QUALITY MANUAL

VERSION 1.0

Guerbet

GUERBET MISSION

Guerbet's men and women are committed to offering health professionals contrast agents, medical devices and innovative solutions indispensable to diagnostic and interventional imaging to improve patients' prognosis and quality of life.

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INTRODUCTION

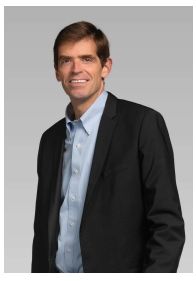
We are pleased to share with you the first Guerbet Group Quality Manual!

Guerbet is a leader in medical imaging worldwide, offering a wide range of pharmaceutical products, medical devices, software and services for diagnostic and interventional imaging, to improve the diagnosis and treatment of patients.

Our Quality Management System is based upon our strong commitment to offering health professionals contrast agents, medical devices and innovative solutions indispensable to diagnostic and interventional imaging to improve patients' prognosis and quality of life. It is our Quality System applied to ensure the quality of all the Guerbet products, services and solutions throughout their life-cycle from discovery to development, manufacturing, distribution and discontinuation for established and innovative products & services. It is operated in a flexible and adaptable model to include quality standards specific to each profile class of the Guerbet portfolio. It is constantly evolving to anticipate regulatory developments and to support the needs of our three franchises: Diagnostic Imaging, Interventional Imaging and Digital Solutions, as well as our Global Functions.

In line with our Guerbet objective of focus and simplification, the Quality Manual provides to all Guerbet personnel as well as to external partners and regulators a concise and useful overview of our Quality System structure and related key processes. Our Guerbet Quality Vision, Quality Policy and Quality Manual constitute the hallmarks of our Quality Documentation pyramid and serve as vectors to ensure a full deployment of our Quality management principles across the organization. They are an important part of our desired Quality Culture focused on patient safety centricity and contribute to our innovation and continuous improvement strategic goals.

We are convinced that, thanks to the commitment to this Quality Manual of each individual at all levels of Guerbet, we will be improving diagnosis, prognosis and quality of life for patients.



David HALE
Chief Executive Officer

Pierre ANDRE
Vice President, Quality Technical Operations
Chief Pharmaceutical Officer

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1.1 EXECUTIVE SUMMARY

This Quality Manual provides specifics on the policies and procedures Guerbet uses to meet cGXPs Quality Management System requirements.
The intent of these policies and procedures is to demonstrate Guerbet's ability to consistently provide products & services that meets our patients, customers and applicable regulatory requirements and to enhance our patients & customers' satisfaction through the effective application of the quality system, including processes for continual improvement of the system and the assurance of conformity to our patients & customers and applicable regulatory requirements.

1.2 SCOPE

The Quality Manual applies to all Guerbet sites including all activities related to research, development, manufacturing and distribution of all Guerbet products & services.

1.3 ABOUT GUERBET

Guerbet is a Global Pharmaceutical and Medical Device group founded in France and supporting healthcare professionals specializing in diagnostic and interventional medical imaging. We provide them with contrast media, injection systems, medical devices and related solutions adapted to their needs.
It all began with Marcel Guerbet's discovery of the first iodinated organic contrast medium in 1901. The company was later founded in 1926 by André Guerbet. Guerbet's innovative workforce has since left its mark on medical imaging technologies and contrast media, taking the company to the next level.
Every second, somewhere in the world a patient undergoes an imaging procedure with a Guerbet product. More than 60,000 health professionals rely on our contrast agents to diagnose disease and assess treatment efficacy.

Guerbet is listed in Euronext Segment B, and a majority of its shares are owned by the Guerbet family.
> For more info about Guerbet, visit www.guerbet.com

1.4 GUERBET PRODUCTS AND SERVICES

Guerbet offers a comprehensive range of imaging products, solutions, and services for Diagnostic Imaging (MRI, CT, Cath Lab, Digital Solutions, Interventional Imaging, Interventional Radiology) and Women's Health to enhance clinical decision-making at each point of the patient journey from diagnosis, to treatment and follow-up, in order to efficiently improve patient outcomes.

Our products and services are available in more than 80 countries through our affiliates and network of distributors.

DIAGNOSTIC IMAGING (DI)

Magnetic Resonance Imaging

- Dotarem®

- OptiStar Elite®

CT & Cath Lab

- Optiray®

- Xenetix®

- Illumena Neo®

- OptiVantage®

- Flowsens®

- OptiOne®

Digital & AI solutions

- Contrast&Care
- Dose&Care
- icobrain
- Patient Synopsis

INTERVENTIONAL IMAGING (II)

Interventional Imaging

- Lipiodol® Ultra-Fluid

- Patent Blue V

- Microcatheters SeQure® and Drakin™

- Vectorio®

1.5 OUR QUALITY VISION

1.6 OUR QUALITY POLICY

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QUALITY RESPONSIBILITIES AND ORGANISATION

2.1 RESPONSABILITIES

Quality Technical Operations Vice-President (QTO VP) & Chief Pharmaceutical Officer

The Quality Technical Operations VP & Chief Pharmaceutical Officer is responsible and has the authority:

- For the implementation of the quality system. The QTO VP delegates to others various aspects of the system but retains the responsibility and accountability,
- To establish a system, which will ensure the flow and further communication of the required information on current regulatory requirements.

Quality Assurance Manager of Departments

The Quality Assurance Manager of departments are accountable for:

- For ensuring compliance of its Department activities to regulatory and internal requirements;
- For monitoring the accurate application of the quality management system of its Department;
- For establishing an audit plan and conducting such audits, based on a risk analysis;
- For representing its department towards competent / regulatory authorities during inspections.

Quality Organisation (Sites, group)

The Quality Organisation is responsible for:

- Recommending strategies to management for meeting quality objectives and monitoring the effectiveness of the quality system,
- Establishing and monitoring suitable audits on products, processes, and systems to ensure that all established quality criteria are met prior to release to the market.

All Departments

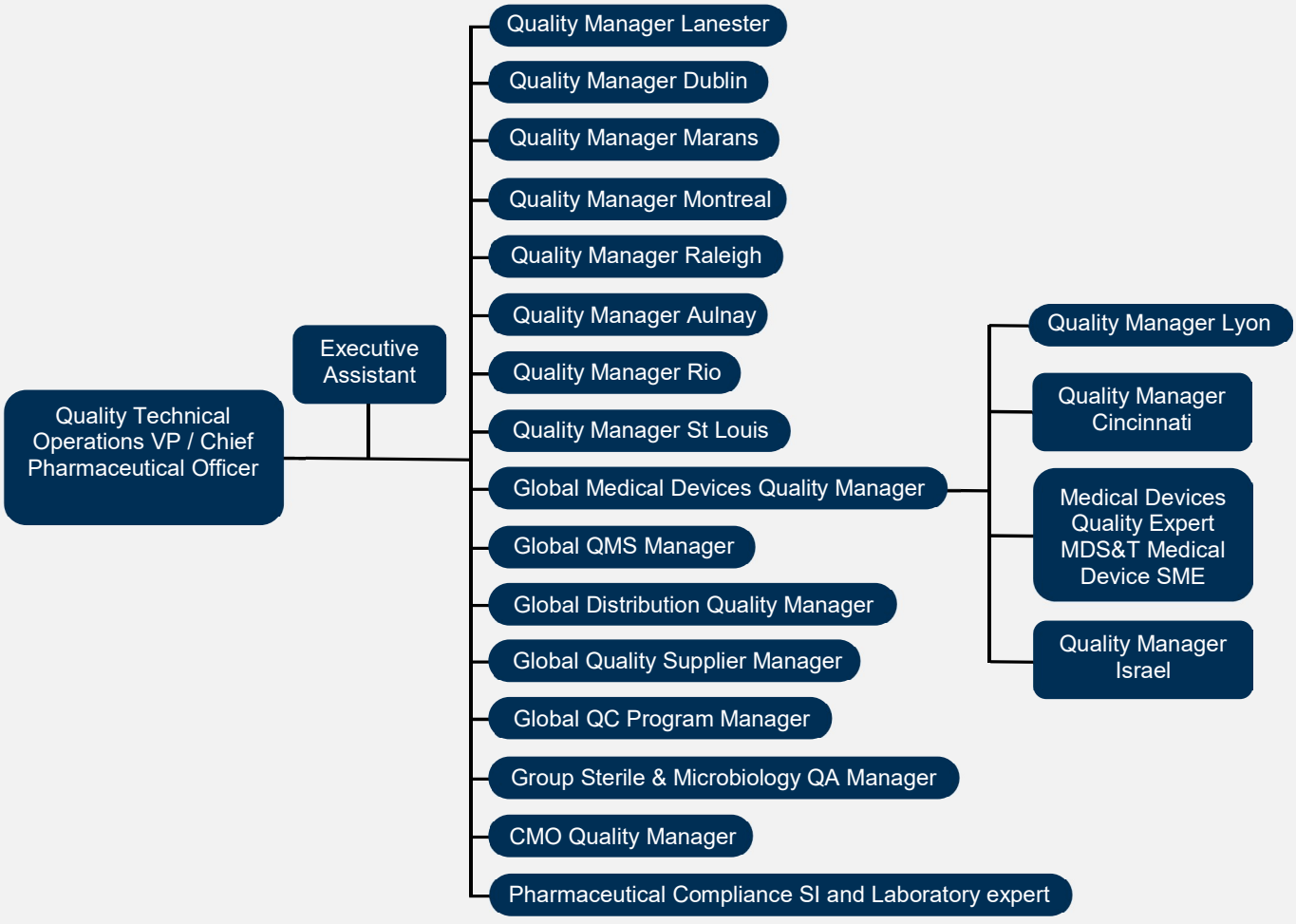
The responsibility for attainment of the established quality levels is shared by all departments. The quality system includes an environment that encourages continuous improvement by everyone – All of management is committed to this and all employees are involved.

Each individual employee is responsible for performing assigned functions or task assignments in accordance with established procedures and guidelines, so that the defined standards of quality are achieved.

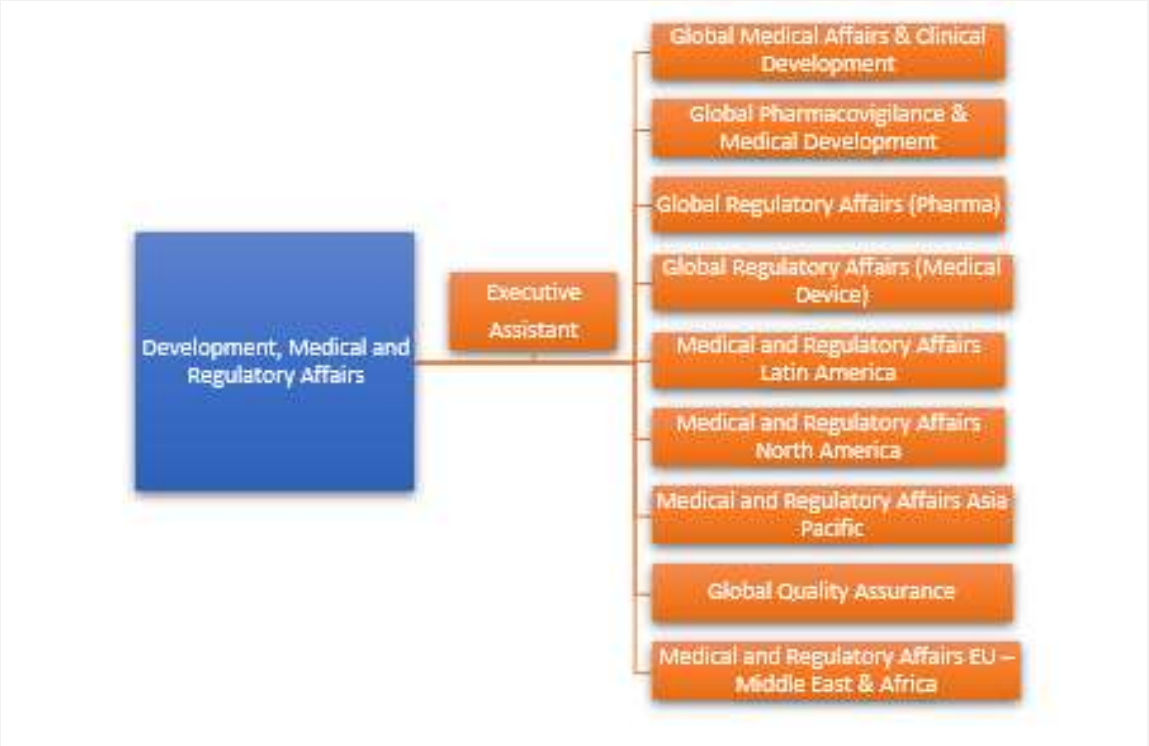
Department Managers are responsible and have authority for creation and implementation of all required procedures.

2.2 ORGANISATIONAL CHARTS

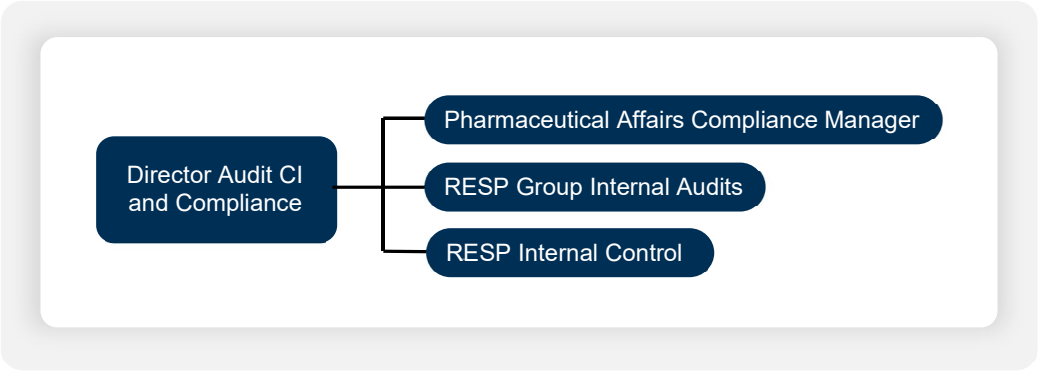
Within the Quality Technical Operations (QTO) there over 300 people. The Quality Technical Operations VP & Chief Pharmaceutical Officer reports into the Chief Technical Operations Officer:



Within the Development, Medical and Regulatory Affairs group there are over 100 people. The Medical Affairs and Regulatory Affairs VP has the following direct reports:



Within the Audit and Compliance group there are about 8 people. The CI audit and Compliance Director reports into the Chief Executive Officer and has the following direct reports:



2.3 SITE QUALITY OPERATIONS

At each manufacturing site there is one Site Quality Manager (SQM) with the mission to lead and coordinate quality and compliance in their sites to ensure that all products and services are designed, developed, manufactured and distributed in compliance with the applicable regulatory and Company requirements.

This includes the following responsibilities, as a minimum:

- Accountable for cGxP compliance and quality performance for products and services at their sites,
- Ensure and harmonize consistent implementation of the Guerbet QMS at their sites,
- Ensure continuous improvement of the quality concepts, promote innovation and systems performance,
- Integrate risk management principles into Quality Systems,
- Ensure inspection readiness and strictly follow-up to GxP regulatory inspections.

The SQM in the Active Pharmaceutical Ingredients (API) and Fill / Finish sites report operationally to the Chief Pharmaceutical Officer, with a dotted line to the Plant Directors.

The Heads of the Operational Quality Units in the Medical Device sites report operationally to the Global Medical Devices Quality Manager, with a dotted line to the Plant Directors.

2.4 QUALITY TECHNICAL OPERATIONS GROUP

The Quality Technical Operations (QTO) group report into the Quality Technical Operations VP & Chief Pharmaceutical Officer.

This group consists of the following:

- Quality Manager for CMOs,
- Global Medical Devices Quality Manager
- Global Distribution Quality Manager,
- Global Quality Management Systems Manager,
- US Quality Technical Operations Manager,
- Global Supplier Quality Manager,
- Pharmaceutical Compliance SI and Laboratory expert,
- Group Microbiology & GMP Compliance,
- Computer System Validation Manager,
- Executive Assistant to Vice President, Global Quality Technical Operations & Chief Pharmaceutical Officer.

2.5 SENIOR MANAGEMENT

Senior Management is the team of individuals at the highest level of authority in their respective organisation who have the day-to-day task to manage that organisation. They have the ultimate responsibility for the overall effectiveness of the QMS. Senior Management ensures that roles, responsibilities and authorities related to the QMS are defined, communicated and implemented throughout the company.

In practice, Senior Management:

- Participates in the design, implementation, monitoring and maintenance of the QMS throughout their organization,
- Demonstrates strong and visible commitment to the QMS,
- Ensures a timely and effective communication and escalation process exists to raise quality issues to the appropriate levels of management,
- Conducts management reviews of process performance, product quality and the QMS effectiveness,
- Supervise relevant staff in their respective field of operation and adherence to Quality principles,
- Advocates for continuous improvement, determining and ensuring adequate resources to implement, maintain and continuously improve the QMS.

2.6 RESPONSIBILITIES FOR THIRD PARTIES (SERVICES PROVIDERS, SUPPLIERS)

The responsibility for service providers and suppliers is with the Global Supplier Quality Manager and with each site Quality Manager. This includes;

- The overall quality and compliance of supplier quality and oversight responsibility for purchasing controls as to relates to quality,
- The assurance of consistency for supplier audits, supplier statuses, supplier selection, monitoring practices, metrics and field action prevention,
- Compliance to GMP, deployment of best practices including developing operating philosophies, establishment and maintenance of a Quality culture and establishing quality systems in alignment with Guerbet Global standards and international GMP regulations.

2.7 RESPONSIBILITIES FOR CONTRACT MANUFACTURERS

The contract manufacturing organization (CMO) team is composed of individuals that manage the day-to-day tasks to ensure production at CMOs sites are effectively performed according to cGXP. They have the responsibility to ensure the Guerbet Group policy are efficiently applied.

In order to ensure an adequate surveillance of the operations performed at CMO sites and quality system is in place, regular governance meetings are organized to review the requirements defined in relevant quality agreements.

Finally, an annual evaluation of each CMO performance is established.

2.8 RESPONSIBILITIES FOR SUPPLY CHAIN

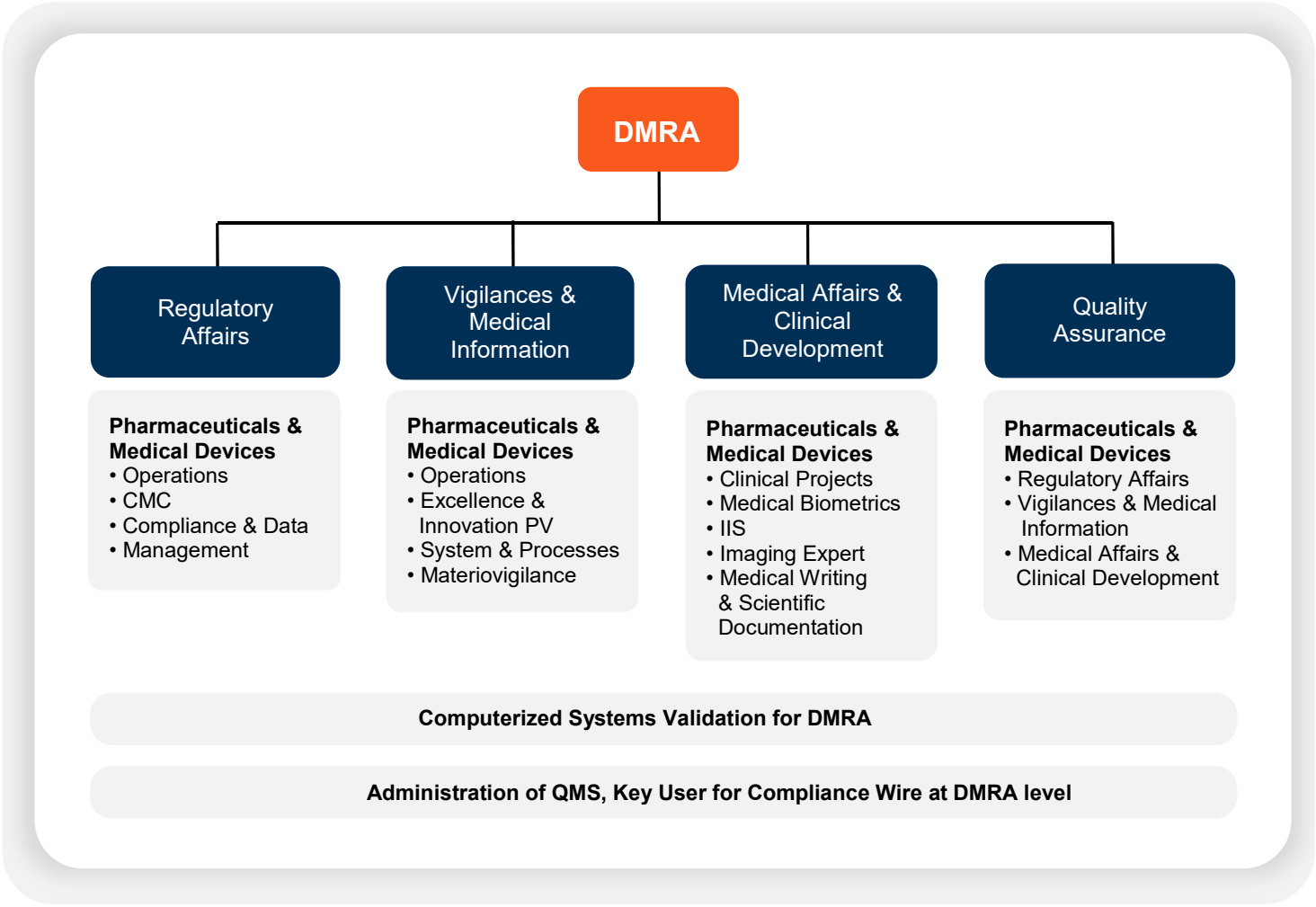
The Quality Supply Chain ensures the control of the distribution chain and consequently maintains the quality and the integrity of medicinal products and medical devices.

In order to guarantee the quality and the integrity of the products, the quality supply chain is responsible for:

- Developing and maintaining a quality system setting out responsibilities, processes and risk management principles in relation to the distribution activities,
- Conducting Quality risk management and ensuring that the evaluation of the risk to quality is based on scientific knowledge, experience with the process and ultimately links to the protection of the patient,
- Defining the shipping lanes and qualify them prospectively or retrospectively,
- Qualifying the transporters and maintain their qualification (Audit and Quality agreement),
- Qualifying the distributors partners (Third Party Logistic and distributors) and maintain their qualification (Audit, Quality Agreement and Quality Review Meeting),
- Tracking and assessing all deviations noted during the distribution activities,
- The training of auditors and other teams involved in the distribution quality activities,
- Managing complaints, returns, suspected falsified medicinal products and recalls and define appropriate action plan to avoid recurrences.

2.9 DEVELOPMENT, MEDICAL AND REGULATORY AFFAIRS (DMRA) ORGANISATION

The main activities covered by the departments of the DMRA Division are described in the chart below:



The Quality Management System is structured so as to reflect the organization described above.

2.10 AFFILIATE QUALITY MANAGEMENT

At each Commercial Affiliate office within Guerbet, a Quality Manager is appointed to define, implement, manage and control the Affiliate Quality Systems, in order to ensure the quality of products and services at market level and to guarantee compliance with applicable regulatory requirements and the Guerbet Quality Management System. The Affiliate Quality Manager reports to the Affiliate General Manager as well as, in some regions, to the Regional Distribution Quality Manager. In countries where local regulations require a Responsible / Qualified Person (QP) for commercial activities, the Affiliate Quality Manager is the Qualified Person or delegates this responsibility to a designated person.

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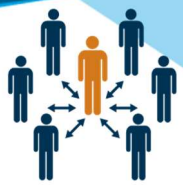


MANAGEMENT RESPONSIBILITIES

Senior Management has the responsibility to demonstrate a strong commitment to the quality management system and share the responsibility and authority for overall administration of quality management system activities. They are responsible for ensuring the implementation and maintenance of the QMS within their respective areas.
Guerbet has provided evidence of its commitment to the development and implementation of the quality management system and continually improving its effectiveness by:

- Communicating to the organization the importance of meeting customer as well as statutory and regulatory requirements,
- Establishing the quality policy,
- Ensuring that quality objectives are established,
- Conducting audits and management reviews; and
  Ensuring the availability of resources.

3.1 MANAGEMENT REVIEW

Technical Operations

Guerbet reviews the quality management system at planned intervals to ensure its continuing suitability, adequacy and effectiveness. This review includes assessing opportunities for improvement and the need for changes to the quality management system, including the quality policy and quality objectives. Records of management reviews are maintained.
Management Review is organised and performed as follows:

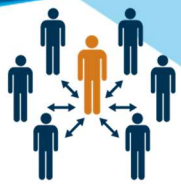
- Quarterly Business Quality Management Reviews attended by the Quality Technical Operations VP / Chief Pharmaceutical Officer and the SVP, Technical Operations at a minimum,
- Site level Quality Management Reviews (at least three times per year),
- Monthly Cluster calls to review the months activities by groups (API, Fill & Finish and Medical Device).

Business Quality Management regularly reviews the quality system, as implemented in the site, to assure its effectiveness in meeting current requirements and company needs. These reviews are physically conducted at the sites with the relevant site leadership team.

Development, Medical & Regulatory Affairs (DMRA)

The management review is organized yearly, based on QMS update plan – established at the beginning of a given year for the subsequent two years between QA, Compliance and Operations. In addition, a monthly review of deviations and action plans is organized between QA and compliance. Finally, monthly indicators are established following the conduct of audits and planning of corrective / preventive actions.

References: EMA/CHMP/ICH/135/1995 Guideline for Good Clinical Practice (GCP) E6 (R2)
EMA/541760/2011 Guideline on Good Pharmacovigilance Practices (GVP)



3.2 PLANNING

The Quality Policy is supported by Quality Objectives that have been established by the sites and the VP, Quality Technical Operations / Chief Pharmaceutical Officer, the SVP, Technical Operations and the CEO. Quality is fully integrated into Guerbet's strategic and operational planning and business processes.

3.3 MEASUREMENT

Quality performance and reporting are completed for key performance indicators (KPIs), Quality issues (both product and system) to the appropriate levels within the organisation. These also include areas for continuous improvement.

3.4 COMMUNICATION

Effective communication is used to promote the Quality Policy and objectives to ensure there is awareness, engagement and involvement of all personnel at every level. In addition, Quality Alerts are shared at and between sites to ensure learnings and escalation occurs within the organisation.

Quality KPIs and key communications are shared and reviewed during the Monthly Tech Ops T/C by clusters, Monthly QTO T/C by clusters, Quarterly Reviews and Annual Tech Ops & QTO meetings.

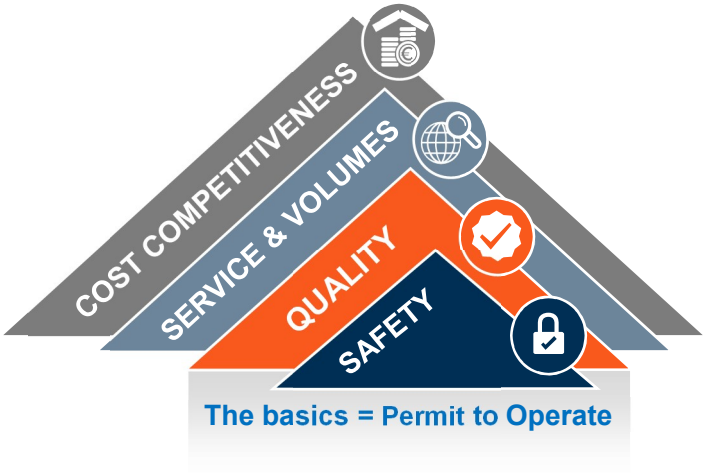
Note:
Reference Quality Management Policy (QMR), (Q019016, GBT-DMS-Quality-Quality Systems-10000008).

Reference Escalation Policy, (Q019706, GBT-DMS-Quality-Quality Systems-10000062).

4

OUR QUALITY CULTURE

- Creates an environment where **Quality is owned by all**, so that every employee can adopt the right behavior and make the right decisions,
- Includes **Patient at the center of our vision**, of our thoughts and our acts,
- Encourages continuous improvement and emphasizes **Simplicity (Keep It Simple & Smart - KISS), Pragmatism & Entrepreneurial attitude,**
- Develop the **right sense of urgency**, pay attention to the right things,
- Execute and live **Gemba**, observe, feed-back and partner with production teams – QuEnSH,
- Take **visible actions to simplify** processes and systems,
- Includes **Quality Risk Management (QRM)** in all our decisions,
- Reinforces our **Priorities**:



5

KNOWLEDGE MANAGEMENT AND QUALITY RISK MANAGEMENT

Use of Knowledge Management and Quality Risk Management will facilitate achievement of the following objectives by providing the means for science and risk-based decisions related to product quality:

- Achieve product realization,
- Establish and maintain a state of control,
- Facilitate continual improvement.

The Manufacturing Development, Science and Technology (MDS&T) group plays an important role in Knowledge Management by providing technical and scientific support with the sites, global functions and third parties to introduce and maintain commercially viable and robust products and services. It helps to ensure effective product/service development, scale up, technology transfer, process validation, continual improvement and post-approval change management that meet all the applicable regulatory and Guerbet requirements. MDS&T is involved as well in new technology surveillance process.

5.1 KNOWLEDGE MANAGEMENT

Product and process knowledge should be managed throughout the product lifecycle from development through the commercial life of the product up to and including product discontinuation.
Knowledge management is a systematic approach to acquiring, analysing, storing and disseminating information related to products, manufacturing processes and components.
Sources of knowledge include, but are not limited to:

- Prior knowledge,
- Pharmaceutical research and development studies – MDS&T…
- Technology transfer activities,
- Process validation studies,
- Manufacturing experience,
- Innovation and Continual improvement,
- Management of Change activities,
- Pharmacovigilance / Material vigilance.

5.2 QUALITY RISK MANAGEMENT

Quality Risk Management (QRM) is integral to an effective quality management system & supports a scientific and practical approach to decision-making. It provides documented, transparent and reproducible methods to accomplish steps of the quality risk management process based on current knowledge about assessing the probability, severity and sometimes detectability of the risk.

It can provide a proactive approach to identifying, scientifically evaluating and controlling potential risks to quality. It facilitates continual improvement of process performance and product quality throughout the product lifecycle.

QRM is integrated into the quality management system including areas such as auditing / inspection program, change management, continuous improvement, quality defects, CAPA and deviation management.

Note: Reference Quality Risk Management Policy (QRM), (Q019219, GBT-DMS-Quality-Quality Systems-10000026)

6

GROUP QUALITY AUDITS AND INSPECTIONS

Guerbet sites and functions are periodically audited to verify compliance with Guerbet's QMS. These audits are managed by the Quality Technical Operations group and the audit teams include personnel from other sites and functions. These audits facilitate readiness of the sites and functions for regulatory authority inspections, ensuring that Guerbet is meeting all regulatory obligations and commitments. The audit frequency, duration and number of auditors is determined using analysis based on risk.

To ensure on-going inspection readiness the following tools and support are provided:

- Mock Audits can be performed by Quality Technical Operations group at request of the site,
- Unannounced audits are also used to assess the state of compliance and associated risks,
- Inspection Preparation can be provided from the Quality Technical Operations group and site Quality departments. This support is provided both prior to and during regulatory inspections,
- Quality Management Review and Monthly Performance Review with Senior Management.

When deviations from internal or external requirements are identified during audits or regulatory inspections, corrective and preventive action plans are put in place and monitored until resolution.

Also, prior to the decision to enter a partnership or purchase of a new product, the Quality Technical Operations group is involved in the evaluation and selection of the company (depending on the criticality / risk of the product being supplied) through a due diligence process, to assess the state of compliance and associated risks to Guerbet.

Note: Reference Quality Audits (Q018966, GBT-DMS-Quality-Quality Systems-10000001)

7

GROUP QUALITY DOCUMENTATION SYSTEM AND DATA CONTROL

Guerbet considers data generated as being a company asset and therefore ensures that data integrity is fundamental within the quality system to guarantee the safety, efficacy and quality of Guerbet products.

Guerbet protects the maintenance and assurance of the accuracy and consistency of data over its life-cycle and ensures that data integrity is critical to the design, implementation and use of a system that stores, processes or retrieves data.

Data should be reliable and accurate and apply equally to manual and electronic data.

Data governance is integral to the quality system allowing for a flexible and risk-based approach to prevent and detect data integrity issues.

7.1 DOCUMENTATION OVERVIEW

Quality system is documented at 4 levels to ensure planning and integration of quality into Guerbet products.

Basic Structure of the Quality Management System Documentation:

The process to establish, review, approve and distribute global quality policies and procedures is detailed in the policy for issuing global quality polices referenced below. Global Quality documents are developed for each type of GxP and public health-related regulation.

Note: Reference Good Data and Records Management (Q019032, GBT-DMS-Quality-Quality Systems-10000014)

7.2 RECORDS MANAGEMENT

Quality records are documents that indicate compliance with the Quality System procedures and provide evidence of a controlled system. Records define and establish the evidence of conformity to requirements and effective operation of the Quality Management System.

Quality records will also include computerised systems data that generate GxP data. The use of validated, effective, GxP controlled computerized systems provide enhancements in the quality assurance of all operations (manufacturing, quality control, release and distribution) related with regulated materials/products and associated data / information management. The extent and type of validation necessary will be based on the assessment of the criticality of operations handled through the specific computerised system.

The requirements for identification, storage, protection, retrieval, retention time and disposition of records are defined.

Note:
Reference Policy for the Control and Issue of Quality Technical Operations Policies, Guidelines and Procedures (Q018924, GBT-DMS-Quality-Quality Systems-10000000).

Reference Policy for Good Data and Records Management (Q019032, GBT-DMS-Quality-Quality Systems-10000014).

Reference Data Integrity Management and Remediation Policy (Q019034, GBT-DMS-Quality-Quality Systems-10000013).

8

PRODUCT REALISATION

8.1 RESEARCH AND INNOVATION

In accordance to Guerbet defined strategy, Research and Innovation objectives are the exploration of new concepts leading to technological innovations to improve overall patient care through advances in medical imaging with new products or the development of new applications and processes for existing products in line with regulatory quality and environment requirements. Products are either pharmaceuticals, medical devices or software.

Guerbet devotes signification resources to research and innovation including about 9% of revenue and 4 R&D centres. There is scientific partnership with public and private players worldwide for the development of contrast media and artificial intelligence.

8.2 DESIGN AND DEVELOPMENT

New contrast media or new chemical entities (NCEs) are developed in several successive phases:

- Phase I to study the clinical and biological tolerance in healthy volunteers and the pharmacokinetics (how the product is distributed, metabolized and eliminated within the organism) of increasing doses of the product, and thereby determine the maximum tolerated dose,
- Phase II to compare the diagnostic effectiveness on patients of several doses of the product usually with a leading product on the market,
- Phase III to confirm, for a large cohort of patients, the diagnostic effectiveness and tolerance profile of the product compared with a leading product or technique.

The main objective of Life Cycle Management (LCM) activities is to manage the changes made on products that are already approved and sold. Typical LCM activities include obtaining approval for new indications, the development of new formulations or presentations, securing registrations in new geographic regions, and the clinical studies that take place after approval (phase IV).

Medical Device Product design and development activities are accomplished as a planned, controlled, maintained, and documented activity. The design and development activities are planned by and assigned to qualified personnel equipped with adequate resources.

Design input requirements (including functional, performance, usability, and safety requirements, previous designs, output of risk management) are documented, as detailed in an approved design procedure. Applicable statutory and regulatory requirements are considered and included in design and development inputs. Design input specifications relating to the product requirements are identified, documented and reviewed for adequacy. Design and development input activities should also address packaging requirements. Design output specifications defining identified product requirements are documented in a form that enables verification against the design and development input and is reviewed for adequacy. Design reviews will be conducted by a cross functional team as required. Such reviews will be documented.

Design verification establishes that design output meets the design input specification by means of design control measures, as specified in approved design control procedures. Design validation is conducted after Design Verification activities and shall ensure that product specifications and product performance will meet the specified requirements of the product definition as per product dossier. Design transfers are to occur per an approved engineering procedure. This procedure ensures that design and development outputs are verified and suitable for manufacturing, and production capability can meet production requirements.

Design History File. This record is of the design and development process and is maintained for each product. This design history file contains or references the records that demonstrate fulfilment of design control requirements.

8.3 DESIGN CHANGES / CHANGE MANAGEMENT SYSTEM (MANAGEMENT OF CHANGE – MoC)

Changes, modifications, or revisions are controlled and distributed through the Change Management System (Management of Change - MoC).

Innovation, continuous improvement, the outputs of process performance and product quality monitoring and CAPA drive change. In order to evaluate, approve and implement these changes properly, Guerbet has an effective change management system.

The change management system ensures continuous improvement is undertaken in a timely and effective manner. It provides a high degree of assurance there are no unintended consequences of the change.

The change management system should include the following, as appropriate for the stage of the lifecycle:

- Quality Risk Management should be utilized to evaluate proposed changes. The level of effort and formality of the evaluation is commensurate with the level of risk,
- Proposed changes are evaluated relative to the marketing authorization, including design space, where established, and current product and process understanding. There is an assessment to determine whether a change to the regulatory filing is required under regional requirements. From a pharmaceutical quality system standpoint, all changes should be evaluated by a company's change management system,
- Proposed changes are evaluated by expert teams with the appropriate expertise and knowledge from relevant areas (e.g. Pharmaceutical Development, Manufacturing, Quality, Regulatory Affairs) to ensure the change is technically justified,
- After implementation, an evaluation of the change is undertaken to confirm the change objectives were achieved and that there was no deleterious impact on product quality.

Note: Reference Policy Quality and EHS Management of Change (MOC) (Q019479, GBT-DMS-Quality-Quality Systems-10000057)

8.4 PURCHASING

Purchased materials and services from suppliers must conform to requirements established by Guerbet. Supplier selection, supplier process control, receiving, and testing are methods to provide purchased material control.

Suppliers are selected on the basis of their ability to meet specified requirements (quality, delivery, service, and cost). Qualified suppliers are on an Approved Suppliers List (ASL) controlled locally at site level.

Critical suppliers and Guerbet work closely together to identify and target areas for improvement, both at the supplier and at Guerbet. Establishing process controls, reducing variability, and accomplishing process improvements, allow both parties to make improvements in terms of quality and service.

8.5 PRODUCT IDENTIFICATION AND TRACEABILITY

Where appropriate, procedures are established and maintained for product and material identification and traceability. Procedures and methods are established that identify materials and products during all stages of delivery and production. These procedures and methods are documented and maintained. When traceability requirements have to be met, individual materials and products will have unique identification assigned and will be recorded.

8.6 CONTROL OF MONITORING AND MEASURING EQUIPMENT

Quality and Site management is responsible for establishing and maintaining a system for the control of all measuring and test equipment used by each site in all phases of product development, inspection, testing, installation, servicing and product acceptance. Designated instruments and equipment are calibrated and traceable to recognized standards.

8.7 CUSTOMER RELATED PROCESSES

Guerbet establishes and implements procedures for the review of contract requirements, sales contracts, customer orders and contract compliance in supplying products and services to customers. Customer complaint communications are handled through the Global Quality Technical Operations group with the Product Monitoring team based in Saint Louis, USA and in Villepinte, France. Customer complaints are handled in accordance with local procedures and in partnership with Pharmacovigilance & Medical Devices Vigilance.

8.8 PHARMACOVIGILANCE PROCESSES

Pharmacovigilance relates to the science and activities ensuring the detection, assessment, understanding and prevention of adverse effects or any other medicine-related problem [Definition by the WHO].

Guerbet has set up a pharmacovigilance system and a quality system dedicated to pharmacovigilance, as specified in the guidelines on Good Pharmacovigilance Practices (GVP). The organization and the processes of pharmacovigilance are described in quality documents (procedures, instructions and forms) and in the Pharmacovigilance System Master File (PSMF) of the Group. Pharmacovigilance activities are performed by some qualified personnel working at headquarters and at partners' level under the oversight of the European Union Qualified Person for Pharmacovigilance (EU-QPPV). Safety Data Exchange Agreements (SDEA) stating the roles and responsibilities in pharmacovigilance have been signed between each partner (affiliate or distributor) and the Pharmacovigilance department of Guerbet.

The pharmacovigilance system is designed to monitor the safety of Guerbet's authorized medicinal products and detect any change to their risk-benefit balance.

8.9 MEDICAL DEVICES VIGILANCE PROCESSES

The purpose of the Medical Device Vigilance System (Materiovigilance) is to improve the protection of health and safety of patients, healthcare professionals, and other users by reducing the likelihood of reoccurrence of incidents related to the use of a medical device.

The Medical Devices regulations states that adverse incidents are evaluated and, where appropriate, information is disseminated in the form of a National Competent Authority Report (NCAR).

8.10 INFORMATION SYSTEMS PROCESSES

The Information Systems (IS) department of Guerbet Group has set up a quality system (“Qual-IT”) ensuring the compliance of the group's Information Systems and Information Technologies with global pharmaceutical requirements and Information Systems good practices. Most of the activities run by Guerbet Group are critically dependent on Information Systems, which are hosted on premises or in the cloud. They are made up of a complex worldwide network of interrelated systems, involving a great variety of stakeholders such as institutions, clients, suppliers and even more.

A dysfunction or cyberattack in the way Information Systems operate can therefore lead to problems that could be severe with possible consequences on product quality, patient safety, our image, turnover, employees, customers, shareholders and environment. IS has issued policies and procedures that govern all our IS processes.

The IS Quality Policy is based on two main pillars:

- Information Security,
- IS Validation.

Information Security Policy is driven by the Chief Information Security Officer who oversees managing IS security. He reports to the Chief Information Officer (CIO). The Chief Information Security Officer (CISO) leads 2 committees: Security committee (Quarterly with CIO), Security report (Monthly with Local Security Officer). Information Security aims at taking adapted measures to ensure the protection of data and Information Systems and compliance with regulations by establishing and implementing the appropriate principles:

- Availability to ensure that authorized users have access to information, application and services when needed,
- Integrity to safeguard the accuracy and completeness of information and processing methods,
- Confidentiality to ensure that information is not made available or disclosed to unauthorized individuals, entities, or processes,
- Auditability which refers to the capability of a system to keep relevant tracks and proofs of what was done and by who.

IS Validation Policy is driven by the IS Validation Engineer who oversees validating Information Systems used for decision making related to product quality or patient safety. The IS Validation Engineer reports to the IS organization & Methods manager with a dotted line to the Chief Pharmaceutical Officer. The Validation Engineer participates to GxP project committees, Change Advisory Boards (CABs) and Quarterly Validation Reviews with the Chief Pharmaceutical Officer.

The purpose of IS Validation is to implement measures to ensure that Information Systems are fit for intended use and compliant with healthcare industry regulations all over their life cycle from conception to retirement. Those measures aim to safeguard product quality and patient safety by reducing the risk to an acceptable level of undermining the integrity of the data and the Information Systems.

Validation consists in obtaining and maintaining compliance with healthcare industry regulations by:

- Organizing qualification activities as part of plans and reports,
- Applying appropriate controls during operation phase of Information Systems in periodic reviews.

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MEASUREMENT, ANALYSIS AND IMPROVEMENT

9.1 MONITORING AND MEASUREMENT

The effectiveness of quality management system and the overall quality performance of manufacturing, distribution, development operations must be continuously monitored and assessed in order that opportunities for improvement and elimination of defects be provided.

Customer satisfaction

Guerbet aims at not only to meeting proactively, but exceeding, if possible, customers' needs and expectations.

Internal inspection / audits

Planned and documented internal site inspections / audits verify the implementation and effectiveness of the quality system and provides self-improvement objectives. Audits are conducted by qualified personnel independent of those having direct responsibility in the area being audited and examine the processes, procedures, systems and premises. They are conducted following a written procedure or plan. Results of audits are used to evaluate the implementation and effectiveness of the quality system. Audit reports are reviewed by site management.

9.2 NON-CONFORMING PRODUCT CONTROL

Guerbet has established and maintains procedures that prevent the inadvertent use of non-conforming material or product. Identification, documentation, evaluation, segregation (where practical), and disposition of non-conforming material or product is controlled. The procedures define the responsibility for reviewing product found to be non-conforming and ensuring the correct disposition authority.

9.3 DATA ANALYSIS

Quality data is collected and analysed to determine the effectiveness of the Quality Management System and to identify areas for improvement. Key Performance Indicators (KPIs) are collected each month for the sites and reported with to the Technical Operations group.

9.4 IMPROVEMENT

Guerbet improves the effectiveness of the Quality Management System by reviewing the Quality Policy, objectives, audit & inspection results, analysis of data/KPIs, and CAPAs.

CAPA:

A planned and documented program for corrective and preventive actions is established to ensure that conditions which adversely affect quality are promptly identified. The causes of discrepancies are determined, and positive steps are taken to prevent recurrence. Changes in procedures resulting from corrective and preventive actions are implemented and documented.

Corrective and preventive actions are reviewed and identified Root Causes are tracked by management as part of the Management Review Process in order to evaluate the Corrective and preventive actions effectiveness.

Note: Reference Policy for the Corrective Action / Preventive Action (CAPA) Management (Q018958, GBT-DMS-Quality-Quality Systems-10000004)

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DOCUMENT HISTORY

Issue date & version	Comment
April 2020 - V 1.0	First version - Global Quality Manual