ASTRAZENECA GLOBAL POLICY

QUALITY AND REGULATORY COMPLIANCE POLICY

1.   PURPOSE

This Global Policy outlines the top level requirements to support product quality and compliance in the development, manufacture and distribution of Active Pharmaceutical Ingredients, Medicinal Products and Devices.

2.   AUDIENCE

This Global Policy applies to all parts of the business to meet the needs of patients, health care professionals, and regulatory authorities through lifecycle management of products.

All AZ SET or business units are expected to follow this policy and any global standards and procedures or, provided they are consistent with this policy, their own local or functional standards and procedures.

3.   SCOPE

This Global Policy covers activities in science unit research & development, product licensing, commercial manufacturing & distribution, through to product discontinuation. It also applies to areas, or parts of them, which support those activities, such as IS/IT, regulatory affairs and marketing companies.

4.   POLICY STATEMENTS

In accordance with the AstraZeneca Code of Conduct and this Global Policy, the development, product licencing, manufacture, and distribution of active pharmaceutical ingredients, medicinal products and devices by the Company must be conducted in compliance with relevant International Codes and Standards, regulations for GXP - Good Laboratory Practice / General Laboratory Standard, Good Clinical Practice, Good Manufacturing /Distribution Practice and AstraZeneca Good Regulatory Practice. Local regulatory requirements, as well as the requirements of the countries to which products or data are supplied, must be satisfied.

The Senior Management of each AZ SET or business unit in scope must:

- Provide the strategic direction with respect to quality and the necessary resources, education, training and environment to achieve this direction.

- Ensure that everyone understands that they are responsible for quality.

- Implement a documented quality management system based upon the applicable laws and company standards as a minimum.

- Regularly review and continually improve the quality management system and its processes.

- Understand customers' and suppliers' requirements in order to facilitate mutually beneficial partnerships and continual improvement.

- Define which parts of this Policy, as described in the following sections, are applicable in their area, and ensure that those parts are implemented and maintained.

- Ensure that there are regular reviews of compliance with this Policy.

The responsibilities of management are further described with respect to eight topic areas.

4.1 QUALITY MANAGEMENT SYSTEM

Management of each applicable SET or business unit must ensure that:

- The Quality Management System ensures that all Company products, processes, supporting documents and product licences, are fit for their intended use.

- An independent Quality Assurance (QA) unit exists to assure management that the defined Quality Management System is effective.

- Management reviews of process performance and/or product quality and of the quality system are conducted.

- Measurable objectives that relate to this Policy are established within each AZ SET or business area, and plans are generated and executed to ensure that systems and processes are continually improved.

- Quality and compliance issues are reported to Senior Management through a defined reporting system to ensure that issues that may adversely affect patient safety or the Company's licences to operate are dealt with by the appropriate level of management. There must be a documented system to assess these issues, and to identify and implement corrective and preventive actions to avoid a recurrence.

- Risk management is integrated into Quality processes that are defined, reviewed and approved.

- Effective change management systems are in place for all changes that could affect the safety, quality or effectiveness of a product or process; the conduct of clinical or pre-clinical studies; documents submitted to regulatory authorities; approved product licences or compliance with applicable laws and Company standards.

- Knowledge must be managed to assure lessons are learned from significant internal issues, good practices, regulatory trends and external inspections and that these are shared within and across AZ SET or business areas as appropriate.

4.2 ORGANISATION AND PERSONNEL

Management of each applicable AZ SET or business area must ensure that:

- Organisational units have sufficient suitably trained staff and that the organisational structure is outlined in a current organisation chart showing key personnel and the independence of QA functions.

- All personnel, including consultants, have the appropriate education, training, skills and experience to carry out their work competently. All personnel must have written and up-to-date job descriptions/role descriptors that clearly outline responsibilities and accountabilities. Management responsibilities must be clear and people in key positions must have appropriate authority.

- Training programmes are in place to ensure that personnel understand the Quality Management System, relevant codes of practice and Company policies, procedures and guidelines. A training programme must include basic, job-specific, continuing and refresher training, which must be recorded and reviewed regularly. Trainers must be qualified.

- All personnel meet any medical or hygiene conditions that apply to their job.

4.3 FACILITIES, UTILITIES, EQUIPMENT AND COMPUTERISED SYSTEMS

Management of each applicable AZ SET or business area must ensure that:

- Facilities, utilities, equipment and computerised systems are designed, constructed, installed, qualified, maintained and decommissioned as appropriate to their intended use, and in compliance with the applicable standards and regulations. Any changes to facilities, utilities, equipment and computerised systems must be defined and controlled.

- The following elements are considered during design and operation of facilities, utilities, equipment and computerised systems:
    - o Adequate size/capacity;
    - o Suitable location;
    - o Logical layout;
    - o Degree of separation of activities;
    - o Ability to clean;
    - o Ability to prevent mix-ups, contamination and deterioration or loss of materials or information.

- Access to, and security of, facilities, utilities, equipment and computerised systems are defined and controlled.

4.4   DATA, DOCUMENTATION AND INFORMATION

Management of each applicable AZ SET or business area must ensure that:

- All paper, electronic or other data, documentation and information (collectively referred to as records) are managed and maintained in accordance with the standards and regulations that apply to the organisation or part thereof that is responsible for them.

- Written procedures are in place for managing records to assure their quality and integrity. As appropriate, procedures must describe record generation, modification, review, approval, retention, disposal and control of access.

- Records must be archived, as necessary, in secure archives with restricted access.

- All records are managed to ensure accuracy, integrity, security, readability and accessibility over the defined lifetime of the records. Transfer of records between media or formats must be controlled and validated.

- Data are recorded, evaluated, reported and communicated as necessary in an accurate and timely manner.

4.5   AUDITS AND INSPECTIONS

Management of each applicable AZ SET or business area must ensure that:

- Audits of internal activities, external suppliers and contractors are conducted, and by sufficiently independent individuals who possess the skills to assess compliance with applicable standards and regulations.

- Written procedures are in place to define scheduling, performing and reporting of audits, and timely follow-up of corrective actions.

- Internal audits are documented in formal reports that include clear details of the outcome of the audit. All audit reports must be issued as confidential documents and the list of recipients kept to a minimum. Audit observations must be classified according to impact and severity.

- Systems and procedures are in place for preparing, managing, conducting and following-up inspections by regulatory authorities, accreditation agencies or third parties.

- Processes are in place to inform Senior Management of all notices of external inspections and of progress and outcomes of external inspections.

- Management and Quality Assurance staff review any proposed Company responses and subsequent communications relating to external inspections.

4.6 CONTRACTS, AGREEMENTS, SUPPLIES AND MATERIALS

AstraZeneca is responsible for the quality and conduct of any work that is carried out on its behalf by any third party, and management of each applicable AZ SET or business area must ensure that:

- Outsourced work complies with applicable standards and regulations. The Company must be satisfied with the Quality Management System and compliance standards of the third party before any work is contracted out.

- A written contract or agreement that defines the quality and compliance requirements and the roles and responsibilities of all parties is in place between the Company and the third party. Similar agreements must be in place between organisational units within the Company to cover any work that one unit carries out on behalf of another unit, or where multiple units have individual responsibilities that must be coordinated to achieve a final outcome.

- Contracts or agreements are reviewed regularly and are readily available.

- The quality of purchased supplies and materials meets applicable standards and regulations. There must also be specifications, defined acceptance criteria, controlled storage, and segregation to preserve integrity, as necessary. The status of the items must be maintained either physically or electronically and procedures must describe sampling, testing, approval, expiration or re-test dating, as applicable.

4.7 ISSUE MANAGEMENT, RECALLS, ADVERSE EVENTS AND PRODUCT COMPLAINTS

Management of each applicable AZ SET or business area must ensure that:

- Systems and procedures are in place to assess the severity of an issue, adverse event or complaint, and for determining its potential impact on the safety, quality or effectiveness of a product or process.

- Systems and procedures are in place to manage major business issues, as well as to carry out investigations into issues that may affect product or patient safety, quality, efficacy or compliance with Good X Practice or related regulations.

- Issues, recalls and adverse events are reported in accordance with both applicable international regulations and the requirements of local regulatory authorities. Actions to be taken if a recall is required must be defined.

- Reported issues, adverse events or complaints regarding the Company's products or investigational materials are assessed and trended.

- Investigations into issues that relate to product quality, safety or efficacy are carried out in a timely manner and are prioritised and resourced appropriately. Investigations must be documented and include the scope, the determination of root cause, and corrective and preventive actions. Investigations must come to a conclusion, and any actions must be followed through until completed.

4.8 PROCESSES AND CONTROLS

A process (such as for example a clinical trial, non-clinical study, manufacture of a pharmaceutical product, regulatory submission or licence change) can include planning, designing, carrying out, monitoring, recording and reporting of the process. Management of each applicable AZ SET or business area must ensure that:

- Processes are designed to be fit for purpose and robust, and that the necessary resources, activities, milestones, responsibilities and accountabilities are defined.

- Documented procedures exist for all processes and controls that are required to meet international standards or the Good Practice regulations, or to comply with the Quality Management System.

- All processes are verified or validated in accordance with applicable requirements.

- Procedures are in place to accept or reject inputs (for example test subjects, test systems, raw materials) according to pre-defined requirements.

- Processes are monitored to guarantee the desired quality of the outputs.

- Procedures are in place to accept or reject outputs (for example clinical data and results, clinical trial reports, raw data and specimens, non-clinical study reports, investigational materials, analytical results, finished drug product, regulatory approval status) according to pre-defined requirements.

- Process performance must be regularly assessed, to evaluate the suitability, adequacy and effectiveness in delivering the defined outputs, and must be continually improved.

5.   GLOSSARY

Terms	Definition
GXP	**Good X Practice (AZ Glossary)** **Definition: Generic Term, Regulatory Agency compliance. X can mean for example Clinical, Laboratory, Pharmacovigilance, Manufacturing Distribution, Regulatory**

6.   REFERENCES

Not Required

7.   REVISION HISTORY

Version	Description of Change
4.0	**Policy reformatted to comply with new AZ PDM Policy Template** **Scope of applicability changed from "SET/Function" to "AZ SET or business area"**