedures

9 APPENDIX A: QUALITY ASSURANCE AT NELSON LABS NV, OVERVIEW OF ROLES AND RESPONSIBILITIES

9.1 QUALITY ASSURANCE

The Quality Assurance Management is committed to dedicated and independent Quality Assurance (QA) and monitoring of Quality Control (QC) processes.

The basic outline of the functional units responsible for data generation and review is as follows:

- Lab Technician
- Data Reviewer
- (Sr.) Lab Operations Manager / Head of QC
- Study Director / Scientific Project Manager
- Quality Assurance Unit (QAU)
- Qualified Person

The first level of QC lies with the trained bench *technicians* conducting the analyses. Proper documentation and peer and data review are important aspects of laboratory quality management at this level.

Responsible management are responsible for ensuring that adequate facilities and equipment are available to the analysts to ensure the production of scientifically and technically valid data. Lab Management interacts closely with the analysts and provides them with adequate supervision in order to ensure that the laboratory- and QC-procedures are strictly adhered to.

Data Review (QC Review): Raw data review is performed within the operational department by a dedicated group of data reviewers which work independent from the lab technicians executing the tests. Additionally, data review can also be performed by others within the company as long as they have sufficient knowledge for performing this review (e.g. Study Directors or scientific project managers).

The *Quality Assurance Unit* is responsible for auditing the laboratory facilities, procedures, processes, equipment and raw data. The results of these audits are presented to the responsible management and may be used, when required, to decide upon preventive and corrective action. By doing so, the QAU assists in maintaining and continuously improving the management systems and technical procedures in the laboratory.

The responsibility of the Qualified Person applies to the quality decisions (GMP) related to QC testing on medicinal products and to the issue of Certificates of Analysis for the QC testing on medicinal products and related GMP study reports.

9.2 RELATED DOCUMENTATION

Management System documentation:

SOP0425	Quality Assurance and Quality Control
SOP0420	Job descriptions
SOP0419	Personnel and training
SOP0445	Conduct of Site Leadership Team, Quality, Lab and SD Meetings
SOP0220	Contents and Final Review of a Completed Project File

MAN0015 Training Policy

10 APPENDIX B: SCOPE OF ACCREDITATION AND CERTIFICATION

Actual licenses, certifications and accreditations can be found on the Nelson Labs website: https://www.nelsonlabs.com/our-company/quality/

Nelson Labs Europe Certifications

Nelson Labs Europe laboratory is:

- GMP inspected and recognized by the Belgian Federal Agency for Medicinal and Healthcare Products (FAMHP)
- GLP certified by Sciensano (ex-Scientific Institute of Public Health (WIV-ISP); Identification number: T02)
- FDA registered (FDA Establishment Identifier (FEI): 3005742674)
- ISO 17025 accredited by BELAC (Identification number: 363-TEST)

The same documents can also be found directly on the website of following notified bodies:

- ISO 17025 by BELAC:
- https://economie.fgov.be/en/themes/quality-and-safety/accreditation-belac/accredited-bodies/testing-laboratories-test

- GMP certificate by FAMHP on EUDRA GMDP: http://eudragmdp.ema.europa.eu/inspections/gmpc/searchGMPCompliance.do

- Listed as GLP facility by Sciensano http://www.glp.be/GLPfacilities.html

- FDA registration: https://www.accessdata.fda.gov/scripts/cder/drls/default.cfm

11 APPENDIX C: NELSON LABS SOP MATRIX

Nelson Labs' SOP Matrix is kept as a "living document" in electronic format on site.

The overview below is dated April 12th, 2024.

11.1 MANAGEMENT SOPS

Cross-reference		SOP's per (sub)cluster	Quality Level		
Old number	MC number		ISO	GLP	GMP
		EHS (Hygiene, Med. Control, Fire prevention, evacuation, ...)			
1.2.2	SOP0432	Occupational health and health assessments	x	x	x
5.1.1	SOP0433	Emergency and Evacuation Procedure	x	x	x
5.1.2	SOP0434	Use and care of Personal Protective Equipment	x	x	x
5.1.10	SOP0438	Use of emergency shower and Eye wash station	x	x	x
5.1.11	SOP0439	Bioveiligheidshandleiding van het laboratorium voor Microbiologie	x	x	x
-	SOP0491	Fire Prevention and Safety	x	x	x
-	SOP0493	First aid	x	x	x
		Human Resources (recruitment, evaluations, ...)			
1.2	SOP0440	Personnel and Organization	x	x	x
1.2.1	SOP0441	Personnel, Recruitment and Evaluations	x	x	x
-	MAN0015	Training Policy	x	x	x
		Facility (Access control, pest control, emergency generator, ...)			
2.1.1	SOP0442	Facilities Description	x	x	x
2.1.3	SOP0443	Visitor Registration at Nelson Labs NV Premises	x	x	x
2.2.7.1	SOP0444	Use and maintenance of the emergency generator	x	x	x
		Sales & Marketing			
4.2.13	SOP0446	Quotation Procedures	x	x	x
		Communication			
1.2.6	SOP0445	Conduct of Site Leadership Team, Quality, Lab and SD Meetings	x	x	x
		Strategies			
1.1	SOP0448	Company organisation table	x	x	x
1.2.7	SOP0449	Management Review Procedures	x	x	x
4.2.10	SOP0450	Customer Survey	x	x	x
KHB / SMF	MAN0010	Quality manual Nelson Labs NV	x	x	x
VMP	MAN0012	Validation Policy	x	x	x
-	MAN0013	Risk Assessment for Mixed Use of Premises, Resources and Systems	x	x	x
-	MAN0016	Nelson Laboratories Leuven (BE) – Environmental, Health, and Safety Management	x	x	x
-	MAN0017	User Access Management Policy	x	x	x
-	MAN0018	Change Policy	x	x	x

11.2 QUALITY MANAGEMENT SOPS

Cross-reference		SOP's per (sub)cluster	Quality Level		
Old number	MC number		ISO	GLP	GMP
		Document management			
4.2.1	SOP0413	Development, Change Control, Periodic Review and Archiving of a Standard Operating Procedure	x	x	x
-	SOP0151	Document management using MasterControl	x	x	x
-	SOP0179	MasterControl Document Management - User guide for general staff	x	x	x
-	SOP0189	MasterControl Document Management - User guide for Document Owners and Management	x	x	x
-	SOP0194	MasterControl Document Management - User guide for Document Management team	x	x	x
-	SOP0475	Training in MasterControl - User guide for Document Management team	x	x	x
4.2.11	SOP0414	Development, Review and Distribution of Sponsor Specified Procedures (SSP)	x	x	x
4.2.9	SOP0416	External Document Control - Library management	x	x	x
4.1.8	SOP0417	Development, review, reconciliation and archiving of forms and raw data	x	x	x
		Training			
1.2.3	SOP0419	Personnel and Training	x	x	x
1.2.4	SOP0420	Job Descriptions	x	x	x
1.2.5	SOP0199	Matrix of (Technical) Competence	x	x	x
		Sponsor- and Self-Inspections			
4.1.13	SOP0421	Internal Audit: Process and Facility Based Inspections	x	x	x
4.2.22	SOP0422	Sponsor Inspections	x	x	x
4.2.33	SOP0423	Periodic Review of (critical GxP) computerized systems	x	x	x
4.2.35	SOP0424	QA program GLP		x	
4.2.34	SOP0425	Quality Assurance and Quality Control	x		x
		Non-Conformance (NCR)			
4.2.20	SOP0426	Non-conformances/Deviations (including retest)	x	x	x
		Corrective & Preventive Actions (CAPA's)			
4.1.14	SOP0427	Corrective/Preventive Action Procedures	x	x	x
		Complaints			
4.1.19	SOP0428	Dealing with Complaints	x	x	x
		Out-of-Specifications (OOS)			
4.1.36	SOP0429	Out-Of-Specification procedure	x		x
		Data integrity			
-	MAN0014	Data Integrity Policy	x	x	x
4.2.5	SOP0430	Good Documentation Practice(GDP) and Signature Policy	x	x	x
-	SOP0481	Audit Trail Review	x	x	x
		Risk Management			
4.2.31	SOP0431	Quality Risk Management	x	x	x

Support Management SOPs

Cross-reference		SOP's per (sub)cluster	Quality Level		
Old number	MC number		ISO	GLP	GMP
		Purchase			
4.1.12	SOP0380	Purchasing Services, Equipment and Supplies	x	x	x
4.1.16	SOP0381	Vendor and Subcontractor Qualification and Monitoring Procedures	x	x	x
4.1.37	SOP0382	Communication and sample flow between Nelson Labs NV/Qualified Contractor and Nelson LLC	x	x	
		Validation			
2.2.2	SOP0383	General Procedures Including Use and Maintenance for Laboratory Systems	x	x	x
4.2.29	SOP0386	System Validation	x	x	x
4.2.30	SOP0387	Operational Change Control for Lab- and IT Systems	x	x	x
4.1.26	SOP0390	Control of Reference Standards and Materials	x	x	x
2.2.6.32	SOP0391	Calibration Weights for Balances	x	x	x
		IT			
		General IT procedures			
6.2	SOP0393	Lab Systems Backup procedure	x	x	x
6.2.1	SOP0394	Servers Backup procedure	x	x	x
6.2.2	SOP0395	Servers Restore and Testing procedure	x	x	x
6.3	SOP0396	User Account Management For Nelson Labs NV Network Systems	x	x	x
6.5	SOP0398	Hardware Inventory SOP	x	x	x
6.6	SOP0399	Virus and Malware Code Protection	x	x	x
6.7	SOP0400	Nelson Labs NV-Network Infrastructure Documentation	x	x	x
6.8	SOP0401	Software Usage at Nelson Labs NV	x	x	x
6.19	SOP0402	Workstation Installation and Configuration	x	x	x
-	SOP0498	User guide for applying compliant e-signatures with DocuSign	x	x	x
-	SOP0456	DocuSign for Administrators	x	x	x
-	SOP0474	Use and Maintenance of Dynamic Templater Application	x		
-	SOP0628	Use of the Excel Audit Trail Add-In (ITS-085)	x	x	x
		IT Systems: Use & maintenance			
6.10	SOP0403	STARLIMS - System Administration	x	x	x
6.11	SOP0404	STARLIMS - Use of the Purchase Manager	x	x	x
6.12	SOP0405	STARLIMS - Use of the Materials Management Module	x	x	x
6.13	SOP0406	Use of Spreadsheet Tools	x		
6.14	SOP0407	Use of Spreadsheet Tools-Lab	x		x
6.15	SOP0408	Open lab ECM User Procedure	x	x	x
6.16	SOP0409	Open lab ECM System Procedure	x	x	x
6.17	SOP0410	STARLIMS - Use of the electronic batchbook module	x	x	x
6.20	SOP0411	STARLIMS - Equipment Management	x	x	x
6.21	SOP0412	STARLIMS - Storage Location Management	x	x	x
-	SOP0196	STARLIMS - Use of the Inventory Management Module	x	x	x
-	SOP0494	STARLIMS: Use of the Recipe Preparation Module	x	x	x
6.18	SOP0455	Server qualification and maintenance	x	x	x
-	SOP0466	LOMS - System administration	x	x	x
-	SOP0881	Use and maintenance of the thermoguard merge script	x	x	x
		Archiving			
4.2.8	SOP0392	Archive procedures	x	x	x

OPERATIONS SOPS

11.2.1 Conduct of a study

Cross-reference		SOP's per (sub)cluster	Quality Level		
Old number	MC number		ISO	GLP	GMP
		Conduct of a study			
4.1.1	SOP0200	Study Logging Procedures, Sample Receipt, Storage and Contamination Control Practices Using Loms System	x	x	x
4.1.38	SOP0201	Management of specially regulated substances	x	x	x
4.2.21	SOP0202	Communication with sponsors	x	x	x
4.1.40	SOP0203	Subsampling of aqueous and organic solvent based extracts/test solutions for extractables and leachables studies	x		
4.1.6	SOP0204	Method Validation	x		x
4.1.28	SOP0205	Measurement of uncertainty and validation for microbiological methods	x		x
4.2.27	SOP0206	Estimation for Measurement of Uncertainty	x		x
3.2.30	SOP0207	Conduct of a Leachable Study	x		
4.1.32	SOP0208	Conduct of a GMP study			x
4.1.41	SOP0209	Conduct of a commercial R&D study			
4.1.30	SOP0210	Assuring the Quality of test results	x		x
1.2.8	SOP0211	Assignment of Study Responsibles - GLP		x	
4.1.22	SOP0213	Study Plan for a GLP Study		x	
4.1.23	SOP0214	Conduct of a GLP Study		x	
4.1.31	SOP0215	Characterisation of test, control and reference items		x	
4.1.20	SOP0216	Reporting and Rounding off Results	x	x	x
4.1.24	SOP0217	Reporting of a GLP Study		x	
4.1.7	SOP0218	Test Report, Test Result Report and Study Report Generating Procedures	x		x
4.1.33	SOP0219	Certificate of Analysis Generating Procedure			x
4.2.7	SOP0220	Contents and Final Review of a Completed Project File	x		x
4.2.37	SOP0221	Sample Return and Sample Destruction procedures	x	x	x

11.2.2 Conduct of a study performing the test: microbiology and toxicological procedures

Cross-reference		SOP's per (sub)cluster	Quality Level		
Old number	MC number		ISO	GLP	GMP
		Conduct of a study			
		Conduct of a study - Performing the test(s): Microbiological & Toxicological procedures			
3.1.1.1	SOP0222	Cell Counting using a Hemacytometer	x	x	
3.1.1.2	SOP0223	Growth and maintenance of mammelian cell lines	x	x	
3.1.1.3	SOP0224	Use and Maintenance of cell and tissue culture room	x		x
3.1.1.4	SOP0452	Gram staining	x		
3.1.1.8	SOP0225	Preparation, storage and control of growth media and rinse fluids	x	x	x
3.1.1.9	SOP0226	Basic Surface Area Calculation	x	x	
3.1.1.10	SOP0227	Culture and maintenance of reference micro-organisms	x	x	x
3.1.2.3	SOP0228	MEM Elution Test	x	x	
3.1.2.5	SOP0229	Sterility Test (USP,EP and ISO)	x		x
3.1.2.6	SOP0230	Validation of a sterility test	x		x
3.1.2.8	SOP0231	Total Bioburden	x	x	x
3.1.2.9	SOP0232	Growth Promotion Test	x		x
3.1.2.24	SOP0234	Bacterial Endotoxins: Limulus Amebocyte Lysate (LAL) Test for Detection and Quantitation of Endotoxins	x	x	x
3.1.2.25	SOP0235	Microbial examination of non-sterile products: Microbial Enumeration Tests	x		x
3.1.2.26	SOP0236	Microbial examination of non sterile products: Tests for specified microorganisms	x		x
3.1.2.32	SOP0239	Bioanalytical ELISA method validation	x	x	
3.1.2.37	SOP0242	Carbohydrate test	x	x	
3.1.2.39	SOP0336	Hemoglobin test	x	x	
-	SOP0454	Aseptic Techniques	x	x	x
-	SOP0460	Monocyte activation test (MAT)	x		x
-	SOP0471	BCA assay for determination of protein content	x	x	
-	SOP0472	Cleaning validation procedures for Healthcare reprocessing	x	x	
-	SOP0476	Steam sterilization validation	x	x	
-	SOP0477	Chemical and thermal disinfection validation procedures for Healthcare processing of reusable devices.	x	x	
-	SOP0514	In vitro irritation test	x	x	
-	SOP0901	Filter integrity testing: determination of compatibility for filters	x		
-	SOP0902	Filter integrity testing: product wet integrity test	x		
-	SOP0903	Filter integrity testing: bacterial retention test	x		
-	SOP0904	Filter integrity testing: growth inhibition test of drug product	x		
-	SOP0911	Filter integrity testing: Culturing Brevundimonas diminuta	x		
-	SOP0913	Filter integrity testing: Conditioning of Filters with Media	x		

11.2.3 Conduct of a study performing the test: analytical procedures

Cross-reference		SOP's per (sub)cluster	Quality Level		
Old number	MC number		ISO	GLP	GMP
		Conduct of a study			
		Conduct of a study - Performing the test(s): Analytical procedures			
3.2.4	SOP0243	Manual Conductivity determination	x		x
3.2.7	SOP0244	Determination of elements by ICP-OES	x		
3.2.8	SOP0245	Determination of semi-volatile organic compounds(SVOCs) in extracts of aqueous and solid samples by gaschromatography-mass spectrometry (GC/MS)	x		
3.2.10	SOP0246	FTIR-Analysis	x		
3.2.11	SOP0247	Determination of Anions by Ion chromatography	x		
3.2.26	SOP0249	Determination of Turbidity	x		
3.2.39	SOP0251	Sample preparation prior to the determination of organic compounds in extractable/leachable studies	x		
3.2.40	SOP0252	Manual pH Determination	x		x
3.2.44	SOP0253	Total Organic Carbon (TOC) Analysis	x	x	
3.2.47	SOP0254	Determination of volatile organic compounds (VOCs) in liquid or solid samples by Headspace GC/MS	x		
3.2.55	SOP0256	LC/UV Analysis of SULPHUR in Dichloromethane, Isopropanol and Hexane using the Agilent 1200 LCMSD	x		
3.2.58	SOP0257	Determination and Quantification of ammonium(NH4+) in Water by Ultra Violet-Visible Light Spectrophotometry (UV-VIS)	x		
3.2.60	SOP0258	Determination and Quantification of hydrogen peroxide (H2O2) in Water for Injection by Ultra Violet -Visible Light Spectrophotometry (UV-VIS)	x		
3.2.69	SOP0259	Determination and quantification of Silicon Oil in hexane and in Utra Pure Water (UPW) by Graphite Furnace Atomic Absorption Spectrometry (GF-AAS)	x		
3.2.73	SOP0262	Measurement of subvisible particles in solutions with the HIAC 9703+ measurement system	x		x
3.2.76	SOP0264	LC/MS Screening using the Thermo Scientific Exactive Orbitrap	x		
3.2.77	SOP0265	Determination of semi-volatile organic compounds (SVOCs) in extracts of aqueous and solid samples by GC/MS after silylation with BSTFA	x		
3.2.81	SOP0267	Quantitative Determination of Irgafos 168, Irganox 168 oxide, Irganox 1010, Irganox 1076 and Bis((2.4-ditert-butylphenyl)phosphate in DCM extracts by LCMSMS	x		
3.2.82	SOP0268	ESI-LC/MS Screening using the Thermo Scientific Q-Exactive Focus Orbitrap	x		
3.2.83	SOP0269	Determination of Mercury (Hg) in aqueous solution by Inductively Coupled Plasma Mass Spectrometry (ICP-MS) Matrix: Ultra Pure Water (UPW)	x		
3.2.84	SOP0270	Determination and quantification of bis(2,4)di-tert-butylphenyl)phosphate using the Thermo Fisher Q-exactive focus instrument	x		
3.2.86	SOP0271	Determination of 16 PAHs in extracts by Gas Chromatography - Triple Quadrupole Mass Spectrometry (GC/MS/MS)	x		
3.2.87	SOP0272	Determination of 11 Nitrosamines in extracts by Liquid Chromatography - Triple Quadrupole Mass Spectrometry (LC/MS/MS)	x		
3.2.88	SOP0273	Non Volatile Residue (NVR) determination	x		
3.2.89	SOP0274	DSC analysis	x		
3.2.90	SOP0275	Determination of acetaldehyde and formaldehyde in aqueous solutions after derivatization wih DNPH by LCUV analysis using the agilent 1260 infinity LC/DAD/FLD	x		
3.2.91	SOP0276	Screening for a selected set of metallic impurities in aqueous extracts and drug products by Inductively Coupled Plasma Mass Spectrometry (ICP-MS)	x		
3.2.92	SOP0451	Determination of volatile organic compounds (VOCs) in liquid or solid samples by Headspace GC/MS using Masshunter	x		
-	SOP0467	Screening of volatile and semi-volatile organic compounds using masshunter	x		
-	SOP0487	Determination of semi-volatile organic compounds(SVOCs) in extracts of aqueous and solid samples by gaschromatography-mass spectrometry (GC/MS) using masshunter	x		
-	SOP0458	Determination and Quantification by means of UV/VIS Spectrophotometry	x		
-	SOP0631	Screening of non-volatile organic compounds in UHPLC-HRAMS data using the Compound Discoverer data processing platform	x		
-	SOP0633	Determination of non-volatile organic compounds (NVOCs) by UHPLC/ESI HRAMS with Compound Discoverer	x		
-	SOP0634	Determination of non-volatile organic compounds (NVOCs) by UHPLC/APCI HRAMS with Compound Discoverer	x		
-	SOP0888	Good Practices for Manual Integration	x		x

11.2.4 Conduct of a study: Use and maintenance and reagentia & standards

Cross-reference		SOP's per (sub)cluster	Quality Level		
Old number	MC number		ISO	GLP	GMP
		Reagentia & Standards			
4.1.2	SOP0377	Management of Inventories (Chemicals and Consumables) at Nelson Labs	x	x	x
4.1.29	SOP0378	Determination of the purity of qualitative and quantitative standards	x		
5.1.6	SOP0379	General Housekeeping and labwaste disposal regulations	x	x	x
		Lab equipment : Use & maintenance			
4.2.28	SOP0278	Monitoring of controlled storage for temperature and humidity	x	x	x
2.2.3.2	SOP0280	Use and Maintenance of Stuart Colony Counter	x		
2.2.3.11	SOP0284	Use and Maintenance of Naber Muffle Furnaces	x		
2.2.3.12	SOP0285	Use, Validation and Maintenance of Depyrogenation Oven	x		
2.2.3.19	SOP0287	Operation and Maintenance of Varian 720-ES ICP	x		
2.2.3.35	SOP0293	Operation and Maintenance of the Agilent 1200 series HPLC VWD.	x		x
2.2.3.38	SOP0295	Use and Maintenance of the BIO-TEK Automated Microplate Reader	x	x	x
2.2.3.39	SOP0296	Operation and Maintenance of the Agilent 6410, 6460 an 6470 LC/MS Triple Quad Mass Spectrometer and Agilent 1200 and 1290 series HPLC	x		x
2.2.3.40	SOP0297	Operation and Maintenance of the Shimadzu Prominence LC-DAD	x		x
2.2.3.42	SOP0298	Use and maintanance of the HACH 2100AN turbidimeter	x		
2.2.3.43	SOP0299	Operation and Maintenance of Perkin Elmer THGA Graphite Furnace AA-600	x		
2.2.3.45	SOP0301	Use and Maintenance of the Agilent (HS)-GC with FID and NPD detector	x		x
2.2.3.48	SOP0303	Use and maintenance of ProLAB 4000 pH/CONDUCTIVITY meter	x		x
2.2.3.49	SOP0304	Operation and Maintenance of the Agilent 1260 Infinity LC/DAD/FLD	x		
2.2.3.50	SOP0305	Operation and maintenance of the Agilent 6120 Quadrupole LC/MS and 1200 LC/DAD/FLD	x		x
2.2.3.51	SOP0306	Operation and maintenance of the thermo fisher scientific UHPLC, Photodiode array(PDA) detector and mass spectrometer exactive incl. HCD	x		
2.2.3.54	SOP0307	Operation and Maintenance of the Perkin Elmer NEXION 300XX	x		x
2.2.3.56	SOP0308	Use and Maintenance of the Agilent 7890A/7000B EI/CI-GC-QQQ	x		x
2.2.3.60	SOP0311	Use and maintenance of Perkin Elmer DSC 4000	x		
2.2.3.65	SOP0312	Use and maintenance of Sievers M9 Laboratory TOC Analyzer	x	x	
2.2.3.66	SOP0313	Operation and Maintenance of the Agilent 7697A static Headspace Sampler/Agilent 6890N, 7890B or 8890B Gas Chromatograph / 5975 inert or 5977A or 5977B Mass Selective Detector (HS-GC/MS)	x		
2.2.3.67	SOP0314	Operation and maintenance of the Dionex ICS-2100 Ion Chromatograph	x		
2.2.3.68	SOP0315	Use and maintenance of the "Tecniplast BS48" Biosafety cabinet	x		
2.2.3.69	SOP0316	Operation and maintenance of the Agilent 7890B/7200A EI/CI-GC-QTOF	x		
2.2.3.70	SOP0317	Operation and maintenance of the Agilent single quad GC/MS systems	x		
2.2.3.72	SOP0319	Operation and maintenance of the Thermo Fisher Scientific UHPLC, Photodiode Array (PDA) detector and Hybrid Quadrupole Orbitrap high resolution Mass Spectrometer Q-Exactive incl. HCD	x		
2.2.3.73	SOP0320	Operation and maintenance of the Cary 630 FTIR	x		
2.2.3.74	SOP0321	Operation and maintenance of the Gerstel Dual Head Multipurpose Sampler – Agilent 7980B/5977B GC-MS	x		
2.2.3.75	SOP0322	Operation and maintenance of the Thermo Fisher Scientific UHPLC, Photodiode Array (PDA) detector and Hybrid Quadrupole Orbitrap high resolution Mass Spectrometer Q-Exactive Focus incl. HCD	x		
2.2.3.76	SOP0323	Use and maintenance of HIAC 9703+ Liquid particle counter	x		x
2.2.6.1	SOP0325	Use and Maintenance of Refrigerators and Freezers	x	x	x
2.2.6.3	SOP0326	Use and maintenance of water baths	x	x	x
2.2.6.4	SOP0327	Use and Maintanance of drying ovens	x		
2.2.6.7	SOP0329	Use and maintenance of syringes and automatic pipettes	x		
2.2.6.10	SOP0330	Use and Maintenance of Integra Pipetboy	x		
2.2.6.11	SOP0331	Operation and Maintenance of Centrifuges	x		
2.2.6.12	SOP0332	Use and maintenance of Elix and Milli-Q Advantage A10 water purification system	x		x
2.2.6.15	SOP0333	Heating and Stir Plate	x		
2.2.6.16	SOP0334	Operation and Maintenance of Incubators	x		x
2.2.6.17	SOP0335	Use and Maintenance of Inverted Microscope	x		
2.2.6.19	SOP0337	Use and Maintenance of Vortex	x		
2.2.6.21	SOP0339	Use and maintenance of Mechanical Shaker	x		x
2.2.6.25	SOP0340	Use and Maintenance of Motic Light Miscroscope	x		

11.2.4 Conduct of a study: Use and maintenance (Continued)

Cross-reference		SOP's per (sub)cluster	Quality Level		
Old number	MC number		ISO	GLP	GMP
		Lab equipment : Use & maintenance			
2.2.6.34	SOP0344	Use and Maintenance of the Lancer Washer	x	x	x
2.2.6.35	SOP0345	Use and Maintenance of TurboVap® II concentration workstation	x		
2.2.6.36	SOP0346	Use and Maintenance of Universal Shaker	x		
2.2.6.37	SOP0347	Use and Maintenance of Grant QBD2 Block Heater	x		
2.2.6.38	SOP0348	Use and Maintenance of binder Climatic Chambers	x		
2.2.6.39	SOP0349	Use and Maintenance of waterbath GD 120	x		x
2.2.6.41	SOP0350	Use and Maintenance of the Steritest Equinox Pump	x		x
2.2.6.45	SOP0353	Use and maintenance of Reference "TESTO" Datalogger	x		
2.2.6.47	SOP0355	Use and maintenance of the Getinge Isotest Sterility Isolator	x		x
2.2.6.48	SOP0356	Use and Maintenance of Dräger Gasdetection Sytem	x		
2.2.6.51	SOP0358	Use and Maintenance of Ultrasonic Waterbaths	x	x	
2.2.6.55	SOP0360	Use and Maintenance of CO2 Incubator	x	x	
2.2.6.56	SOP0361	Use and maintenance of the Fisher Scientific Accuspin Micro 17 Centrifuge	x		
2.2.6.63	SOP0364	Use and maintenance of the air-monitoring system : SAS super IAQ and 180	x		
2.2.6.65	SOP0365	Use and Maintenance of CISA steam sterilizer	x		x
2.2.6.67	SOP0367	Use and Verification of Thermometers	x		
2.2.6.68	SOP0368	Use and maintenance of the Precision Balance Entris 623I-1S	x		
2.2.6.69	SOP0369	Use and maintenance of Climatronix climatic chambers	x		x
2.2.6.71	SOP0371	Use and maintenance of the Bioquell QUBE Sterility Isolator	x		x
2.2.6.74	SOP0373	Use and maintenance of the automated cell counter (nucleocounter)	x		
2.2.6.75	SOP0374	Use and maintenance of the Sartorius Semi-Micro Balance ME215P	x		
2.2.6.76	SOP0375	Use and Maintenance of Mettler-Toledo XSE + XSR 205DU Analytical Balance	x		
5.1.5	SOP0376	Cleaning and Preparation of Glassware and Labware	x	x	x
-	SOP0198	Use and maintenance of sterility room	x		x
-	SOP0457	Operation and Maintenance of Perkin Elmer THGA Graphite Furnance AA	x		
-	SOP0459	Operation and maintenance of the Lambda 25 UV/Visible spectrophotometer	x		
-	SOP0464	Use and maintenance of BAGMIXER® 400 W	x		
-	SOP0465	Use and maintenance of the Clariostar microplate reader	x	x	
-	SOP0469	Use and maintenance of the Washer-Disinfector Belimed WD290 IQ	x	x	
-	SOP0168	Use and maintenance of Spatula balance	x		x
-	SOP0468	Use and Maintenance of TUTTNAUER steam sterilizer	x	x	x
-	SOP0509	Use and Maintenance of BAVnp-01-Laminar-S-1.8 Lorica	x	x	x
-	SOP0510	Use and Maintenance of BMB-II Laminar-S Savvy SL 1.8	x	x	
-	SOP0627	Use and Maintenance of ThermoCouples	x	x	
-	SOP0638	Use and maintenance of the Precision balance ML6002T/00, XSR603SN	x		
-	SOP0511	Operation and maintenance of the Thermo Fisher Scientific Vanquish Orbitrap QE LCMS system	x		
-	SOP0851	Operation and maintenance of the Thermo Fisher Scientific Dual Vanquish Orbitrap Exploris 120 LCMS system	x		
-	SOP0894	Use and Maintenance of S Sonic irrigator		x	
-	SOP0912	Use and maintenance of the Flow Test	x		

11.2.5 Global Nelson Policies

Published or drafted by April 10th 2024

POL0001 Global Quality Policy
POL0003 Document control Policy
POL0004 Training Policy
POL0005 Data Integrity Policy
POL0006 Change Control Policy
POL0007 Quality Event and CAPA Policy
POL0008 Audit Policy

11.2.6 Sotera Health IT Policies

Published by April 10th 2024

IT.SIRP.001	Incident Response Policy	Policy
IT.ISP.001	Information Security Policy	Policy
IT.VMP.001	Vulnerability Management	Policy
IT.INFP.001	IT Infrastructure Policy Statement	Policy
IT.LA.001	General Security Settings	Policy
IT.LA.002	Password Settings	Policy
IT.LA.002a	Password Settings Matrix	Policy
IT.LA.003	Privileged IT Access	Policy
IT.LA.004	User Access Management	Policy
IT.LA.005	Physical Access Security	Policy
IT.MC.001	Change Management	Policy
IT.OP.001	Backup and Recovery	Policy
IT.OP.002	Job Scheduler Access	Policy
IT.OP.003	Management of Failed Jobs	Policy
LA5A	New/Modified User Access Management Process	Procedure
LA5B	Terminated User Access Management Process	Procedure
LA5C	Periodic Access Review Process	Procedure
MC1-MC5	Manage Change Process	Procedure
OP1	Backup Process	Procedure
OP2	Job Scheduler Access Process	Procedure
OP3	IT Operations Process	Procedure

12 APPENDIX D: GMP JUSTIFICATION FOR THIS DOCUMENT AS SITE MASTER FILE

The principles of EudraLex Volume 4, EU Guidelines to Good Manufacturing Practice (Medicinal Products for Human and Veterinary Use) are applicable to all processes and systems where GMP is marked in Appendix C of this document (section 11).

12.1 AUTHORIZED PHARMACEUTICAL MANUFACTURING ACTIVITIES OF THE SITE

Nelson Labs has no capability for the manufacture of drug substances and/or drug products. Nelson Labs is a Contract Research Organization solely engaged to provide QC services to the Pharmaceutical industry, in compliance with EudraLex GMP (§1.1).

Nelson Labs is periodically inspected according to the national inspection program by the Federal Agency for Medicines and Health Products (FAMHP) related to the following Manufacturing Authorizations:

- n° 1844 H, in accordance with Article 40 of Directive '2001/83/EC', for human medicinal products;
- n° 1844 V, in accordance with Article 44 of Directive '2001/82/EC', for veterinary medicinal products;
- n° 1844 IMP, in accordance with Article 13 of Directive '2001/20/EC', for investigational medicinal products.

Nelson Labs holds the following GMP certificates:

- BE/GMP/2022/052 for human medicinal products;
- BE/GMP/2022/053 for veterinary medicinal products;
- BE/GMP/2022/054 for investigational medicinal products.

12.2 QUALITY MANAGEMENT SYSTEM OF NELSON LABS

The Quality Management System of Nelson Labs is described throughout this entire document. Roles and responsibilities of the quality unit are described in detail in section 9.

Additionally, the tasks and responsibilities of the Qualified Person (QP) are described below:

- Final responsibility for all quality decisions directly related to GMP release testing independently from the Top Management
- Final responsibility to issue Certificate of Analysis and, if requested by sponsor, GMP study reports or test result reports. The results of each test or series of tests shall be reported accurately, clearly, unambiguously and objectively, and in accordance with any specific instructions in the test methods and protocols
- Final evaluation of Deviations, Complaints and Out-of-Specifications (OOS)
- Use QA audit information to determine the extent to which the management system objectives are being met (e.g. complaint & CAPA resolution) and responsible for handling and implementation of CAPA's
- Approval for all quality management SOPs related to the GMP release testing

12.3 RELEASE PROCEDURE OF FINISHED PRODUCTS

Nelson Labs QP never holds final certifying/batch release responsibility but supports the sponsor's certifying QP with a confirmation statement indicating that Nelson Labs testing is performed according to GMP.
GMP release testing of drug products / active substances / intermediate products is managed by the Head of QC (technical), the QA department (compliance) and the QP (compliance and release) according to the written monographs, validated test methods and approved specifications from the Contract Giver. After data review and technical release of the data package from the laboratory by the Head of QC, a Certificate of Analysis or other result report (test result report or study report) is generated, which is reviewed by QA. Subsequently, QA informs the QP of all critical aspects with possible impact on the test results. The reviewed results/report are released by the Qualified Person.

12.4 MANAGEMENT OF SUPPLIERS AND CONTRACTORS

See section 6.6 of this document.

12.5 QUALITY RISK MANAGEMENT (QRM)

The approach for Quality Risk Management is based on the general risk management process as outlined in ICH Q9. See section 8.5 of this document.

12.6 PRODUCT QUALITY REVIEWS

Not applicable.

12.7 PERSONNEL

See sections 0 and 6.2 of this document.

12.8 PREMISES AND EQUIPMENT

12.8.1 Premises

Every room is labelled and the facilities description (floor plan) is available as AUX1802 via the document management system. Nelson Labs' quality system is harmonized to such an extent that every room can be considered for potential GMP activities.

See section 1.1 of this document.

12.8.1.1 HVAC system

All laboratories are equipped with individual computer assisted HVAC systems and separated air-handling of each room by means of extraction and pulsing which minimizes the risk of cross-contamination.
Overpressure of rooms and inlet of HEPA-filtered air is installed for critical areas, i.e. Microbiology department.

12.8.1.2 Water system

The reversed osmosis water (Water type II) produced by the Elix system can be used for general lab applications and as feed water for the Milli–Q Advantage A10 system. Purified water (Water type I) is used for analysis.

12.8.2 Equipment

See section 6.4 of this document.

12.8.2.1 GMP Critical computerized systems

Paper represents the authoritative form of site documentation. In addition to paper, electronic records as generated by computerized lab systems are securely managed. Computerized lab systems comply with the requirements set down in Annex 11 of the EU GMP Guideline.

12.9 DOCUMENTATION

See section 0 of this document.
All raw data used for GMP release activities is subject of form reconciliation.

12.10 PRODUCTION

12.10.1 Type of products, Process validation, Material management and warehousing

Not applicable.

12.10.2 Quality Control

As a Contract Laboratory, Nelson Labs performs Quality Control Testing for third parties (Pharmaceutical Industry).
These GMP testing activities include, but are not limited to:

- Method development
- Method validation
- Method transfer
- Pharmacopoeial testing
- Stability study

In view of the different types of analytical activities and studies and their respective quality systems (ISO 17025 & GLP), Nelson Labs has evaluated the 'mixed use' of the Nelson Labs premises, resources, systems and equipment (MAN0013).

The tasks and responsibilities of Head of QC are interchangeable with those of Technical Management as defined in §9.

Nelson Labs ensures the quality of its test results by review prior to issuing results. All reported results are double checked by reviewing raw data sheets, instrument print-outs, draft reports, and all other necessary documentation which guarantees the traceability of the reported results.

All test results that fall outside the established specifications, acceptance criteria or expected result as described in guidelines, test procedures or written agreements between Contract giver and Nelson Labs, are subjected to an Out-of-Specification investigation according to the written procedures.

12.11 DISTRIBUTION, COMPLAINTS, PRODUCT DEFECTS AND RECALLS

12.11.1 Distribution

Distribution is under the responsibility of the Contract Giver.

12.11.2 Complaints

See section 7.9 of this document.

12.11.3 Product defects

Not applicable.

12.11.4 Recalls

Not applicable.

12.12 SELF-INSPECTION

See section 8.8 of this document.

12.13 QUALIFIED PERSON APPROVAL OF SMF JUSTIFICATION

I undersign that the Quality Manual of Nelson Labs in combination with this appendix D related to:

- Management responsibilities
- Process and system audits (processes are clearly defined and systematically reviewed in order to demonstrate the required quality and comply with their specifications)
- Validation of critical steps of the processes and significant changes to those processes
- Qualified and trained personnel
- Adequate premises and space
- Suitable equipment and services
- Correct materials
- Approved procedures and instructions
- Suitable storage
- Documentation (records which enable the complete history of a batch to be traced)
- Test methods (validated and approved for all testing operations described in the marketing authorization)

is in compliance with the GMP principles set forth in EudraLex Volume 4, EU Guidelines to Good Manufacturing Practice (Medicinal Products for Human and Veterinary Use).

Approval by QP of this document

Signature:

Leo Aerden
Qualified Person
Industrial Pharmacist No. 1253

13 APPENDIX E: LIST OF GXP CRITICAL SOFTWARE AND APPLICATIONS

13.1 NON-EQUIPMENT RELATED COMPUTERIZED SYSTEMS

See AUX1794 current version for current detailed list of validated excel spreadsheets, self developed tools and scripts (not Excel-based), Commercially available software, Qualified servers and others. The list below is a relevant summary of qualified IT systems (ITS) of AUX1794.

Software application name	Nelson ITS Identifier	Scope	Quality level		
			ISO	GMP	GLP
Self-developed tool (Excel-based)					
>50 validated excel spreadsheets	ITS-xyz	Validated and controlled excel spreadsheets as per SOP0386.	As identified on AUX1794		
Self-developed tool (not Excel-based)					
Validated scripts (<10)	ITS-xyz	Scripts to document data migration (e.g. data copy or data delete or merge)	x	x	x
LOMS: Laboratory Organisational Management system	ITS-022	Access interface on SQL database managing the lab organization (project and sample identification) and aspects of the electronic QMS.	x	x	x
Report Templator	ITS-069	Application to automatically generate reports for E&L after ingestion of result sheets (excel)	x		
Excel Audit trail system	ITS-085	Application to generate audit trail on validated excel spreadsheets used to ingest to Report Templator	x		
Software (commercially available)					
STARLIMS	ITS-018	Operational Lab management system	x	x	x
Thermoguard	ITS-020	Environmental monitoring system (Temperature and Humidity)	x	x	x
OpenLAB ECM	ITS-032	Data Integrity tool to capture and store initial raw electronic data (datafile, audit trail, method, sequence)	x	x	

MasterControl	ITS-066	Document management and training system, aspects of electronic QMS	x	x	x
Docusign	ITS-073	Validated tool used to electronically sign 21CFR11	x	x	x
Masshunter add-in	ITS-091	Software for quantitative processing of screening analyses of GC/MS data	x		
Compound Discoverer add-in	ITS-092	Software for quantitative processing of screening analysis of LC/MS data	x		
Kantech Entrapass Global Edition	ITS-093	Badge Control System	x	x	x
Commvault	ITS-104	Data back-up and restore	x	x	x
Acronis Cyber Protect	ITS-111	Imaging Software (restore and disaster recovery purposes)	x	x	x
IT-Server Landscape					
>15 qualified servers	ITS-099	Qualified on premise server infrastructure	x	x	x

13.2 EQUIPMENT RELATED COMPUTERIZED SYSTEMS (ACQUISITION/PROCESSING SOFTWARE)

Laboratory systems are typically operated with acquisition software and processing software (where applicable). The table below identifies the different softwares used at Nelson Labs in relation to the test method which is descriptive for the analytical technique. Sofware updates and traceability of actual software versions is documented in the configuration documents or use and maintenance SOPs as respective life cycle documents. IT maintains a historical software distribution list as per SOP0401.

Test method	Data Acquisition (supplier)	Data Processing (supplier)
HS-GC/MS, GC/MS, GC/QQQ, GC/QTOF, LC/QQQ	Masshunter (Agilent) Maestro (Gerstel, only for systems with sampler robot)	Masshunter (Agilent)
GC/FID/ECD, LC/UV	OpenLab Chemstation (Agilent); Labsolutions GPC (Shimadzu)	OpenLab Chemstation or Masshunter (Agilent); Labsolutions GPC (Shimadzu)
LC-Orbitrap	Xcalibur (Thermo Fisher Scientific)	Sieve, ToxID, Compound Discoverer (Thermo Fisher Scientific)
FTIR	Microlab (Agilent)	N/A
ICP-OES	ICP Expert (Agilent)	ICP Expert (Agilent)
UV-VIS	UV WinLab ES (Perkin Elmer)	N/A
GF-AAS	Syngistix (Perkin Elmer)	Syngistix (Perkin Elmer)
ICP-MS	NexION and UV WinLab ES (Perkin Elmer)	NexION and UV WinLab ES (Perkin Elmer)
TOC	DataPro 2 (Sievers)	DataPro 2 (Sievers)
DSC	Pyris Manager (Perkin Elmer)	N/A
Particle determination	Pharmspec (Beckman Coulter)	N/A
Ion Chromatography	Chromeleon (Thermo Fisher Scientific)	Chromeleon (Thermo Fisher Scientific)
Plate Reader (Cytotox, Bacterial Endotoxin, Elisa)	WinKQCL (Lonza); Endoscan-V(Charles River) CLARIO software (BMG Life Sciences)	N/A
Valprobe (temperature measurements)	Valprobe RT (Kaye)	Valprobe RT (Kaye)

14 APPENDIX F: LIST OF GXP CRITICAL SUPPLIERS

Suppliers generated in the topics below are based on the approved qualified supplier list on May 15th 2024.

14.1 RAW MATERIAL SUPPLIERS

N/A as Nelson Labs only performs QC testing as manufacturing activity.

14.2 PACKAGING MATERIAL SUPPLIERS

N/A as Nelson Labs only performs QC testing as manufacturing activity.

14.3 EQUIPMENT SUPPLIERS

Suppliers of manufacturing equipment, including machinery used in testing, and packaging processes. This includes calibration and maintenance services. Included in the maintenance activities are preventive maintenances and Operational Qualification by suppliers (if applicable).

14.3.1 Calibration service suppliers

Cal Particle Counter
CMI
Cal Temp/ Hum/ CO2
AMPHENOL Advanced Sensors Germany GmbH
TRESCAL NV
Calibration
TESTO
Cal Balances and Weights
METTLER TOLEDO
TRESCAL NV
Cal Manometer
TRESCAL NV
Cal Isolator
TRESCAL NV
Cal Stopwatch
TRESCAL NV
Cal Caliper/schuifpasser
TRESCAL NV
Cal Air Sampler
VWR INTERNATIONAL
Cal Pipettes and Syringes
VWR INTERNATIONAL

14.3.2 Maintenance service suppliers

Equipment (analytical) supplier, maintenance	Equipment (non-analytical) supplier, maintenance
AGILENT TECHNOLOGIES	AGIDENS Life Sciences NV
ANALIS	AGILENT TECHNOLOGIES
BELIMED B.V.	AMPHENOL Advanced Sensors Germany GmbH
CHARLES RIVER ENDOTOXIN MICROBIAL SOLUTIONS	BELIMED LIFE SCIENCE AG
CHARLES RIVER MICROBIAL SOLUTIONS INTL. LTD	BEUN-DE RONDE
CHEMOMETEC	BIOTAGE SWEDEN AB
CMI	CHEMOMETEC
GETINGE	CISA PRODUCTION S.r.l. Unipersonale
ISOGEN LIFE SCIENCE BV	CLIMATRONIX BVBA
METROHM BELGIUM	DUOMED Belgium NV/SA
METTLER TOLEDO	EGILABO
M-FILTER BV	FISHER SCIENTIFIC
PERKINELMER (Belgium) BV	JOHNSON CONTROLS BV/SRL
PMT BENELUX	KÖTTERMANN
RIC	LONZA SALES
SHIMADZU	MEDTRADEX BV
TECNILAB-BMI BV	MERCK LIFE SCIENCE BV
THERMO FISHER SCIENTIFIC	PRESA SA/NV
THERMOGUARD	RfQ-Medizintechnik GmbH & Co. KG
	SCHNEIDER ELECTRIC
	TESTO
	THERMO FISHER SCIENTIFIC
	TOP CLASS PRODUCTS & SERVICES TCPS nv
	VWR INTERNATIONAL

14.4 Laboratory Suppliers

Providers of laboratory consumables, and reagents necessary for quality control testing and analysis.

Reagents, standards, column, media, strains, ...	Spec. Reg. Sub. standards
AA BLOCKS, INC.	ANGENE INTERNATIONAL LIMITED
ABCAM (Netherlands) BV	Apotheek Bierbeek
Absolute Standards, Inc	BIOTRADING BELGIUM BV
acCELLerate GmbH	CHEMOS GmbH & Co. KG
ACHROM	CHIRON AS
AGILENT TECHNOLOGIES	COUNCIL OF EUROPE
AGORA CULINAIR VLEMINCKS B.V	FISHER SCIENTIFIC
	LGC STANDARDS

Alfa Chemistry
ANGENE INTERNATIONAL LIMITED
Apotheek Bierbeek
ASAS Labor GmbH
ASTATECH
BENELUX SCIENTIFIC
BIESTERFELD FRANCE S.à.r.l.
BIOMÉRIEUX BENELUX
Bioquell UK Ltd
BIO-RAD Laboratories N.V.
BIOSYNTH s.r.o.
BIOTRADING BELGIUM BV
BLDPHARM
BMD (Biomedical Diagnostics)
BOC SCIENCES
BUCHEM
CAMPRO SCIENTIFIC
CHARLES RIVER ENDOTOXIN MICROBIAL SOLUTIONS
CHARLES RIVER MICROBIAL SOLUTIONS INTL. LTD
CHEM-LAB nv
CHEMOS GmbH & Co. KG
CHIROBLOCK GMBH
CHIRON AS
Clearsynth
COUNCIL OF EUROPE
Culture Collection of Switzerland AG
DA VINCI Laboratory solutions B.V.
Dr. LOHMANN DIACLEAN GmbH
DR. WEIGERT BELGIE NV
FISHER SCIENTIFIC
FLUOROCHEM Ireland
GETINGE
INTERSCIENCE
J.H. RITMEESTER BV
LGC STANDARDS
LONZA SALES
MAT Biotech BV
MATRIX SCIENTIFIC
MatTek In Vitro Life Science Laboratories
MERCK LIFE SCIENCE BV
MERKALA
MILTENYI BIOTEC B.V.
NELSON LABS
MERCK LIFE SCIENCE BV
SANTA CRUZ BIOTECHNOLOGY
THERMO FISHER SCIENTIFIC
TORONTO RESEARCH CHEMICAL
VWR INTERNATIONAL

Spec. Reg. Sub. standards R&D

ANGENE INTERNATIONAL LIMITED
MOLEKULA GmbH

Standards (R&D)

A2B Chem LLC
AA BLOCKS, INC.
ANGENE INTERNATIONAL LIMITED
ASTATECH
BLDPHARM
BOC SCIENCES
CAMPRO SCIENTIFIC
Chem Service Inc.
CHIROBLOCK GMBH
INstruchemie BV
INVIVOGEN
KEY ORGANICS Ltd
MatTek In Vitro Life Science Laboratories
MOLEKULA GmbH
PARAGOS E.K
PROMEGA BENELUX BV
Rocky Mountain Biologicals,Inc.
SynHet UAB
TECO medical Benelux

Consumables

ACHROM
AGILENT TECHNOLOGIES
Apotheek Bierbeek
BELIMED LIFE SCIENCE AG
BIOMÉRIEUX BENELUX
BIOTAGE SWEDEN AB
BIOTRADING BELGIUM BV
CHARLES RIVER MICROBIAL SOLUTIONS INTL. LTD
CHEM-LAB nv
CHEMOMETEC
CHIRURGICAL MAINTENANCE
Confalonieri Luciano
DULIS BELGIUM
DUOMED Belgium NV/SA
EURO-SCIENTIFIC BVBA

NODIA BV	FISHER SCIENTIFIC
PERKINELMER (Belgium) BV	GETINGE
PHENOMENEX	INTERSCIENCE
PROMEGA BENELUX BV	LEAFSIS, LDA
SANTA CRUZ BIOTECHNOLOGY	LONZA SALES
STAXSBELGIUM	MERCK LIFE SCIENCE BV
STERIS NETHERLANDS BV	MERKALA
STERIS NV/SA	METROHM BELGIUM
SYNQUEST LABORATORIES INC.	METTLER TOLEDO
TCI EUROPE	MILTENYI BIOTEC B.V.
TCS BIOSCIENCES	MULTIMEDI BV
TECNILAB-BMI BV	NELSON LABORATORIES LLC
THERMO FISHER SCIENTIFIC	NELSON LABS
TLC PHARMACEUTICAL STANDARDS Ltd.	PERKINELMER (Belgium) BV
TORONTO RESEARCH CHEMICAL	PMA-HELEON NV
TRINOVA BIOCHEM	PMT BENELUX
USP	RS COMPONENTS
VWR INTERNATIONAL	RUHOF
WATERS	SARSTEDT
	SHIMADZU
	STAXSBELGIUM
	STERIS NETHERLANDS BV
	TECNILAB-BMI BV
	THERMO FISHER SCIENTIFIC
	VWR INTERNATIONAL

14.5 Transportation and Logistics Providers

Nelson Labs is not responsible for controlled logistics. When controlled transport conditions are required our customers are responsible to organize the shipment or pick-up. In the case Nelson Labs is allowed to return spare samples to the customers, typically FEDEX or DHL will be used to ship.

14.6 Cleaning and Sanitization Suppliers

Laboratory benches are to be cleaned by Nelson Labs personal only. The floor and other rooms within Nelson Labs are cleaned by a local cleaning company (JM cleaning service).

14.7 Utilities Suppliers

EP Purified Water is supplied by qualified equipment inhouse. Endotoxin free water for BET testing is purchased as a consumable (Lonza or Charles River). Compressed air is generated through onsite compressors. Gasses, if not considered a consumable, are provided through an onsite tank maintained by Air Liquide Belgium.

14.8 MISCELLANEOUS SERVICES

14.8.1 Waste Management and Disposal Services

Companies offering services for the safe disposal of waste generated during manufacturing processes, including hazardous and non-hazardous waste. Qualified suppliers for waste management are SGS Ewacs NV and RPB (Renewi).

14.8.2 Pest Control

Nelson Labs partnered with Rentokil for monitoring, treatment and control of relevant pest organisms on premise.

14.8.3 Off-site Archiving

Nelson Labs partnered with MERAK for offsite archiving of paper and electronic records.