AZIND: MCOQ LOCAL QUALITY MANUAL FOR ASTRAZENECA INDIA

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Associated Document for 1-P63-cv-X: Standard Operating Procedure for Local Quality Management for GXP Activities

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1. PURPOSE AND SCOPE

AstraZeneca Pharma India Limited (AZPIL) is committed to the development, manufacture and supply of high quality medicines in compliance with company standards, international codes and regulations and local regulatory requirements.

This Work Instruction outlines the steps to the quality management system in the local markets, AstraZeneca Pharma India Limited (AZPIL), for the GMP/GDP activities carried out by or on behalf of AstraZeneca Pharma India Limited (AZPIL) to the SOP 1-P63-CV-X: LOCAL QUALITY MANAGEMENT FOR GXP ACTIVITIES. The Quality Manual describes how AstraZeneca Pharma India Limited (AZPIL) meets the standards for quality management set out in the Global Standard: **Quality Management System (QMS) and Quality Policy**.

GXP activities are:

GCP - Good Clinical Practice
GVP - Good Pharmacovigilance Practice
GMP - Good Manufacturing practice
GDP - Good Distribution Practice
GRP - Good Regulatory Practice

The Quality Management System (QMS):	
Ensures the required standards for activities that underpin all GxP activities	Training; document management; contract management
Provides adequate systems for dealing with issues and errors in GxP activities	Product complaints; adverse event reports; issue management and product recalls; deviation and CAPA (Corrective and Preventative Actions) management
Pre-empts and prevents issues and errors	Risk management; change management; self-assessment; continuous improvement; Preventive Actions (from deviation and CAPA management)
Performs a strategic review of the quality management system to address risks and opportunities and determine resource allocation	Management review; continuous improvement
Provides and responds to independent review of the quality management systems and processes	Audit; inspection

Figure 1: Elements of the Quality Management system

This instruction applies to all AZ personnel working for AstraZeneca Pharma India Limited (AZPIL) involved in or accountable for any GMP/GDP activity, including quality management of GxP activities in AstraZeneca Pharma India Limited (AZPIL).

This Quality Manual describes the quality management system (QMS) supporting GMP, GDP with links to Medical Evidence GCP, GVP and GRP activities carried out by AstraZeneca Pharma India Limited (AZPIL). It includes how quality is managed for GxP activities carried out by third parties on behalf of AstraZeneca Pharma India Limited (AZPIL)

This document supports the **AstraZeneca Standard: Quality**. See the references.

2. WHAT YOU NEED TO DO (INSTRUCTION)

2.1 Quality Management and Continuous Improvement

2.1.1 Management Responsibility and Reviews

Why Do This:	How To:
To ensure the Country President and other senior leaders accountable for the GxP QMS have the information to make decisions on strategy, priorities and resources for GxP activities. To ensure there is a review of key data and trends. **Status:** Formal process is **mandatory** **Frequency: Management Review Meetings must be quarterly.** Escalation of significant issues and risks should occur as these become known.	1. **Prepare the agenda (Management Review Inputs):** to assess the performance of the QMS and find areas where improvement is needed. The review includes the following: • Minutes of the previous meeting • Audit and inspection findings, including assessment of 3rd party providers • Risks • Issues (number of minor and description of major and critical) • Outcomes of Self-Assessments • Relevant changes • Local performance on global and local KPIs • Monitoring outcome of any outsource activities (when applicable) • Follow up on the completion and any updates of the local training plan (when applicable) Ensure QRM agenda and slide decks are as per template issued by Global MCOQ. 2. **Management Review Outputs:** The output from the Management Review Meetings will include any decisions or actions in relation to: • Improvements needed to maintain the effectiveness of the QMS and associated processes • Resource needs • Required audits or self-assessments Minutes of Meeting should be approved by senior management (either by Director Regulatory Affairs or VP-Medical Affairs or Country president) Presentation slides used for QRM should be signed off by MCOQ Lead. Records of Management Reviews are recorded and retained in company sharepoint (Box Folder).

2.1.2 Risk Management

Why Do This	How To
Identifying and analysing risks is essential to mitigate and control those risks. **Status:** A formal risk management process is **mandatory** **Frequency:** on a **quarterly** basis Risks registered prior to 31 December 2021 can be accessed at GXP Portal as extracted noneditable excel: Archived tools (Link or within Toolkits (Link) From 1 January 2022 a global tool - Veeva Quality Vault (VQV) is used (Link).	Refer to Risk-'How Do I' Guides at VQV End User Portal. **1. Create 'MC GMP/GDP & Quality Risk Register' in VQV** (once created keep it active) **2. Create and assess individual risks** • Define the risk (hazard), i.e. activity that might go wrong. Determine with the risk owner "what might go wrong?" (Use the "Techniques to Assess Risk", GUID-0021152. • Describe the risk: *"Due to **XXX** there is a risk of **YYY** which could lead to **ZZZ**".* XXX= failure mode(s), means reasons/root causes, YYY=risk (hazard) ZZZ= harm(s), means consequences • Identify the owner of the risk • Create failure mode-sub records, i.e. the reason(s) of the risk-"why it might go wrong?") and their root causes • Create the harm(s) sub-records - "What are the consequences should it go wrong" • Perform risk analysis as per 1-P57: severity (impact) of harms/consequences, likelihood (probability) of harms/consequences, detectability of hazard/risk. System will automatically calculate the risk score and classify as critical, major, medium, low • Decide if a risk will be accepted (no mitigation actions needed, with justification) or it will be mitigated (mitigation actions to be created) • If decided, create mitigation actions addressing the failure modes and/or harms • Perform risk analysis after mitigation action(s) completed and check if additional mitigation actions needed or if a risk can be moved into 'controlled' state. **3. Risk review and control** • Create Periodic review records to review the risks in the Risk register (quarterly and/or more frequent as needed) • If needed re-evaluate the risks that are in controlled state **4. Risk documentation and communication** • Report and manage the risks in the VQV Risk tab (Link) • Newly identified risk and any other open risks are reviewed and discussed in the regular AstraZeneca India GxP team meeting before completing the periodical review in VQV Risk tab. Senior managers are communicated about the risk e.g. LCC or similar or management review meeting. • **Include updates in Management Meetings –** see Management Review: section 2.1.1

2.1.3 Knowledge Management & Continuous Improvement

This includes using knowledge to drive continuous improvement and good document management. For document management, see section 2.4.

Why Do This	How To
Helps to reduce issues, manage risks and reduces duplication of effort. Informs allocation of resources. Supports simplification, redesign and improvement of GxP activities. **Status:** Formal continuous improvement assessment is **Mandatory.** **Frequency:** Quarterly review during the Management Review Meeting.	**1. Collect data for review** • Deviations & CAPAs • Risks • Audit and inspection findings • Change management • Self-assessment • Other sources e.g. best practice from other business units or companies **2. Convene a meeting** • Include quality experts, GxP experts and management as appropriate • Review data from 1, above • List areas needing improvement & opportunities for improvement • Determine top 2 to 5 priority improvement areas. The Ideas ranking Tool (FORM-0033278) may be used to help with this • Agree the area(s) for improvement and improvement actions **3. Enter area(s) for improvement (as identified above)** Enter data on improvement areas into the Continuous Improvement Plan Tracker tool **4. Review and update actions.** Reminders will be sent to *review and update progress in the* Continuous Improvement Plan Tracker tool **5. Include updates in quarterly Management Meetings – see Management Review: 2.1.1** **6. Job Handover/Knowledge transfer** • GxP Resource who is leaving the organization must complete the Handover prior to leave the Organization as per TMP-0011183 – AZIND:Job Handover Checklist • Soft copy of the document/data must be uploaded in the common box folder. Box - Link • Respective Line Manager is responsible and ensure all required documents are uploaded prior to resource leaving the Organization. • Hand over checklist to be completed and duly signed & dated by both the Resource and the Line Manager. • Scanned copy of the duly signed Hand over checklist to be retained in company sharepoint (Box Folder) Box - Link.

2.1.4 Change Management

Planned changes in GxP processes may occur for many reasons, including Regulatory changes, outputs of continuous improvement, a change in an external partner; system changes and many more.

Why Do This	How To
When a system undergoes change, it can lead to unintended effects which should be proactively identified and managed. Failure to implement a fit for purpose Change Management System can lead to serious problems. This area is under scrutiny by regulatory inspectors. **Status:** A formal change management process is **mandatory for major changes** **Frequency:** For each change as it occurs. Major changes included in senior management review meetings as minimum.	**1. Identify and assess the change** • Each GxP function should be alert to relevant changes. • The Local Change Control Log, FORM-0122057 (for minor changes) and TMP-0009102 (for major changes) serve as the local GxP tools to document the information relating to any change within GxP area. Any new GxP relevant changes will be discussed and followed up in regular GxP meeting • Check if the change is managed by a global change process, as this may limit or remove the need for a separate local change management process. **2. Categorize the change** • Determine if the change is major or minor. A major change is one that has a potential impact GxP activities in a way that could affect product quality, patient safety, study data integrity or breach internal standards or external regulations. Major changes must be formally assessed and documented. Other changes are minor. Log all your changes into the Local Change Control Log at Box folder. Box-Link If a change is major, the change and the actions needed is captured in Major Change Control Form Template, TMP-0009102. If a change is minor, the change and the actions needed is captured in AZIND: Minor Change Control Form, FORM-0122057. **3. Risk assessment (required for major changes)** • Before a decision is made to implement a major change, complete a quality risk assessment of the proposed change • If there is a risk associated with the change, proceed as in section 2.1.2 of this manual **4. Evaluate the change and approve the plan (required for major changes)** • Evaluate the change to ensure it is justified technically and from a business perspective. • Get agreement on the change management plan by MCOQ lead or Regional lead as apllicable • Implement the change management plan and review progress • Update the plan if additional requirements are identified **5. Track the major and minor change to completion** • Complete second part of the Change Control Form once the change control is ready to be closed.

	• Close the change request once the change has been implemented and the change management actions are completed. **6. Effectiveness check** Include details on how the effectiveness check will be performed once the major change is completed in the Change Control Form, TMP-0009102 **7. Include updates in quarterly Management Meetings:** see Management Review: 2.1.1 **8. Change control numbering:** Issue the Change control number to all GxP changes in following sequence. **AZPIL-CC-YYYY-XXX** Where: AZPIL – AstraZeneca Pharma India Limited CC – Change control YYYY – Calendar year (Example: 2023) XXX – Chronological number start from 001

2.2 Personnel and Training

2.2.1 Organisation Charts

Organisation charts are obtained from Workday.. Historic charts can be obtained on request from Human Resources.

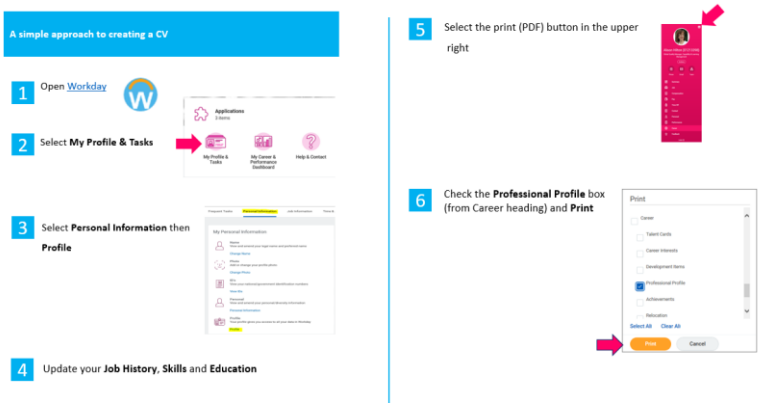
2.2.2 Training management

Why Do This:	How To:
Staff working in the GxP areas must have the skills, qualifications and training to their role. This also applies to third parties providing GxP services or GxP quality management services **Status:** training records must be available in Cornerstone SBX or a similar validated system. **Frequency:** Initial training when a person joins a new role, ongoing training such as when a new procedure or a standard is effective or repeat training as a reminder of key	Staff involved in any GxP activity must receive adequate job specific training. This consists of initial or 'induction' training and ongoing or 'continuous' training. Induction training will provide the knowledge to allow initiation on the GXP activities. GxP new starter follow the GUID-0024639 AZIND: GXP New Starter checklist. Also MCOQ personal will follow the MCOQ induction programme GUID-0023056 Ops_MCOQ_Activities Onboarding New Starter GMP/GDP & Qualityfollowing the instructions included in the excel. All the activities in the onboarding tool must be performed by the new starter unless not under the new starter´s responsibility (supported by the Job description) Role wise training requirement is defined in GUID-0023888 AZIND: Local Training Matrix. Ongoing training may provide new information or be refresher training to ensure information is being retained. Training should be relevant to trainees' individual needs and be appropriate to their duties and responsibilities. Training is managed in the company training management system, Cornerstone SBX, or can be delivered directly in live training sessions.

information. The need for training must be regularly assessed (at least annually) by the individual and the responsible manager.	**1. Assigning training** Each person working in a GxP function is assigned the required global training for their function. This is done by assigning the appropriate globally managed “MC role” and the “OQ Quality Operation ALL” to the individual. The list of applicable Global MC and Local roles can be found in GUID-0023888 AZIND: Local Training Matrix Each person should have all applicable MC roles and the “OQ Quality Operations ALL” assigned to them , that is they can have multiple MC roles assigned.The Guide for Managing Training in Saba Cloud, GUID-0021150 explains how to assign training roles. There is also guidance in the Cornerstone SBX system. The training included in each of the Job Roles is known as the ‘certification list’ and is reviewed and updated by the global role owners on a quarterly basis and as new procedures are published. Any new training added to the certification list will automatically be assigned to anyone with the training role assigned to them. Training on local procedures and other required local training is assigned to individuals as single items of training or managed via local training roles. The certification list in local training roles is updated as procedures or training change. The local job role (equivalent to ‘training role’) and the correspondence certification list (local procedures training list) is captured in GUID-0023888 AZIND: Local Training Matrix. Line managers ensure those working in their GxP area are being assigned the necessary global and local training. Local job role is assigned for new hires based on local training matrix. Line managers are responsible to ensure individuals working in GxP areas are assigned the correct globally managed ‘MC role’ and ‘local job role’ prior to commencing a GxP task. Training is assigned as either Core or JIT (Just in time) training • Core training is mandatory training for a specific role and has automatically assigned certifications. • JIT training is mandatory training for a specific task and is manually assigned by the learner or their manager when the task is planned, and the training becomes relevant. • Each item of required training is given a time-line in which to complete the training, usually 30, 60 or 90 days. When staff go on extended leave (>30 days) the line manager can assign a temporary ‘On Leave’ Jobrole instead of the usual training. This ensures training is not assigned to be completed while the individual is on leave. For documentation of training conducted outside of SABA Cloud system, Training Attendance Sheet can be used. Upon completion, each trainee shall log in and upload this training record into SABA Cloud using these steps. **2. Refresher Training** Refresher training is repeated training or retraining to ensure that the required level of knowledge, awareness and competence in GxP skills is maintained. The need for refresher training is based upon assessment of:

	• Any prolonged time interval since a task was last performed • any quality incident, deviation or procedural failure where training was a factor or part of a CAPA • Detection of an adverse trend • Returning from an extended absence • The need for regular training, such as annual training **3. The Training Plan** In addition to the MCOQ training plan A local training plan is developed on an annual basis using the Training Plan and Tracker, PLAN-0119363AZIND: Annual GxP Training Plan taking into account: • Changes in local procedures • Audit and inspection findings • Changes to facilities, processes, systems, regulations etc. • Changes to the organisation and/or teams. • Any recurring problems • Quality deviation, incidents or findings • Regional or global training plans, to avoid duplication of sessions • Individual training needs The annual training plan captures all training across GxP functions and will be captured as a topic for follow up in regular GxP Meeting

2.2.3 CVs

Why Do This:	How To:
To demonstrate alignment of the job responsibilities to the, education and experience of the employee. **Status:** CVs are mandatory for those with GxP responsibilities and must either be uploaded (or signed) by the employee **Frequency:** CVs should be reviewed, re-signed and re-uploaded every year (If required)	1. Each employee with GxP responsibilities writes their CV. The CV Template, TMP-0009097 can be used and is completed with details of training, qualifications and experience. Other recommended alternative is to create a CV using Workday, see the steps below:  (For additional information, reference SOP-0107573 2-P13-cv-M) 2. If the template is used, owner of the CV to upload CV into Cornerstone SBX using the instructions for upload of job description and CV, *Learner - Cornerstone SBX – How To Upload CV/Resume and Job Description in Saba Cloud.* If the CV is

	uploaded by someone different than the owner, the owner of the CV needs to sign it. 3. There is no need to re-sign and date if your CV reflects your current Job, Job History, Skills and Education

2.2.4 Job descriptions

Why Do This:	How To:
Providing written job descriptions (JDs), ensures individuals are clear on their accountabilities which contributes to ensuring all vital GxP tasks are done. Management can map the allocation of tasks across groups of JDs to ensure all required tasks are covered and aligned with local GxP systems and the organisational structure. Inspectors check JDs against these factors. **Status:** JDs are **mandatory** for every employee involved in GxP activities. **Frequency:** for every new employee, when there is a change in accountabilities and and at least every year	Employees involved in GXP activities must have an approved job description defining their accountabilities and responsibilities. The Human Resources Job Role Profiles (Job Catalogue) are not to be used as local GXP job descriptions. Job descriptions can be individual or general, that is, applicable to a group of people. "TMP-0012419 AZIND: Generic Job Description Template for GxP" can be used for preparation of Job Description. 1. Contact Human Resources department to check your local process 2. Refer to JD MCOQ generic templates, Responsibilities are described for each role, ensuring all necessary GxP activities area included in the JDs. . An MCOQ JD should be approved by the local MCOQ Lead. 3. Once completed, the owner of the JD will upload it to their Cornerstone SBX profile as evidence of the individual acknowledgment. If not uploaded by the owner, the JD will require his/her signature. The line manager has access to the JD in Cornerstone and can review it at any time. See instructions Cornerstone SBX. *Learner - Cornerstone SBX – How To Upload CV/Resume and Job Description in Saba Cloud* 4. Review the JD at least every year, add the new review date. The owner of the JD will then upload the updated document into Cornerstone SBX. Every year, at the beginning of the year, the local MCOQ lead or delegate sends an email to all GxP personnel involved in GMP/GDP activities to remind of the annual JD review and re-upload There is no need to re-sign, date or upload if your Job Description is current. 5. Review the JD if: • There is a relevant change in the activities described in the JD • The person is changing to a new role in the GXP area The Country President JD does not require the line manager signature nor review every year but the Country President must have a JD which includes the GXP accountabilities. Refer to Generic Country President JD with NEW GXP accountablilites-template, TMP-0011216 which includes the minimum requirements for the GXP accountability

2.3 Infrastructure

2.3.1 Tools and Validation of Tools

It is in scope for any software used for a GxP business process including decisions, transactions or storage of GxP data. This can range from large enterprise wide IT systems which are globally validated such as Cornerstone SBX through to any local desktop applications such as Excel Spreadsheets or SharePoint sites used for GxP. AstraZeneca Pharma India Limited (AZPIL) must validate **local** tools which fall in scope. Global or regional tools will be validated by the respective global or regional team.

Why Do This:	**How To:**
To ensure our systems are designed, constructed, installed, qualified, maintained, operated and decommissioned according to their intended use. Tools must be reliable and data integrity assured because of the importance of GxP activities in ensuring product quality and patient safety. **Status:** Validation of GxP tools is **mandatory**	**1. Planning** • Determine if the system is a GxP system requiring validation using the Risk Impact Determination (RID) TMP-0008377. • Define the validation plan – activities are scaled based on risk (GxP impact, system size, complexity) • Consider the business practices and the technical requirements • Involve the local IT partners • Consider if a supplier assessment is required **2. Specification** • Define the functional requirements of the system • Identify potential areas of GxP impact • Define non-functional requirements such as access management, backup/restore, security, electronic records, signatures requirements. • Identify the need for a procedure or operating manual for the system. • Specify connections with other systems and any data/record migration required. **3. Configuration** • IT configures the technical requirements to fulfil the functional requirements **4. Verification** • IT defines the system tests required to verify the correct technical functionality. • User performs the user acceptance tests to verify correct operation for the business process, SOPs and users. • User to report the outcome of the test. • Decide on the test acceptance, checking the results against the specifications for the system. **5. Reporting** • IT creates a validation report. • Owner checks the validation is completed, according to the validation plan.
Frequency: Before the system is in operation and each time there is a significant change to the system	

	• IT determines the “go live”. • Owner implements the training. **6. System lifecycle management** • Owner reviews the maintenance process. • If changes are required, a change request is raised which starts the process of validation again (from point 1 above). • Owner performs periodic reviews to confirm the system is in control and remains in a validated state. • All the validation documents must be retained and available to auditors and inspectors. These are stored in ECMS (Enterprise Content Management System)

2.4 Data and Documentation

AstraZeneca Pharma India Limited (AZPIL) uses validated sites for hosting GxP documents, to maintain data integrity and support inspections. Systems ensure that only current versions of documents are accessed, except when providing an earlier version for audit and inspection.

The Local MCOQ lead is responsible for quality oversight of the AstraZeneca Pharma India Limited (AZPIL) GMP/GDP Quality documentation system, including control of documents.

The Document Owner is responsible for determining the archiving requirements for a document, in compliance with local procedure (SOP-0103759 - AZIND: Procedure for Archiving & Records Management) and the new GRAD site

Different GxP documents types are stored on different platforms, as specified by global procedures. Where the repository for a specific document type is not specified by global procedures, a validated global or local system is used.

2.4.1 Procedural Documents

Local procedures are maintained in the global Enterprise Content Management System (ECMS) reviewed as needed and at least every three years.

See section 2.2.2 for management of training, including procedural training. All personnel involved in GxP must comply with the procedures relevant for their role.

Refer to SOP-0103761: Procedure for Document Control and Management for management of local procedures.

2.4.2 Records management

GxP records are retained on AZIND electronic shared folder system (Box folder). Other quality management and continuous improvement records are retained within the global platforms (ECMS, EQV, VQV etc.)

Why Do This:	How To:
Ensures staff are following current procedures. Supports knowledge and communication. Required for inspections. **Status:** Required **Frequency:** Annual check of the GRAD timeliness applied to documents against the GRAD schedule. Procedural documents, reviewed at every 3 years or earlier if there are major changes in content.	**1. Generation and control of documents** Each document should have a clear title, unique number and version number. ECMS manages version control of documents so that only current versions are visible to general users. Only valid official records and procedures should be included in ECMS. **2. Document creation, review and revision** For procedures, use the global templates: • Standard (TMP-0009192), SOP (TMP-0009189), Guidance (TMP-0009190), Work Instruction (TMP-0009191). Documents migrated from AZ-Doc to ECMS have new document ID (ECMS number) and they are searchable by the ECMS number and the AZDoc number. The author or editor of Standards, SOPs, Work Instructions or Planned Deviations and the approver cannot be the same individual. Revision of global GxP procedures does not require a major change control process as changes are described in the company written procedures. Document owners are responsible for monitoring procedural documents that are due for review and ensuring the review happens in a timely manner. ECMS reporting and searching functionality facilities this review. Refer to SOP-0103761: Procedure for Document Control and Management for management of local procedures. Procedural document monitoring must include changes to relevant global procedures to assess if they have impact on local procedures. Refer to the Global Procedure Change Log" to check if changes to global procedures have a local impact: • The local MCOQ Lead or delegate monitors Global Procedure Change Log" updates of global GMP/GDP and QMS procedures. • The local MCOQ lead or delegate undertakes a gap analysis against local procedures using FORM-0122058 AZIND : QCM Assessment Form to determine if there is local impact and retain all assessment forms in company sharepoint GXP | Powered by Box • If the gap assessment results in a change to local processes and/or procedures and training impact, record the outcome in the local Change Log (with local actions to be taken, for which not necessary to raise AZIND: Minor Change Control Form, FORM-0122057). If the level of change is major (multiple processes and/or procedures) manage the change using the major change form and the Change Control process described in this document. If the local impact bears a

risk at local level, make an additional entry in the Risk log.

If the gap assessment results in no local impact, this should be documented in the FORM-0122058 AZIND : QCM Assessment Form.

- Manage changes to local procedures using the change control processes within ECMS (DCR for minor items to address at next periodic review, DCC for immediate changes).

Good Documentation *Practice* must be followed.

To create, update (new version) or withdrawn a mandatory procedural document (Standard, SOP, Work Instruction or planned deviation) the MC must create a Document Change Control (DCC) in ECMS. ECMS DCC Work Instruction and DCC-related training material is available at ECMS sharepoint site (Link). See Job Aid on Managing Procedural Documents in ECMS, GUID-0022758.

3. Retention of documents

Records are archived only when they are the official record (no drafts or copies) and they are no longer active (do not require frequent or immediate access). Archiving of documents must be in accordance with new GRAD

AZPIL documents are physically stored in the AZPIL office or externally archived at P N Writer & Co. Pvt. Ltd., a company incorporated in India and having its registered office at 105, Dr. Ambedkar Road, Chinchpokli, Mumbai-400033 and its branch office at Writers Information, Address: No 89/3, Bidarahalli Hobli, Seegehalli Village, Kadugodi Post. Bangalore – 560067.

Refere local procedure “SOP-0103759 - AZIND: Procedure for Archiving & Records Management”

Physical archives are in a secure building, constructed and maintained to ensure that documents and any other types of media are kept secure, complete and retrievable throughout the specified retention period.

Access control to the physical archive must be maintained. The name date, reason for the visit and time of personnel accessing the archive, except for authorized personnel, working in the respective GxP function is recorded on the Access to Archive Log,. Such personnel must be accompanied by the Archive staff for the duration of the visit.

If a record needs to be removed from the archive, a record of the material removed must be kept using the Temporary Removal of Documents from Archive FORM-0105834. When the document is ready for destruction according to the GRAD schedule, the owner of the document should approve the destruction using the Permanent Removal/Destruction of Documentation from Archive Template, FORM-0105833..

	4. Electronic records Electronic records follow the same principles as paper records. GxP documents (Electronic) are stored in Global Documentation Management System. There must be procedures in place to cover backup, restoration, archive, storage and retention of the computerized system and its data, including associated audits trails and metadata

2.5 Audits and Inspections

2.5.1 Audits

Audits may assess personnel, systems, processes, procedures, facilities, products, studies, reports, records and/or data for compliance with policies, standards, procedures, guidelines, regulations or regulatory submissions. Audits may assess both in-house and external/third party activities and may be planned or undertaken on a 'for-cause' basis.

Personnel undertaking audits must have the appropriate skills, training, experience and personal attributes to conduct the audits they perform. Auditors must have sufficient independence to be able to openly report adverse findings to management to satisfy internal and external corporate governance expectations.

AstraZeneca's Global GxP audit functions run an audit programme that includes audit of AstraZeneca Pharma India Limited (AZPIL).

Refer SOP-0034148 GMP and GDP Auditing of Suppliers and AstraZeneca Sites Global Procedure.

Why Do This:	**How To:**
To assess compliance with regulations and company procedures and to identify issues requiring CAPAs and improvement. **Status:** Formal process is **mandatory**. **Frequency:** Set by the audit functions. Internal GxP audits of MCs operate on an approximate 3-year cycle risk base approach. Local audits can be commissioned, if required	1. Ensure AstraZeneca Pharma India Limited (AZPIL) is always prepared for a local inspection/audit by ensuring good quality management principles are adhered to on an ongoing basis. 2. Determine who will co-ordinate local activities for the audit. 3. Agree the date, scope and objectives with the audit group (either in AZ or if locally organized with the external auditor) 4. Determine the team to be interviewed and identify systems and document to be audited. 5. Agree CAPAs and their timescale with the audit group and any findings to be escalated. Create CAPAs associated to the findings reported in the Global tool as instructed by the auditors. See details in the EQV Portal-GPQS Audit 6. Include audit findings in management reviews. 7. Follow up CAPAs to conclusion in the EQV Portal-GPQS Audit

2.5.2 Inspections

Why Do This:	How To:
Regulatory authority inspections: • determine if the marketing authorisation holder has personnel, systems and facilities in place to meet their obligations; • identify, record and address non-compliance which may pose a risk to public health; • use the inspection results as a basis for enforcement action, if necessary.	1. The format, performance and conduct of Regulatory Inspections are largely dictated by the regulatory Inspector but follow a similar agenda and process to internal audits. 2. Refer local procedure SOP-0103763: Procedure for GxP Audits, Inspections and Self-Inspection. 3. The AstraZeneca Pharma India Limited (AZPIL) must send an email to the Global GXP function as soon as the inspection is announced, notifying them of date of the inspection. 4. The relevant local MCOQ lead informs the CP, Medical Director and members of staff who may be called upon to support the inspection. It is important to ensure there will be adequate support during the inspection process, including those who will be interviewed and people to prepare and check documents for the inspection (also from the global function as applicable). 5. Records, documents and data requested by an Inspector must be provided promptly. 6. Financial data, sales or pricing data, personnel data (other than CVs, job descriptions, training records) are not subject to inspection unless mandated by regulation. 7. Inspectors may be allowed to photograph and record any activity determined by the inspector to be necessary to effectively conduct the inspection. Duplicate records of any pictures or recordings should be retained by AstraZeneca Pharma India Limited (AZPIL) 8. During the inspection a daily summary of the inspection must be provided by the AstraZeneca Pharma India Limited (AZPIL) to the relevant Global GxP function using the Regulatory Inspection Daily Summary Report Template, TMP-0009101. 9. Immediately after the end of the inspection, Regulatory Inspection Summary Report Template, TMP-0009106 must be sent to the relevant Global GxP function. 10. Post inspection: • Acknowledge receipt of the inspection report. • Distribute the report to relevant functions in AstraZeneca Pharma India Limited (AZPIL), *the Regional lead, the Head of MCOQ support and the Head of MCOQ*. • Draft responses within the set timelines. • Findings must be followed up as described in section 2.7, 'Issues management and product complaints', below. Findings must be included in management reviews. • Consult the AstraZeneca Pharma India Limited (AZPIL) legal team on any findings with potential legal implications. • Provide a final response to Regulatory Agency within required timeline. 8. Retain the inspection report, response to the Regulatory Authority, evidence of closure of observations in accordance
Status: Whether announced or unannounced, Regulatory Authority inspections are a **priority** and inspection activities must not be delayed, limited or denied. **Frequency:** Determined by the regulatory authorities.	

	with the GRAD code. Documents are retained within VQV. Record the whole Inspection process in the Global Veeva Quality system for all GXP areas (if Inspection coordinator role is in the MC), prepare responses to Inspection findings with CAPAs and follow up until CAPA closure. Add any attachments in the Veeva Global Quality system. Details are in the "How do I"- VQV portal (Inspections and CAPAs section)

2.5.3 Self-Assessment

Why Do This:	How To:
Provides the first line assurance level that processes are robust and follow regulations and AstraZeneca procedures. **Status:** It is **mandatory** to complete: • The GMP/GDP & QMS checklist • To perform mock recalls • To implement an annual self-assessment plan **Frequency:** • GXP check lists annually • Mock recall annual unless there is a real recall. • Annual self-assessment plan with a realistic number of self-assessments as needed each year	**Self-assessment:** **1. Scheduling and planning** In Q1 of each year, an annual self-assessment plan will be created by the local MCOQ Lead or delegate. The plan will based on a review of previous and new risks, issues, major change projects, audits and inspections and the outcomes of the annual self-assessment checklist. Activity areas which have not been reviewed for some time will also be considered. The plan should be realistic on the number of the audits and approved by the CP or MCOQ cluster Lead. Additionally, audit plan for external vendors should be prepared separately each year in Q1. . Use the Global Veeva Quality system to create the annual self-assessment plan. See details under the "How do I"- VQV portal (audit module). Include as part of the plan the individual Audits (self-assessments), related Findings and CAPAs. Include evidence of CP or MCOQ cluster Lead approval in the attachment section. Include the role who will conduct the self-assessment (lead-auditor). They should be performed by skilled and knowledgeable staff working in the concerned area with sufficient independence to be able to openly report observations to management in order to satisfy internal and external corporate governance expectations. They must not assess activities they have conducted. They must proved **experience** through: • Knowledge as having completed the core MC jobrole assigned in Cornerstone SBX according to the GXP activities under assessment and • Basic knowledge of QMS AND/OR training in 1-P63 and the local Quality Manual) • Knowledge of auditing tool (completion of the VQV QA user role training) Considered as **personal attributes** for the role conducting the self-assessment must have:

- Technical skills: strong understanding of the QMS, to stay current with local regulations and internal requirements
- Communication skills: speaks and writes clearly and concisely, good listening skills

And strongly recommended personal atrtributes such as:

- Behaviours: organized and planning skills, to be observant, integrity and honesty, remains polite in difficult situations
- Competencies: able to schedule, conduct and report self-inspections and internal audits that are compliant with internal and regulatory expectations, to identify non compliances with local procedures and ways of working, to ensure local controls are in place, in use and operating effectively, to identify opportunities for improvement

Optional and further developed training: ISO 9001:2015, Internal auditor training course https://www.bsigroup.com/en-SE/quality-management-iso-9001/training-courses-for-iso-9001/iso-90012015-internal-auditor/>.

Mock recalls must be part of the annual self-assessment (see section 2.7.3, IMTs)>

The self-assessment plan will be monitored by the local MCOQ lead or delegate.

2. **Performing the self-assessment**

Observations are documented and discussed with the personnel involved in the activity and the head of the function, preferably at the time they are observed, to ensure they are accurate and fully understood.

3. **Self-Assessment Reporting and follow-up**

Observations from self-assessments are entered and managed in the Veeva Global Quality system. These observations will be presented during Management Review. Observations made during the self-assessments should be classified as Critical, Major or Minor as per Classification and categorisation of Quality Events, Guideline, GUID-0008746. See details in the "How do I"- VQV portal (audit module)

Reports can be extracted from VQV to distribute locally as needed.

Corrective actions for critical observations are included in local Compliance Improvement Plan.

In addition to the local self-assessment, an annual Check list is completed on request by the Global MCOQ team.

2.6 Partnering and Outsourcing

Any GxP activity that is outsourced must be covered by a legal contract which defines the contractual obligations and a quality agreement describing roles, responsibilities, systems for communication and oversight to ensure compliance with procedures and regulations. AstraZeneca retains full accountability for GxP activities the AstraZeneca Pharma India Limited (AZPIL) has outsourced.

Why Do This:	How To:
To ensure: effective co-ordination of GxP activities, that standards are maintain activities are performed. **Status: Mandatory** when outsourcing: • To a third party • To a separate legal entity within AstraZeneca if not covered in an AstraZeneca written procedure. **Frequency:** For each outsourced activity.	1. Contracts and agreements require legal review and can be based upon the templates in the Global Legal Template Repository. Contracts and agreements must be signed and dated by both parties. The quality agreements cover roles, responsibilities, training, applicable procedures, quality checks and communication procedures. *2.* When contracting an external vendor AstraZeneca Pharma India Limited (AZPIL) must perform an assessment of the vendor and ongoing review to ensure oversight of the vendor. The Contracts and Agreement Guide, GUID-0021149 will illustrate on the main steps for the contract process For already contracted suppliers, to complement the regular oversight of the vendor in all applicable GXP areas, use the Global Veeva Quality system yearly Supplier assessments programme to assess their performance. See details under the "How do I"- VQV portal (audit module). Include as part of the programme the individual Supplier Audits (assessments), related Findings and CAPAs. An audit plan for external vendors which should be prepared each year in Q1 by the local MCOQ lead or delegate Also, Refer SOP-0034148 GMP and GDP Auditing of Suppliers and AstraZeneca Sites Global Procedure 3. Stand alone issues coming from vendors will be included in the Veeva Global Quality system (Quality Issue module)(see section 2.7.1)

2.7 Issue Management and Product Complaints

2.7.1 Issue Management

Why Do This:	How To:
Deviations from routine procedures (e.g. SOPs) or non-compliance with GxP requirements must be reported and managed to maintain control of GxP activities and correct and prevent errors. This area is a focus for regulatory inspections. **Status: Mandatory.** **Frequency:** As issues are detected. Issues registered prior to 20 July 2020 can be accessed at GXP Portal	• Anyone can identify a quality issue • The owner of the issue investigates the quality issue to clarify and validate the details. Follow SOP-0060443 Quality Issue Management and Reporting If the issue is confirmed, the creator/owner of the issue enters the issue in the Global Veeva Quality system. Details are in the "How do I"- VQV end user portal (Quality Issues and CAPAs section) • A Root Cause Analysis, GUID-0021151 or Level 0 is performed for at least the major and critical issues. Contact the RCA facilitator to facilitate the investigation. • Establish an immediate corrective action to contain the issue and define corrective and preventive actions which will address the root cause. • Define a reasonable time for actions implementation and follow up for completion. • Management review meetings must include review of issues and any trends in these, including recurrent issues.

as extracted noneditable excel: Archived tools (Link or within Toolkits (Link) From 20 July 2020 a global tool - Veeva Quality Vault (VQV) is used (Link).	• Global/Regional MCOQ teams are responsible for reviewing trends and repeat deviations across MCs.

2.7.2 Product Complaints

Why Do This:	How To:
A system and procedures for managing complaints, including potential quality defects, is required to prevent reoccurrence and, if necessary, recall medicinal products for human use, including investigational medicinal products, from the distribution network. This is critical to protect patients. **Status:** A process for documenting, investigating and escalating product quality complaints including complaints associated with adverse events (combined complaints) is **Mandatory** **Frequency: complaints must be reported within the target of one (1) working day.**	**1. Handling product complaints, including possible quality defects** AstraZeneca Pharma India Limited (AZPIL) is responsible for receiving, registering and closing complaints for India and for acting as the primary contact with the complainant regarding commercial products, including medical devices. This may apply to investigational medicinal products. The process for handling complaints in described in SOP-0121782: AZIND: Procedure for Management of Product Quality Complaints. Complaint management process includes receipt, documentation and assessment of the complaint to establish if there is a quality defect or other issue.. For complaints assessed to be product quality complaints, include: • Documentation of the quality defect. • Determination of the extent of the quality defect, including checking or testing of reference and/or retention samples and batch production records. • Requesting and managing a sample, or the return of the defective product, from the complainant. • The assessment of the risk(s) posed by the quality defect, based on the severity and extent of the quality defect. • The decision-making process for risk-reducing actions in the distribution network, such as batch recalls and warning letters. • The process for assessment of the impact of any recall action on the availability of the medicinal product to patients. • The need to notify the local health authority. • Identification of the potential root cause(s) of the quality defect. • The need for Corrective and Preventative Actions (CAPAs) to be identified and implemented and the assessment of the effectiveness of those CAPAs. • Retention of the records of each complaint. • Reporting and decision-making time-lines, according to the risk to patients posed by the product quality compliant.

- Any local process for an acknowledgement letter to the complainant Content can include thanking the contact, indicating that AstraZeneca has rigorous processes in place to assess and monitor product complaints received and will take appropriate steps to evaluate this matter .

A complaint might arise from:

- Commercial Marketed Product
- Investigational Medicinal Product (IMP)
- Materials/Supply (internal complaints)

Complaints are categorised into the following types:

- Product Quality Complaints (PQC)
- Combined Complaints.
- Supply and Logistics Complaints
- Temperature Excursions Complaints
- Product Security Complaints
- GDP Complaints

Establish whether the complaint or suspected quality defect relates to a product security issue.

2. **Registering a complaint**
   - All complaints that represent a potential quality defect are entered into the EQV/GPQS within one (1) working day. The EQV/GPQS tool assigns a unique identification number and provides the status and tracking of the compliant. Reports and dashboards in EQV allow trend analysis. Information is available on the EQV/GPQS sharepoint site

3. **Handling reports that are not product quality complaints.**
   If a complaint is an adverse event, medical inquiry, investigational study or product ordering inquiry and does not represent a potential quality defect, document the details and forward these to the relevant department. These events are not captured as a product complaint.

4. **Combined complaints.**
   If there is a quality defect associated with an adverse event it is considered a combined complaint and is entered into the EQV/GPQS tool and reported to Patient Safety as an adverse event.

More information in the PQC manual, GUID-0021793

2.7.3 Issue Management Teams (IMT)

AstraZeneca has clearly defined arrangements for issue management and recall of traded product, free goods, physician samples, medicines for Compassionate Use, Medicines for Named Patient use, Expanded Access medicines and Foreign Medication medicines.

Issue management aims at crisis prevention, regardless of whether the issue arises from internal or external activities. An Issue Management Team is initiated when a Product Quality Issue poses a potential threat to patients, a product or the business as a whole, to decide if in-market action is needed.

Why Do This:	How To:
A process for rapid and efficient establishment of an IMT to address a product quality issue is essential to ensure effective action in the event of a product quality issue that has the potential to impact patient safety. **Status:** A formal recall management process is **mandatory** **Frequency:** Mock recall must be conducted **once a year** to demonstrate that material can be traced to customers and that the arrangements for management of the recall, product return and reconciliation are adequate. (AZ Bangalore ops is responsible for IMT, Recall/Mock recall	When appropriate Global operations will convene a global IMT that may require a MC representative, as described in the global procedure 7-P10-cv-X Management of Product Quality Issues Affecting Distributed Product that may require In-market Action, SOP-0033749. For investigational products refer to 7-P11-CV-X Issue Management (Including recall) of Investigational Medicinal Products (IMPS), SOP-0075544. Details for the report of the IMT in the Veeva Global Quality system are in the "How do I"- VQV end user portal (Quality Issues-Quality issue investigation) Site procedure SOP-0046958 - " In-market Action" is followed for this process An annual mock recall test is performed to provide a holistic evaluation of the recall system and train staff on their tasks and responsibilities in the event of a recall. As per the Quality Agreement (AGR-0003467) with AZ Bangalore site, Recall responsibility is delegated to AZ Bangalore site . Any improvement action identified by the mock recall should be included in the compliance improvement plan.

3. REFERENCES & ASSOCIATED DOCUMENTS

Title
1. Global Standard - Quality Management System (QMS) and Quality Policy, STND-0001965
2. Research & Development Procedural Document Model, Standard, STND-0001445
3. Manage Procedural Documents in R&D and Commercial, SOP-0108676
4. Information Retention Global Standard, STND-0000673
5. GPF Global Standard - Engaging Third Parties (English), STND-0002095
6. 1-P3-cv-X GXP Compliance Management Review and Reporting, SOP-0033766
7. 1-P57-cv-X Quality Risk Management (QRM), SOP-0034065
8. Work Instruction: How to manage Quality and Compliance Manual (QCM) global procedural documents, WI-0015719
9. 1-P63-cv-X Local Quality Management for GXP Activities, SOP-0034048
10. 1-S1-CV-X Standard for Marketing Company Good Manufacturing Practice (GMP) and Good Distribution Practice (GDP), STND-0002250
11. 1-S4-cv-X Risk Management in the Quality and Compliance Area, STND-0000427
12. 2-S1-cv-M Personnel, STND-0000417
13. 2-P14-cv-M Designing And Delivering GMP Training, SOP-0107575
14. 2-P15-cv-M Managing GMP Training Programs and Learning Plans, SOP-0107576

15. 2-P16-cv-M Managing and Maintaining GMP Training Records, SOP-0107574
16. 3-S2-cv-M Premises and Equipment, STND-0000411
17. 3-S10-CV-XIS Computerised Systems, STND-0000429
18. 4-P49-cv-X How to Manage Content in the AZ Enterprise Content Management System (ECMS), SOP-0107560
19. 4-S1-cv-X Data Integrity Standard, STND-0000425
20. 4-S3-cv-X Archive Facilities Standard, STND-0000394
21. 5-S1-cv-X Quality and Compliance auditing, STND-0000419
22. 5-P34-cv-X National Competent Authority Inspections, SOP-0033764
23. 5-P38-cv-M GMP and GDP Auditing of Suppliers and AstraZeneca Sites, SOP-0034148
24. 6-P2-CV-M: Quality Management of Suppliers, SOP-0033739
25. 6-P5-cv-X Handling of Study Drug and Medical Devices in Clinical Studies, SOP-0075542
26. 7-S2-cv-X Standard for Complaints, Quality Defects and Recalls, STND-0002320
27. 7-P10-cv-X Management of Product Quality Issues Affecting Distributed Product that may require In-market Action, SOP-0033749
28. 7-P11-CV-X Issue Management (Including recall) of Investigational Medicinal Products (IMPS), SOP-0075544
29. 7-P28-CV-X Management of Combined Complaints, SOP-0107504
30. 7-P29-cv-X: Global Complaint Management, SOP-0107502
31. 7-P30-cv-X Product Quality Complaint Reporting, SOP-0107501
32. 7-P38 Deviation Management, SOP-0107503
33. 7-P42-cv-MO Selecting Appropriate Corrective and Preventive actions (CAPA) and Effective Assessments, SOP-0107541
34. Quality Risk Management for R&D and C-SET-Work Instruction, WI-0013423
35. Classification and Categorisation of Quality Events, GUID-0008746
36. Quality Issue Reporting and Management, SOP-0060443
37. Corrective and Preventive Actions (CAPA) Management, SOP-0060442
38. Critical Quality Event and Serious Breach Management and Reporting, WI-0013556
39. Global GMP/GDP Documentation Standard, STND-0002249
40. Global GMP/GDP Documentation Procedure, SOP-0107564
41. Global Quality Audit (GQA) Audits of Suppliers and AstraZeneca Sites Enterprise Quality Vault (EQV), SOP-0035612
42. Work Instruction: Managing GMP/GDP Audits in Enterprise Quality Vault (EQV), WI-0010005
43. Supplier Quality Management Process Responsibilities in EQV Audit Module, SOP-0040738
44. Supply and Logistics and Temperature Excursions Events, SOP-0114835

*Please consult the **AstraZeneca Glossary** for clarity on definitions as needed.*

4. DOCUMENT HISTORY

Version	Description of change
4.0	• QRM agenda and slide decks are referenced to Global template • QRM Presentation slides sign off requirement is captured. • Box folder link is provided where required • AZIND: Minor Change Control Form, FORM-0122057 is incorporated • GUID-0024639 AZIND: GXP New Starter checklist is added • PLAN-0119363AZIND: Annual GxP Training Plan is added • "TMP-0012419 AZIND: Generic Job Description Template for GxP" is added • FORM-0122058 AZIND : QCM Assessment Form is incorporated • Self assessment plan approval requirement by CP or MCOQ cluster Lead is added • Level 0 RCA tool added • Refrences are updated • Withdrawn references are removed. • Referenced SOP-0034148 GMP and GDP Auditing of Suppliers and AstraZeneca Sites Global Procedure
3.0	Revised the whole Quality manual inline to "Ops_MCOQ_Quality Manual template_English (TMP-0011217)" for MCOQ India due to transition of GMP/GDP activitities to MCOQ as of 1-Sep-2023. Please refer to change control CC-India-CCL-010 - GxP Future of Work.

2.0	• Updated in alignment with V.11.0 of TMP-0009120 - C-SET_ All _Quality Manual Template_English
	  ○ PQC manual added
	  ○ Links updated
	  ○ Update of references
	  ○ Removal of legacy numbers
	• QRM agenda template TMP-0011269 is referenced under section 2.1.1. (1)
	• Requirement of Senior managemnet approval for QRM minutes is captured under section 2.1.1. (2)
	• Job Handover/Knowledge trasfer procedure is captured under section 2.1.3 (6)
	• Box folder link is provided for change control log under section 2.1.4 (2)
	• Local change control numbering section is added under the section 2.1.4 (8)
	• Local job role asignement process is captured under the section 2.2.3 (1)
	• Periodic JD review requirment is captured under section 2.2.5 (3)
	• Local SOP "SOP-0103761" is referenced under section 2.4.1 & 2.4.2
	• Global procedures assessment process is captured under the section 2.4.2 (2)
	• Local SOPs references updated where required
	• Mock recal responsibility is captured under section 2.7.3
	• Appendix 1 : GxP Organogram is updated

1.0	• New Version • Prepared in alignment with V.9.0 of TMP-0009120 - C-SET_ All _Quality Manual Template_English

5. APPENDIX

Optional section can include visual examples, flows, and tables that help better explain the required practices covered herein within this document.

Appendix 1 Relevant GXP sources

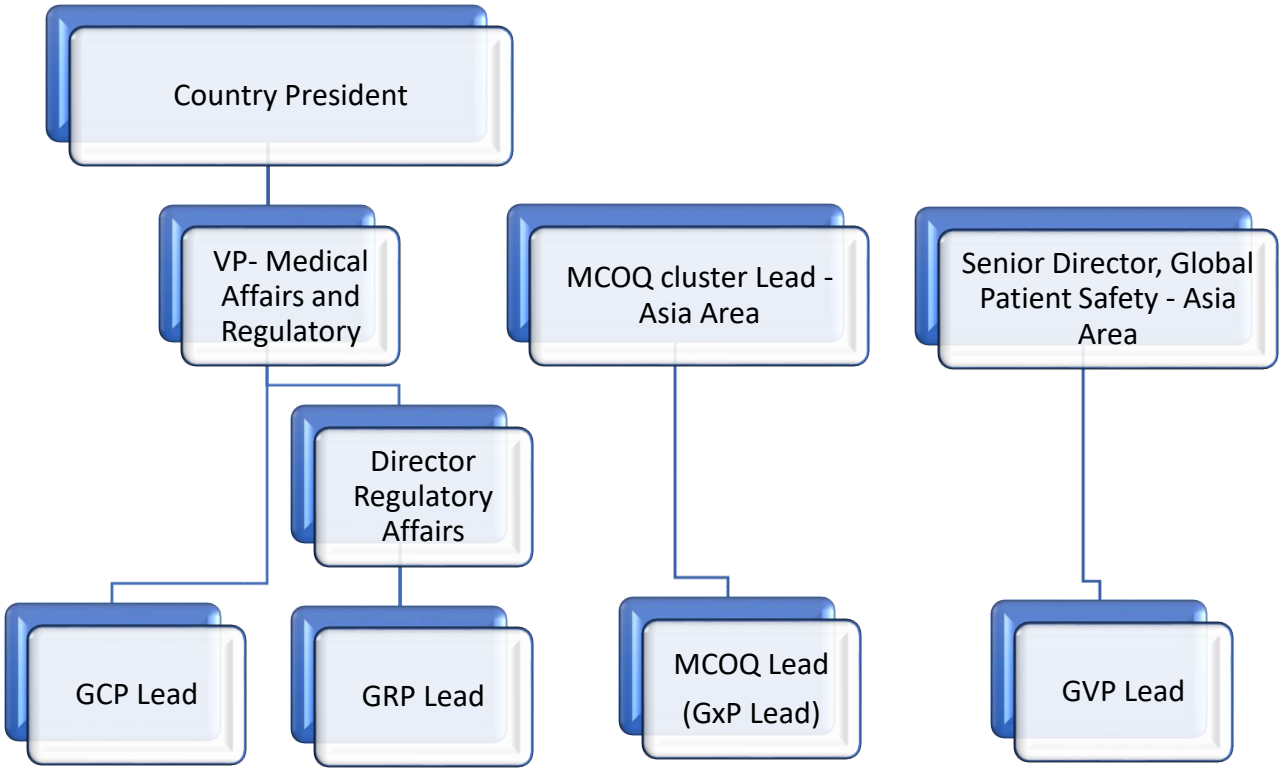
RACI for GXP areas impacting local markets, GUID-0023021

GVP Manual link GVP Manual

GRP Manual link MC Regulatory Process Manual

Medical Evidence website
https://azcollaboration.sharepoint.com/sites/TSM843/SitePages/Global-Medical-Delivery-Hub.aspx

Appendix-2 GxP organogram



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