White paper:

How to implement a Pharmaceutical Quality System (PQS)

This Whitepaper will guide you to implement your PQS.

As the size, type and nature of organisations vary, this Whitepaper may not cover all circumstances unique to your company, however, it details the typical process that we use at PharmOut when implementing a PQS at a client site.

Pharm✓ut®

Introduction

This Whitepaper is intended as a guide to implementing a Pharmaceutical Quality System (PQS) within your organisation. As the size, type and nature of organisations vary, this Whitepaper may not cover all circumstances unique to your company, however, it does provide the typical process that PharmOut consultants use when implementing a PQS at a client site.

This Whitepaper is based on the ISO 9001 framework as it provides an excellent and practical model. Specific Good Manufacturing Practice (GMP) requirements for a pharmaceutical or medical device company can easily be integrated with this model (ICH Q10, PIC/s and/or ISO 13485). PharmOut recommends careful consideration of the relevant compliance standards to ensure all requirements are included.

Managing the change

Migrating an organisation from a pre-quality system state to one that operates with the rigours of quality and control is not a casual task. There is a tightening of how processes are managed and often changes in staff interactions, responsibilities and accountability. Such a change is unlikely to succeed without the dedicated support of both the executive and operational management.

The greatest resource of a company is its people, and strategies for managing both real and perceived change, or concerns and attitudes, should be addressed during the initial planning of the PQS.

It is likely that during the first 6 to 12 months, executive management will need to positively reinforce the PQS requirements on a routine basis to ensure that staff maintain motivation and do not lapse back into old habits. Tweaking of the PQS documents should also be expected as staff become accustomed to the requirements and begin to suggest usability improvements.

The benefits to the organisation of a properly functioning PQS are not just restricted to the knowledge that it complies with regulatory requirements, but that it has the discipline to manage customer requirements effectively.

PQS documentation requirements

A company requiring GMP and/or ISO compliance must establish, document, implement and maintain a PQS, as well as maintain its effectiveness, following the required quality standard.

PQS documents require the following elements:

- documented statements of a quality policy and quality objectives
- a Quality Manual that includes:
  - the scope of the PQS including details of, and justification for exclusions
  - documented procedures for the PQS or reference to them
  - a description of the interactions between the processes of the PQS.
- documented procedures required by the compliance standard (if not located within the Quality Manual)

- documents needed by the organisation to ensure effective planning, operation and control of its processes
- records required by the compliance standard such as evidence of conformity to requirements and the effective operation of the PQS.

Using a documented procedure ensures that:

- all staff perform the same duty in the same way, every time
- all data is recorded in a similar manner
- new staff are trained to a consistent standard.

Records, including monitoring data, batch records, audit findings, labels, QC testing results, non-conformance reports, corrective actions, etc. are evidence that the PQS is being used and that processes are effective.

Controlling documents

Documents within the PQS must be controlled so that only the current version is available to staff while performing their duties, and procedures must be in place to reflect the day-to-day management of all controlled documents.

Documents must have the following key elements to be compliant:

- a unique identifier, typically a letter code for the type of document (for example, SOP, WI, FRM, LST) and a sequential number
- version control where each update to the document must result in an incremental increase in the version (revision, edition etc.) number
- a change history that summarises the changes made to a document each time it is updated
- signatures from the preparer and authoriser (or approver) of the document. A verifier signature is also usually required to confirm that the content of the document is accurate
- the date of revision, if not updated before a specified review period.

Controlling records

Records should be controlled and managed by assigning unique identifiers to individual record types to ensures that they are traceable and retrievable. Appropriate systems to manage records should be documented.

PQS document hierarchy

Controlled documents are typically organised and written according to a hierarchy:

Document Type	Description
Quality Manual	This is the high-level document that provides policy on the company's processes (that is, how the company's PQS works). It details: ▪ PQS requirements ▪ management responsibilities ▪ management of resources for all aspects of the company ▪ how manufacturing will be designed, validated and conducted ▪ customer-related processes ▪ Quality Assurance processes.
Policies	A high-level document that details overall business decisions or strategy. Policies are usually shorter documents that describe why something is done or the high-level rules. Policies are not procedural. It is acceptable to document policy-type material in either the Quality Manual or a procedure if preferred.
Procedures	Details all the procedures required by the company to plan, operate and control its processes. Procedures for smaller/simpler PQSs may also be incorporated into the Quality Manual or multiple procedures may be combined (where appropriate).
Work instructions	Details the step by step instructions required to perform a section of a procedure.
Forms	Captures records for all data/information required to support or confirm the company's processes. A company may prefer to capture forms either as separate controlled documents or within the associated procedure.

Additional controlled document types may also be used at the discretion of the company depending on requirements or preferences. These may include:

▪ manuals
▪ training assessments (or other training documents)
▪ engineering drawings or plans
▪ lists, logbooks or templates.

Where do I start?

The following sections outline a general approach for preparing the PQS. You may also use the *PQS Preparation Checklist* at the end of this Whitepaper to ensure that the documentation requirements have been met.

Generate templates for the controlled documents

Templates should be written for all the controlling document types intended to be used. All templates should have consistent styles and formats so that the documents are easy to navigate and read.

Each template must meet the controlled document requirements (e.g., have a unique identifier, version control, etc). Templates for procedures and instructions should typically include a Purpose, Scope and Responsibilities section (or equivalent).

A company logo can be included with the document header details if required. This is optional depending on preference or concerns regarding logo size, colour, file size or whether the documents will be primarily used online or hardcopy.

Identify current procedures

Most companies already have some written policies and/or procedures, however, these may be incomplete, lacking specific detail, out of date, or not integrated with other business processes. It is recommended that you make a list of all these documents and their status (such as current, out of date, inaccurate, etc).

There may be some areas of the business which you may decide are out of scope for the PQS, such as finance, billing, marketing or business development. Such areas must not have an impact on product quality or safety to be deemed out of scope.

Map your processes

It is advised to map the processes used to manage the quality framework, including their sequence and interaction with each other (typically using a flow chart). You should consider running a brainstorming session or workshop with multidisciplinary team members (and all appropriate stakeholders). During these sessions, gaps should be identified e.g. where documents are missing or where a process needs to be updated to meet regulatory requirements.

It is very helpful to map the controlled documents in their hierarchy, in a similar fashion to an organisation chart (see example below).

Note: Document names in the following figure are for illustrative purposes only and are not intended to be document examples nor represent the total number of controlled documents required.
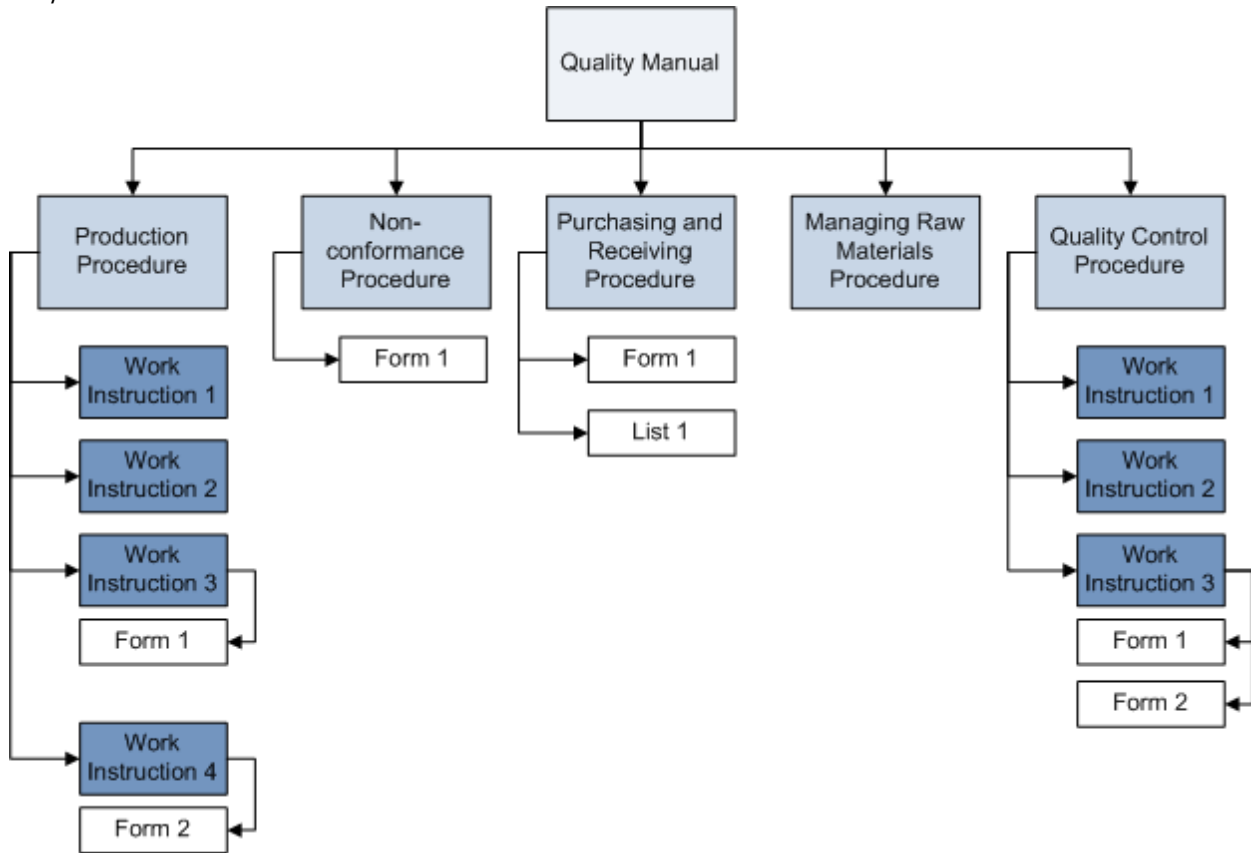
Document numbering can be based on the hierarchy so that work instructions, forms and list numbering reflects the parent procedure numbering, however, alternate document numbering conventions are also acceptable.

Draft the documents

When drafting documents, you should consider the primary audience (and where they are likely to use the document) and use language and vocabulary that is appropriate. For example, if the company has a significant number of bilingual staff, then documents should be written to reflect that level of literacy.

A plain English style is always best when drafting documents. The following general rules also apply:

- if you stumble over a sentence when reading it aloud, then it is probably too complicated or poorly worded
- the size/type of fonts and page layouts should be appropriate for how the documents will be predominantly used (electronic vs hardcopy)
- avoid using colours or backgrounds that can make it difficult for staff with vision or reading difficulties

- consider the writing style is appropriate. For example, work instructions lend themselves to be very structured with numbered steps whereas procedures may be more appropriate in a paragraph style

- don't mix information types. Keep theory, technical background and rules/warnings separate from procedural steps. Mixing information types can create confusion and misunderstanding which may lead to a task being performed incorrectly.

You can increase the readability of your procedures by using simple sentences. You may like to use an online tool such as http://www.online-utility.org/english/readability_test_and_improve.jsp to test readability.

You can also check that the procedure is usable by performing a 'usability test' and asking someone unfamiliar with the task to follow it. Make notes about where they found the document difficult to follow.

Manage electronic drafts

Once drafting begins, PharmOut suggests saving the PQS files with a document control suffix in the file name in a separate folder to the original files. This ensures that the original templates are always available and helps track draft/review stages.

Some examples may include:

- track the draft version - QM001 Quality Manual_v01a, b, c etc.
- track the date of review (1ˢᵗ Jan 2021) – QM001 Quality Manual_010121
- track a reviewer – QM001 Quality Manual_JBloggs
- a combination of the above.

It is important to maintain consistency in the document control mechanism you decide to use during the drafting process.

Make a list (spreadsheet) of all documents with the document number, title, version number, and status of the review. This document can also then easily be amended to form the Master Document List when the PQS is ready to go live.

Review the documents

Ensure that all documents are reviewed by subject matter experts (SMEs) from all areas that are affected by the scope of the document.

Issuing a controlled document that affects an area where staff have not had the opportunity to review may cause unnecessary friction, reduce compliance, and increase the risk of deviation.

Issue the documents

Prepare hard copies of all documents and obtain the appropriate approval as dictated by the compliance standard. Issued original hard copies (and usually MS Word versions) should be filed in a secure location.

Once the PQS documents are approved and are ready to be implemented (issued), the files should be saved and published according to the document control procedure.

Using MS Word functions

The following section suggests the functions that may be used when preparing a PQS (using MS Word). Help for specific problems or different versions of MS Word should be sourced from the Microsoft Office help: https://support.microsoft.com/en-us/office.

Using document styles

The Styles function within MS Word applies a set of formatting characteristics to a document, such as a font name, size, colour, paragraph alignment and spacing.

It is recommended to use document styles so that:

- the same set of styles are available to generate all PQS documents
- consistent formats can be quickly and easily applied throughout the document
- MS Word features like header numbering, table of contents and the document map are easily generated and then maintained during editing and review.

Using fields

MS Word uses fields to perform a variety of functions, including:

- inserting the date and time, footnotes, tables of contents
- inserting information to multiple places within the text (e.g. Company Name)
- performing mail merges.

Using page breaks

Page breaks should be reviewed when you paginate your document. Insert a page break rather than pressing the Enter key multiple times to break the information to the next page. This ensures that subsequent changes in the text appearing before a page break do not alter the pagination.

Using section breaks

These allow the document to be divided into separate sections containing different layouts (e.g., portrait versus landscape page orientation) or formatting (e.g. different section headers/footers).

Important: Headers and footers can be linked or separated from one section to another. Deleting a section break before breaking the link can alter headers/footers linked to the previous header/footer throughout the document.

Using bulleted and numbered lists

Always use a stem sentence to start a bulleted list. Bulleted lists should be used when order is not important.

Reserve numbered (or lettered) lists when it is necessary to show priority or chronology. Use bulleted lists for all other options.

PQS Preparation Checklist

The following checklist may be used during the preparation of PQS documents.

Step	Description	Completed? (✘ / ✔)
1	Identify your company's key processes, existing procedures, and management and control systems needed for the PQS.	
2	Map the key processes and procedures so that their sequence and interaction is clear. Highlight any area that is missing a process or procedure that is required as part of the PQS.	
3	Draft the Quality Manual using the document map.	
4	Draft the remaining procedures and forms required for the PQS.	
5	Review the content of all PQS documents with subject matter experts (SMEs) for their sequence and interaction.	
6	Finalise the PQS documents before approval. Ensure: ▪ company name, logo etc. has been inserted into each document ▪ all Procedures and Forms are cross-referenced as appropriate in the Quality Manual. References to compliance/quality standards have been included where required ▪ all styles are consistent within the PQS documents.	
7	Obtain the appropriate document approval signatures required by the compliance standard and as dictated by your PQS procedure.	

PharmOut is an ISO 9001 certified international GMP consultancy serving the pharmaceutical, medical device and veterinary industries, as well as related hospital and pharmacy operations. PharmOut specialises in PIC/S, WHO, United States FDA, European EMA, and Australian TGA GMP consulting, architecture, engineering, design, project management, training, validation, continuous improvement and regulatory services.

For more information please visit www.pharmout.net or contact us at info@pharmout.net.