
# Competences of Qualified Persons

## A Framework for Individuals Seeking Nomination as a Pharmaceutical Qualified Person

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## About TSET

The Technical Specialist Education and Training group was originally founded to address manpower issues for the various pharmaceutical technical specialist roles in the NHS, notably production, aseptics, quality assurance and radiopharmacy. The group has developed a vital role in identifying training requirements and stimulating the provision of targeted educational programmes. More information can be found at www.tset.org.uk

## Introduction

The purpose of this document is to provide a guide, primarily intended for the NHS, to the competences required by those seeking nomination as a pharmaceutical Qualified Person (QP), as defined in EU legislation.

It is not intended to take the place of the QP Study Guide (published jointly by the Royal Pharmaceutical Society, the Royal Society of Chemistry and the Society of Biology) which lays down the practical experience and underpinning knowledge requirements necessary for nomination. However as competence is a blend of knowledge, skills, attributes and the ability of an individual to apply this in practice; this framework aims to draw together these elements into a set of composite competences. The framework takes underpinning knowledge from the Study Guide, attributes from the Sponsor Form and legal professional duties of the QP, to form the competences which a candidate can utilise to aid their personal development and hence pathway to nomination.

The competences are compiled into clusters, for convenience predominantly mirroring the Study Guide. Within each cluster is additional supporting information. The framework can be used by both nominee and sponsor as a checklist of competence already attained, an assessment of nominee strengths and weaknesses, and as a gap analysis, therefore pinpointing where the nominee has training needs and should focus their personal development. Completion of the framework should act as reassurance that the nominee has covered the requisite body of knowledge necessary to support their application.

| Expert Professional Practice | |
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| **1. Pharmaceutical Law and its Administration - Competences** | |
| | Demonstrates a comprehensive knowledge of National and European Law relating to the manufacture, testing, storage, sale and supply of licensed or investigational medicinal products.<br><br>Demonstrates awareness of the drivers and evolution of key guidance documents, their inter-linkage and relationship with UK law.<br><br>Recognises the statutory obligations with regards to the release for sale of any pharmaceutical product.<br><br>Demonstrates comprehensive knowledge of marketing, manufacturing and wholesaler authorisation structure, content, application and approval procedures, and responsibilities. |
| Associated Skills and Knowledge | |
| The Qualified Person should demonstrate knowledge of the following European Directives and UK Statutory Instruments:-<br>• EPD 2001/20/EC<br>• EPD 2001/82/EC<br>• EPD 2001/83/EC<br>• EPD 2003/94/EC<br>• EPD 2004/24/EC<br>• EPD 2004/27/EC<br>• EPD 2004/28/EC<br>• SI 2004/1031<br>• SI 2005/2789<br>• EC 726/ 2004 | |

In addition the Qualified Person should have knowledge of, interpret and apply:-

- The Medicines Act (1968) plus amendments
- Veterinary Medicines Regulation, plus amendments
- Role, legal status and structure of the European and British Pharmacopoeia
- Marketing, manufacturing and wholesaler dealer licensing processes
- Mutual recognition agreements (**MRA**)
- Pharmaceutical Inspection Co-operation Scheme (**PICS**)
- International Conference on Harmonisation (**ICH/VICH**) guidelines (ICH Q8 and specifically Q9 and Q10)
- Health and Safety at Work Act
- Federal Food Drugs and Cosmetics Act
- Product liability and Trade Description Act

Organisation, role, structure , responsibilities of and documents published by the following authorities / agencies:-

- Medicines and Healthcare products Regulatory Agency (**MHRA**)
- European Agency for the Evaluation of Medicinal Products (**EMA**)
- **European Directorate for the Quality of Medicines** & HealthCare (EDQM)
- The European Federation of Pharmaceutical Industries and Associations (EFPIA),
- Veterinary Medicines Directorate (**VMD**)
- Committee for Medicinal Products for Human Use (**CHMP**) and guidelines on quality
- Committee for Medicinal Products for Veterinary Use (**CVMP**) and guidelines on quality
- Non European Union medicinal product regulators with whom activities relate

This is not a prescriptive list and other documents should be sourced as required

| 2. The Role and Professional Duties of a Qualified Person – Competences | |
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| Releasing | Demonstrates ability to fulfil ethical, legal and professional obligations of the licence holder [(MA, MIA(IMP)].<br><br>Able to assess batch disposition, defend and approve certification, release or non release and reprocessing.<br><br>Able to demonstrate an understanding of the key factors, information or metrics that confirm that a batch of pharmaceutical product has a suitable pedigree demonstrated throughout the manufacturing supply chain and has been made to GMP.<br><br>Demonstrates ability to oversee and delegate duties as appropriate.<br><br>Understands role when acting as independent contractor or on behalf of third parties. |

## Associated Skills and Knowledge

**Skills will not be specific to this section but will encompass those found throughout this document.**

- The GMP requirements for Import and Export of medicinal products within the borders of the EU and between the EU and "Third Countries".

| 3. Quality Management Systems - Competences | |
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| Principles of GxP QA and QC | Can demonstrate an in-depth knowledge of EU guidance on GxP and functions of QA/QC. |
| Design criteria of QM Systems | Understands that which makes up the scope and content of a robust QMS.<br><br>Able to design and implement a QMS.<br><br>Describe an effective organisational structure. |
| Audit and self inspection and regulatory affairs, including product quality reviews | Able to appropriately prepare for and respond to regulatory inspection. 6<br><br>Able to perform requisite audits and self inspections. 1<br><br>Able to provide the interface between the licence holder and regulator.<br><br>Able to perform product quality reviews.<br><br>Able to carry out root cause analysis.<br><br>Able to advise on CAPA where necessary. |
| Audit and Inspection - External Technical agreements, contract acceptances | Able to draw up technical agreements.<br><br>Able to design Key Performance Indicators.<br><br>Able to perform requisite external audits including API suppliers.<br><br>Able to adjudicate, accept and award contracts. |
| Deviation and change control | Demonstrates understanding and implementation of deviation and change control systems.<br><br>Monitors and assesses deviations and approves or declines changes. **2** |

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| Documentation control | Able to design, prepare, review and approve documentation, master templates and control master plan.<br><br>To include:<br>• Master templates<br>• Operation specific SOPs<br>• Logs and action limits<br>• Product specific worksheets (batch manufacturing records) and labels<br>• Site master file<br>• Laboratory test and recording documentation<br>• Clinical trial documentation<br>• Final product and active pharmaceutical ingredient specification documents |
| Design, qualification and maintenance of the environment/premises and equipment | Demonstrates knowledge of URS development, DQ,IQ OQ PQ. 3,4<br><br>Understands their application in procurement and qualification processes calibration, planned preventative maintenance for premises and equipment used for the manufacture of intermediate and final products.<br><br>Demonstrates an understanding of the key equipment used in own products.<br><br>Demonstrates understanding of environmental standards and monitoring requirements. 7 |
| Materials Management<br>Supplier certification | Demonstrates knowledge of Pt II of EU Guide to GMP (APIs)<br><br>Understands responsibilities with regards third country suppliers (MRAs) |

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| Production planning | Demonstrates an understanding of production scheduling on inventory. |
| Provision of Training | Possesses requisite skills to develop, deliver, assess and record effective GMP training.<br><br>Sponsors/supervises/mentors QP trainees/applicants. |
| Complaints and Recall | Demonstrates ability to handle complaints and apply and coordinate recall procedures appropriately. 5<br><br>Liaise appropriately with the MHRA Defective Medicines Reporting Centre.<br><br>Able to process product / service complaints.<br><br>Understands responsibilities with regards reporting non conformances. |
| Distribution | Understand the role of brokers, distributors and repackagers.<br><br>Understand the monitoring and control of both raw material and finished product storage transport and distribution. |
| Process Validation | Understand the principles of process validation design, control and evaluation. |

| Associated Skills and Knowledge |
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| 1. Content and practice of audit<br>2.Impact and risk assessment methods and evaluation.<br>3. Underlying principles of validation design and evaluation<br>4. Design and function of cleanrooms including ventilation and water systems.<br>5. Defective Medicine evaluation and categorisation<br>6. MHRA role, inspection processes and sanctions<br>7.Principles and requirements for environmental monitoring and establishment of limits pertaining to specific dose forms<br>8.Measures for prevention of counterfeiting and illegal activities |

| 4. Statistics – Competences | |
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| Standards | Demonstrates knowledge of standards pertaining to sampling, validation, acceptable quality, process control and analytical methods. |
| Statistical Tools | Demonstrates the ability to choose and apply statistical tools in the evaluation of data pertaining to processes, acceptability of results and setting of limits etc.<br><br>Demonstrates understanding of, precision, accuracy, linearity and range, specificity, selectivity, LOD / LOQ, in the use and choice of statistical tools and when interpreting or comparing data sets. |

**Associated Skills and Knowledge**

The QP must demonstrate knowledge of statistical tools such as:

- BS6000-6001 (Sampling Plans)
- BS6002 (Sampling by variables)
- ISO2859 (Sampling procedures for inspection by attribute and declared quality level)
- Statistical Process Control and Process Control Charting (Trending), including but not limited to, Shewhart Charts, Cusum Charts, Pareto Analysis and Cpk.
- Acceptable Quality Levels (AQLs subset 6001/2)
- Fiducial Limits
- Other common statistical tools such as standard deviation, geometric mean, Dixon's Q Test, 'T' Test and their application
- Data processing methods
- Principles of Six Sigma

| 5. Medicinal Chemistry and Therapeutics - Competences | |
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| | Demonstrates understanding and appreciation of the actions and uses of medicinal products in clinical practice.<br><br>Demonstrable knowledge of 'own product' including risks, contraindications and alternative therapies.<br><br>Judge where, clinical practice and medicine use, impact on product design/development or process and facility design.<br><br>Evaluate or predict where process needs and user indications may collide.<br><br>Evaluate significance of clinical data in product complaint or incident.<br><br>Understand responsibilities of Qualified Person for Pharmacovigilance (QPPV). |

Associated Skills and Knowledge

- Basic physiology
- Describe key therapeutic drug classifications with examples
- Pharmacology- absorption, distribution, metabolism and excretion.
- Pharmacovigilance- Risks, adverse effects and quality/complaints and post market surveillance
- Pharmacoenvironmentology- risks and responsibilities
- Disease states and their treatment
- Knowledge of the properties of drugs/chemicals/materials and their relationship to design of facilities, health and safety, scheduling, campaigning or segregation, equipment choice and cleaning.
- Knowledge of the chemical structures and relationship to pharmacological actions.
- Describe key routes of administration
- Underlying principles of Homeopathy
- General implications of clinical knowledge of drugs in relation to investigating incidents and deviations.

| 6. Pharmaceutical Formulation and Processing – Competences | |
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| | Able to ensure safe and appropriate product development. |

Associated Skills and Knowledge

- Actions and uses of excipients such as preservatives, emulsifiers, thickeners, and suspending agents.
- Manufacturing processes for major dose forms, their limitations and critical control parameters.
- Sterilisation methods.
- The factors that could potentially affect purity, content uniformity, stability (chemical, physical and microbiological) and bioavailability in manufacture.
- The principles of technology transfer and production scale-up.
- Pre-formulation studies and product development.

| 7 . Pharmaceutical Microbiology - Competences | |
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| | Understands the source and range of organisms present related to pharmaceutical production.<br><br>Able to apply microbiological knowledge to product and process design.<br><br>Able to draw up policy relating to environmental control and testing.<br><br>Contributes to the setting of policy with regards personnel health related issues.<br><br>Approves policies and procedures pertaining to the prevention of contamination of starting materials, finished product. |

Associated Skills and Knowledge

- Microbiology- microbial classification, morphology, identification, growth, cultivation and inhibition etc.
- Endotoxins and pyrogens- origins and nature, destruction/removal and tests for
- Contamination risk- Sources and pathways
- Product protection methods
- Selection and efficacy testing of preservatives and disinfectants
- Microbiology/sterility test methods (Including , product development, in- process and environmental and QC)
- Sterilisation methods
- Microbiology of water, its production and distribution systems; inc different grades of water, their use manufacture and control
- Rapid methods of microbiological testing.

| 8 . Analysis and Testing | |
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| Analysis and Testing | Demonstrates knowledge of range of analytical, biological and stability test methods and their validation.<br><br>Able to accurately interpret data and possess and understanding of the limits of test methods, data and results.<br><br>Able to identify out of specification, out of trend or non-conforming data/results.<br><br>Understand organoleptic test methods and applications.<br><br>Demonstrates requisite knowledge to appropriately design sampling regimes.<br><br>Understand responsibilities for contract testing/analysis.<br><br>Approves test methods and limits. |

**Associated Skills and Knowledge**

- Knowledge of the significance of degradation, contamination, adulteration of pharmaceutical materials and finished products
- The underlying principles of and interpretation of qualitative and quantitative analytical methods in common use for the analysis of medicinal products
- Sample retention and retesting
- Out of specification result implications, significance, monitoring and control
- Bioassay
- Pharmacognosy
- EU GMP Annex 19
- GcLP (Good Control Laboratory Practice)
- The underlying principles, methods and types, purpose, significance and management of systems of in-process control
- The underlying principles, application and interpretation of stability testing (protocols & methods), used during development

to determine product shelf life and support ongoing marketing of the product
- The underlying principles, application and design of sampling regimes
- The underlying principles, application and design of analytical method transfers
- The ICH guidelines for method validation, impurities and stability testing;

Radiopharmacy QP/IMPs would additionally require:
- Knowledge of Paper and thin layer radiochromatography and radioHPLC
- Knowledge of electrophoresis followed by radiochromatography
- Knowledge of Light microscopy
- Knowledge of particle sizing by ultrafiltration methods
- Knowledge of electrospray mass spectroscopy , receptor binding assays using cell lines, and animal biodistribution studies

| 9. Pharmaceutical Packaging - Competences | |
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| | Demonstrates knowledge of packaging material properties, design and testing such as to facilitate approval of packaging material choice and test methods.<br><br>Understands the common causes of component and label mix-ups and applies to the approval of reconciliation, line clearance processes and production pathways/process designs.<br><br>Understands the chain of systems which ensure the integrity and accuracy of textual information from originator to routine production, including artwork generation, text approvals and regulatory submission requirements.<br><br>Demonstrates familiarity with different types of packaging and labelling processes and equipment. |

**Associated Skills and Knowledge**

- Knowledge of tamper-evidence, supply chain security and anti-counterfeiting measures
- Knowledge of the properties of packaging materials and their potential effects on product stability
- PS9000
- Knowledge of test methods for ascertaining the effect of packaging on product and vice versa
- Knowledge of Labelling Regulations 1976, MHRA guidance, use of Braille, barcodes and PILs
- Control of packaging components by suppliers and throughout production
- The testing of packaging materials as part of incoming goods checks, including the application of sampling regimes and Vendor Assurance programmes
- The potential root causes of label and other printed component mix-ups and how they can be identified and eliminated
- The underlying principles and application of in-process controls conducted during packaging operations, including line clearance, pack integrity testing, challenge testing reconciliation,; bar coding and optical systems

| 10. Active Pharmaceutical Ingredients - Competences | |
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| | Understands how Active Pharmaceutical Ingredient and excipient attributes along with manufacturing processes, may influence the quality of finished product<br><br>Demonstrates familiarity with API manufacturing processes and controls |

Associated Skills and Knowledge

- Analytical chemistry
- Excipients - effects, purpose and limitations
- Impurities- generation, identification, quantification elimination and prevention
- Physico-chemical/biological properties of active ingredients, attributes and effects on dose form, preparation methods and use
- Homeopathic products and associated directives and regulations
- Registered Herbal Medicinal Products and associated directives and regulations
- Non traditional, atypical actives
- The steps commonly taken in the manufacture of Active Pharmaceutical Ingredients (API) and excipients (*including, where specific to the applicants chosen dosage form and ML experience, biopharmaceuticals*, blood products, immunological, cell therapy, gene therapy and herbal products), their purpose and limitations
- The requirements of Good Manufacturing Practice as applied to the production of APIs
- The underlying principles and application to the EDQM for Certificate of Suitability; (CEP)
- The potential and avoidance of contamination and adulteration of API and verification of the supply chain pedigree
- The requirements for API intended for use in sterile products
- The requirements for control and declarations regarding adventitious infectious agents e.g. Transmissible spongiform encephalopathy (TSE)
- API audit and Certification requirements.

| 11. Investigational Medicinal Products (IMPs) - Competences | |
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| | Understands the difference between manufacture of licensed products and IMPs.<br><br>Understands IMP, placebo and comparator procurement, importation, control and release.<br><br>Understands the role of Ethics Committees in research and development.<br><br>Able to set up a Product Specification File for a clinical trial.<br><br>Able to prepare a Clinical Trial Authorisation application.<br><br>Able to prepare Investigation Medicine Product dossier and Summary of Product Characteristics (IMPd and SmPC).<br><br>Demonstrates understanding of trial subject protection issues.<br><br>Demonstrates knowledge of analytical tests specific to IMP development, testing and use.<br><br>Demonstrates understanding of the conduct and obligations of Clinical Trial Sponsors and IMP providers. |
| Associated Skills and Knowledge | |
| • Understanding of trial blinding, emergency un-blinding and randomisation<br>• Use of placebos and comparators<br>• GCP<br>• An appreciation of World Medical Association (WMA) Declaration of Helsinki<br>• EU GMP Annex 13 and 16<br>• The underlying principles and application of the manufacture and control of active and placebo dosage forms | |

- The control and release of imported IMPs, comparators from EU/EEA countries, MRA countries or “Third Countries”
- Controls surrounding the procurement, storage, distribution and control of IMP, NIMPs, Placebo and licensed and un-licensed Comparators
- The underlying principles, interpretation and application of Good Clinical Practice (GCP), including protection of trial subjects, data integrity, the role of the Sponsor and Ethics Committees and Pharmacovigilance requirements
- The structure and contents of the Clinical Trial Applications (CTA), including the EUdraCT forms, protocols, IBs and IMPD and subsequent authorisation
- An understanding of clinical trial design at all phases (I, II, III and IV) including early stage safety and dose ranging (SAD/MAD) studies through to post marketing studies
- Understanding of the requirements for specific dosage forms and drug types. Use of radioactive Positron Emission Tomography (PET); and interpretation of tissue tracer activity

| 12. Personal, Management and Leadership - Competences | | |
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| | Is able to maintain good working relationships. | ACLF 2. No 2 |
| | Demonstrates ability to communicate effectively using varied skills (written and oral). | ACLF 2. No 1 |
| | Is assertive. | |
| | Demonstrates flexibility and open mindedness. | |
| | Demonstrates the ability to work under pressure. | |
| | Is able to plan and organise effectively. | ACLF 4 No 8 |
| | Operates ethically and with integrity. | |
| | Demonstrates reliability in attendance and performance of duties. | |
| | Demonstrates problem solving skills. | |
| | Demonstrates ability to lead and act as role model. | ACLF 3. |
| | Demonstrates ability to mentor others. | ACLF 5. No 2 |
| | Able to demonstrate advocacy skills (including Devil's) and debate rationale. | |

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| | Able to apply judgement skills.<br><br>Able to manage risk effectively, detecting and resolving threat.<br><br>Able to assess learning needs, plus plan and deliver successful training.<br><br>Able to generate and apply research evidence.<br><br>Acts consistently.<br><br>Able to translate and extrapolate their working knowledge and understanding, taking a logical and defensible approach even in unfamiliar territory.<br><br>Demonstrate commitment to professional development and staying up to date with current developments in the field.<br><br>Demonstrate networks and fora for ensuring currency of knowledge. | ACLF 1. No 3<br><br>ACLF 4. No 4<br><br>ACLF 5 No 4 and 6<br><br>ACLF 6<br><br>6 |

6 ACLF- Advanced and Consultant Level Framework 2009 (Competency Development and Evaluation group .**CoDEG.org**)