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**SUMMARY**

**GLOSSARY**

Some quality standards you may hear about
SCOPE

This workbook will concentrate on the core, underlying principles of quality that are pivotal – explicitly or implicitly – to all quality management standards that impact on research and development.

These principles are also fundamental to the conduct of efficient, reliable and credible scientific and clinical work and will help you to design and implement a practical Quality System; a Quality System that works for your organisation, to make it more productive and compliant, rather than making you work for it, by producing unnecessary bureaucracy.

Finally, the workbook should help you in the task of persuading others of the importance of such a system and therefore give you good leverage in your efforts to improve the system.

The workbook is aimed at the doers; you have either been delegated the task or are that rare individual, a volunteer who has seen the need for a Quality System.

Generally, you have a job title of QA or governance manager or designated individual; however the one thing that’s almost guaranteed is that you’ll have no or limited budget, a pile of documents written in legalese and support so long as you are not ‘interfering’ with the smooth operation of the organisation.

The workbook includes sections on key principles and exercises to work through. There are also Tools and Tips sections giving additional information, examples and options for ways of doing things.
**INTRODUCTION**

**What is Quality?**

This means different things to different people, but central to all definitions is that Quality is about meeting a standard, and one definition states that quality is ‘the degree to which a set of inherent properties of a product, system or process fulfil requirements’. The standards or requirements involved will be defined by circumstance. What does need to be clear is what the standard is. Measuring and demonstrating whether the work is up to the standard is part of Quality Assurance.

**What is a Quality System?**

A Quality System sets out the standards that you are working to, and how you are going to meet them. The system should define what people, actions and documents are going to be employed in order to carry out the work in a consistent manner, leaving evidence of what has happened. It may include manuals, handbooks, procedures, policies, records and templates. The terminology used is less important than the purpose and use of the documents. The fundamentals of a Quality System are the same regardless of what your work is. The same principles can be applied whether you are an academic research laboratory, a medical device manufacturer or a hospital clinical trials unit.

*Figure 1*

Some of the key areas of a Quality System are illustrated in Figure 1 above. These will be explored further later, in the workbook.

Understanding, interpreting and implementing a Quality System is a skill in its own right. The aim of this workbook is to provide tools and a practical approach to develop a Quality System that works for you.

**What is the aim of a Quality System?**

A Quality System aims to ensure reproducibility and reconstructability, and compliance with whatever standards you have set.

This is the essence of good science. A good Quality System ensures the documentation of a testable hypothesis, agrees resources to test the hypothesis in a reproducible manner, ensures that the testing is carried out by competent people with minimal risk of falsification or accusation of falsification of data and ensures that, whatever form the reporting of that data takes, it reflects the evidence generated during the testing.

A Quality System will also encourage those involved to manage change in a proactive way and to learn from instances where things didn’t go as planned.
What is the aim of your Quality System?

This will be completely dependent on the organisation you are in, the standards you are required to meet and the environment you are working in. This workbook will help you determine the aims of your system and help you prioritise actions based on risk.

The criteria will change over time so your Quality System will need to be reviewed from time to time as aims and environment change within your organisation.

**Exercise 1**

What is the scope of your Quality System? What activities are going to be covered? List them here.

*e.g. clinical trials, laboratory animal work, work with Human Tissues*

What are the specific regulations you need to comply with? Consider all standards that may apply.

*These may include international and national Clinical Trials Regulations and Guidelines, the Human Tissue Act, the Data Protection Act, as well as hospital/local policies, client contracts, good practices, etc.*

Do you know enough about these standards, or do you need to know more?

*Don’t forget that there are colleagues, groups and websites you can contact that can provide help and knowledge.*

Are there managerial expectations you are being asked to meet? Are there specific timelines involved? Is there an inspection due, for example?

Ensure you list all the requirements and expectations that your Quality System needs to meet.

Are there any conflicts or doubling up of requirements?

Does one standard take precedence, or is one stricter?

Do all standards apply to all areas of activity or do different areas have different standards?

You could find it helpful to draw a map of what applies where....
For example, it may be of a specific physical area, see Figure 2 below.

*Figure 2*

Or it may be a wider remit, so your ‘map’ will be of departments, clinics or groups. An example showing some of the regulations that may apply in one situation is shown in Figure 3 below.

*Figure 3*

Individual circumstances will be different so you will have to build your own suitable system. It will need to be realistic and you will almost certainly want to build the system in a phased way. In general Quality Systems have the same principles and a well designed system can meet multiple aims. Later on in the workbook we look at these principles in some more detail.

Having completed exercise 1 you will have defined the scope of your Quality System.
What does a Quality System normally include?

There are a number of things that all Quality Systems need to do and some things that apply only to the requirements in the scope of your system. N.B. refer back to Figure 1 on page 2. The requirements of your system will be determined by the individual standards that are applicable in your organisation.

These requirements usually appear as quality policies, but as long as the requirements are documented somewhere, what they’re called doesn’t really matter.

Definitions of roles and responsibilities

Usually part of Job Descriptions are necessary to make sure that people know what to do and who can do what. This may sound obvious, however many organisations aren’t clear about who has authority to sign certain documents and what an individual’s responsibilities actually are (as, for example, a Principal Investigator).

Document control

Document control within an organisation assists in the setting and maintenance of standards including written procedures. The written procedures are necessary to ensure consistency between individuals, they provide structure and simplify how things are done (prevent everybody doing the task in a slightly different way). This usually involves designing templates for the documents you use and detailing how they are created, reviewed and approved. A vital part of document control is version control. This ensures that only the current version of a document is in use and that everyone is trained to use it.

Change control

It is not just documents that change. The best way to manage any change, e.g. changes in procedures or equipment, software, is to plan it and consider the impact such a change will have on those involved. Consultation with those involved in advance of a change will help identify potential flaws in the plan or issues that will result from the change. Pre-empting these will be really valuable in ensuring a successful change process.

Deviation and amendment

This is how the organisation learns from things going wrong (unplanned changes are deviations) and how it plans for changes to activities.

Training records

This is how individuals prove they are qualified to carry out their job. Training against the regulations, requirements and local procedures is critical to ensure that the right people are doing the right job, well.

Review and checking

The Quality Control aspect of Quality Assurance. This includes formal self-inspection (audit) and processes for ensuring that data is accurate.

Facilities and equipment

Where you work and the equipment you use to do a job can be critical. There are many controlled environments involved in research activities, from fridges and freezers to Class A clean rooms, and you need to ensure that the necessary requirements are documented and processes put in place to ensure they are monitored and maintained. Equipment needs to be operated correctly and appropriately maintained to make sure the results it generates are accurate and reproducible.
Exercise 2
What systems, processes and documents do you have in place in your organisation already?
*Consider both formal and informal processes/documents, established staff development systems, standard procedures, induction training.*

If you tabulate this against your requirements you will see what gaps you have.

<table>
<thead>
<tr>
<th>Requirements</th>
<th>What we have in place</th>
<th>Does that achieve the goal for now?</th>
</tr>
</thead>
<tbody>
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<td></td>
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</tbody>
</table>

Have you got any critical gaps that need fixing fast?
*Have you experienced patient death, loss of Intellectual Property, Regulatory Inspection findings, etc?*

*On completion of Exercise 2 you have done a gap analysis.*
To improve, where do I start?

The place to start should always be the place of most risk. Risk will also be dependent on your organisation, your aims and your activities.

Risk is normally made up of two components, Impact and Likelihood. These can be quantified to provide an indication of the priority to assign against each risk. So, in a given situation, a number of things can go wrong. Each thing that can go wrong has an Impact and a Likelihood.

The Impact gives a measure to the possible outcome(s) of the risk. In medical research, death is usually at the top of the scale, impact on subject or staff safety next, someone going to jail next and so on, down to doing something relatively simple again with minimal impact.

The Likelihood is a measure of the chance a particular risk will result in a particular level of Impact. One would hope that the risk of death when doing an activity is less likely than that of major injury and in turn that will be less likely than minor injury; however this needs to be determined for each activity.

The same situation may have different potential Impacts, each with their own Likelihood and therefore different risks. You may also be more ready to accept the same risk in one circumstance compared to a different situation. For example the impact from a business perspective may not be the same as that from a quality perspective.

There are also two ways of assessing this:

**Either**

Assess the basic risks disregarding anything you have in place to mitigate the risks. An example of a mitigating factor would be having an alarm on a freezer. Then add your mitigations to give a second (hopefully lower) mitigated risk score. This will help you keep an eye on how changes impact the risks you have by detailing all your mitigating factors.

**Or**

Assess the situation as it stands, including the mitigations you have in place. This is quicker, but may leave gaps later.

You have already done some of the work to identify risks. Don’t be de-railed by things you see others doing – their risks might be very different to yours.
Exercise 3

Look at the gaps and critical gaps you identified in Exercise 2. Additionally, try to think of any other things that could go wrong.

List all events in column A below.

For each item, classify it for the impact it would have (1 = little, 5 = huge) and the likelihood of it happening (1 = unlikely, 5 = almost certain). Nominate the number quickly - go with your gut instinct. Insert these numbers in columns B and C.

Multiply the scores together to give a risk score (column D). Prioritise the highest scores as what to tackle or be aware of first.

Example:

<table>
<thead>
<tr>
<th>Risk (A)</th>
<th>Impact (B)</th>
<th>Likelihood (C)</th>
<th>Risk score (D)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not recruiting enough patients</td>
<td>4</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>Specialist scientist leaving the organisation</td>
<td>3</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Serum sample not being provided at a specified timepoint</td>
<td>2</td>
<td>3</td>
<td>6</td>
</tr>
</tbody>
</table>

For these examples the area to prioritise would be patient recruitment which could be tackled by increasing awareness of the study or by reducing the target recruitment for that site in the clinical protocol. Next would be the serum samples which could be tackled by ensuring the relevant staff knew which samples were required when and how important they were to the outcome of the study. Finally the training up of other scientists might alleviate the risk of specialist knowledge being lost from the organisation.

Now look at what you’ve done. Does it make sense? Has it identified what you already ‘feel’ is the highest risk? Does risk of death, risk of imprisonment, risk of being sued come out the highest?

Having completed Exercise 3 you have done a risk assessment. You can now use this to guide your implementation.

Before you go any further, you need to ensure that you have management buy-in to taking this Quality System further. The next section shows you the core principles of Quality Systems and explains how each plays its part to ensure success.
**THE CORE PRINCIPLES**

Quality Systems are founded on four principles:

1. **Managing**
   Organisations must manage their physical and human resources to ensure that plans can be converted to delivery. Activities must be managed so that they are under effective and visible control.

   An ‘Activity’ is any organised piece of work such as a study, project or testing campaign. Individual tests will be conducted according to standard procedures or instructions. The plan is about how the tests are organised within the activity.

2. **Planning**
   All research and development should be a planned process, not a series of random occurrences. Planning is a continuous process, not an event. It controls the predictable and reacts to the unpredictable to ensure that the process is under control at all times and that there is clear understanding of cause and effect. Planning needs to happen for every Activity to be undertaken.

3. **Delivering**
   Management and Plans come together to provide the environment in which effective research and development is delivered. Delivery must ensure that inputs and processes are controlled to minimise or remove variability and that outputs (results, reports, papers, etc) are robust and reliable.

4. **Measuring**
   It is important to measure the actual output against the planned aims. Equally important is the setting of acceptable standards for the performance of the work and ensuring that there are mechanisms to demonstrate that these are met or exceeded. Such measurement includes actions known as internal Quality Control and internal performance assessment, as well as independent confirmation of the acceptability of the Activity and its output.

   The core principles are not about the specific content of the Quality System but about its organisation and management.

   **Keep it simple and relevant**

   The two biggest enemies to successful implementation come in the form of statements like:

   “I don’t understand the system.”

   “I don’t understand why we need the system.”

   These can then be used as an excuse to avoid engaging with the Quality System. The antidote to these statements is (a) to keep the system simple and (b) to understand and explain clearly why each requirement is necessary.

   In practical terms it is useful to start a Quality System with the essentials and move forward from there.

   One of the surest ways to fail from the start is to have even the slightest whiff of ‘unnecessary bureaucracy’. Developing lots of documents can be seen to equate to this.
IMPLEMENTATION

We will now look at each of the core principles of implementing a Quality System in a little more detail.

Managing

There are two types of ‘management’ – management of organisations and management of Activities (delivery of research projects, of processes, etc).

Managing organisations

The management of an organisation needs to oversee strategic direction of the whole organisation: this will influence what Activities are to be delivered in order to achieve strategic goals, and the resources and staffing required to deliver them. The principal functions of organisational management are:

• Strategic direction
• Set standards
• Accountability
• Provide resources
• Ensure that their standards are implemented
• Ensure that resources are used properly

There should be a clear definition of how these responsibilities will be discharged and who is responsible for them.

Examples of organisational management include:

• Dean of Faculty
• R&D Director
• Finance Director
• Research Governance Board / Committee
• Senior Management Team

It is critical that organisational management is aware of, and supports the implementation of the Quality System, as it is from here that the authority and resources will come. This can be a difficult thing to achieve, but it is important if you are to be successful. If you are tasked with implementing a Quality System you should consider how best to influence your organisation’s management (see Influencing organisational management on page 11). Organisational management need to be aware of the benefits of having a Quality System and the risks of not having one. They may also be only too well aware of the risks to your organisation of implementing an inappropriate Quality System, and so may need some reassurance that you are going to take a risk-based approach.

Management of Activities

Once organisational management has given authority and responsibility to conduct a specific Activity, it becomes imperative to ensure that the Activity has a single point of control. Therefore each Activity should have an Activity Leader appointed, who is responsible for overseeing the management of the Activity.

Examples of Activities and their Leaders, might be:

• A research project (leader is Chief Investigator)
• A tissue collection (leader is a Designated Individual or Tissue Bank Manager)
• Analysing laboratory samples (leader is a Lab Manager)
• Dispensing drugs (leader is Chief Pharmacist)

Activity Leaders must ensure that appropriate plans are put in place before the Activity starts, and that they take responsibility for the Activity. As part of your Quality System, you may ask Activity Leaders to ‘sign-off’ specific tasks (e.g. completion of plans) at pre-agreed milestones to demonstrate that the Activity they are leading is being conducted in a controlled manner. Any documentation should be proportionate to the risks they are being asked to manage. The roles and responsibilities of the Leader should be defined and documented by organisational management.
For an Activity Leader to be affective they need to be appropriately trained and experienced. Organisational management should ensure that any additional training or support required by Activity Leaders is made available to them so that they can fulfil their role. Organisational management should replace the Leader if this becomes necessary (e.g. because of absence over a period which could affect the management of the Activity).

**Warning**

*Where no one is in control or when a number of people are trying to run the same Activity at the same time, problems commonly arise.*

*Beware of too many signatures on any document – each signatory thinks the others will read it and take responsibility, so no-one actually does. Ensuring that a statement exists to indicate what each signatory is signing for can alleviate this.*

Although each Activity requires a leader, the successful completion of a controlled Activity will usually require input from others. A tool that is commonly used to illustrate who is Responsible, who is Accountable, who should be Consulted or Informed about an Activity is the RACI model. A RACI chart is one method of communicating what is expected of everyone who is involved in delivering each Activity. See Tools and Tips (p15).

**Why is it important to get organisational management buy-in?**

If there is no management buy-in, there can be no system, as there will be no authority and no commitment to providing the necessary resources.

Without leadership and designation of authority there will be no clarity of roles, which in turn will cause confusion, duplication, omission, inconsistency, and potentially waste time, money and other resources.

**Influencing organisational management**

There are risks of not implementing Quality Systems; which will differ from organisation to organisation (see below for the reasons why you might implement a Quality System). However it is also important to acknowledge that there are significant risks to research organisations of implementing an inappropriate Quality System. It is vital that the system is fit for purpose and risk-proportionate. Understanding, interpreting and implementing an appropriate Quality System is a skill in its own right. The aim of this workbook is to provide tools and a practical approach to develop a Quality System that works for you.

The reasons for implementing a Quality System are varied but may include:

- Good quality underpins good research
  - Robust, reproducible data
  - Establishing a secure evidence base
  - Reputation of organisation
  - Clarity and communication
  - Refinement
  - Risk management
- Increased scrutiny
  - Increased regulation and application of regulations, for example in academic and NHS research programmes
  - Funding/grants – in an increasingly competitive market for research funding a means of demonstrating the quality of the project planning and the work carried out may be a means to differentiate grant applications
  - Intellectual Property and Patents – The commercialisation of ideas and the registration and defence of patents relies on Intellectual Property (IP) being appropriately protected, with evidence that stands up in court. An appropriate Quality System will help protect your work.
Anyone who does not believe that quality management can support good science should consider the following examples:

- The money wasted and reputations dented as a consequence of researchers working on what they believed to be specific cell lines which were later demonstrated to be HeLa cells, when validation tests were conducted
- Bovine Spongiform Encephalopathy was believed to have entered the UK sheep flock only because there was no Quality System in place that assured the origin of brain samples was reliable
- Compliance with regulatory requirements
  - For an idea, be that a drug or device, to be approved for use in the general population regulated studies must be performed
  - For work involving human tissues, the Human Tissue Act requires a Quality System to be in place
- Changing expectations
  - Increased regulation and expectations of academic and hospital research
  - Peer review – publicity around certain claims, such as climate studies at the University of East Anglia, means that access to primary data and critical peer review are major issues of concern
  - Media – Medical research stories are, increasingly, making headline news, and it is usually not the good news stories that get the highest billing
  - Activists – Medical research involves the use of animal models. Animal activists are becoming increasingly sophisticated in their attempts to disrupt research and any perceived lack of Quality or Control could attract unwanted attention
How can you achieve what you want to achieve?

Exercise 4
Here are some questions to help you identify the management situation of your own organisation.

Who do you identify as ‘organisational management’?

*These are the people you want to influence*

Is there management support for a Quality System in your area?

Who are the Leaders of your Activities? Are they distinctly identifiable?

Do you believe there is overlap or gaps in responsibilities for Activities? Is this recognised or is it a hidden issue?

Are there other stakeholders who will be affected or who need to be appropriately consulted?

Have you considered all the stakeholders? [See Tools and Tips on page 15]
What do you see as the barriers to implementing a Quality System?

What are the objectives (in priority order) for your:

- **Organisation?**
  
  *e.g. medical research, patient treatment, diagnostics, teaching*

- **Activity?**
  
  *e.g. clinical trials, research projects, sample analysis, tissue storage*

Are there sufficient resources or skills to achieve those objectives?

Can you describe what your role is for each Activity you are involved in?

*Having completed Exercise 4 you have considered the Activities and stakeholders involved with your organisation, and started defining responsibilities.*
Tools and Tips

- Keep management involved. Arrange regular meetings to keep them up to date with what you are doing. The amount of detail management requires may vary; consider the need for minutiae and the need to retain interest.
- Ensure everyone knows who’s doing what and who has responsibility for each part of the Activity. The RACI model is one way of managing this.

**RACI**
This model can be used to help look at risk and involvement. The following definitions are used:

**Responsible**
The those who do the work to achieve the task are responsible for it. There is typically one role with a participation type of Responsible, although others can be delegated to assist in the work required. Those who are delegated to help out with a task are considered to be in a supporting role.

**Accountable**
Also referred to as, Approver or final Approving Authority. This refers to the leader who is ultimately responsible for the correct and thorough delivery of the task. The Accountable person must sign-off or approve the work of the Responsible person. There must be only one Accountable person specified for each task.

**Consulted**
Those whose opinion is sought; and with whom there is two-way communication.

**Informed**
Those who are kept up-to-date on progress, often only on completion of milestones; and with whom there is just one-way communication.

<table>
<thead>
<tr>
<th>Task</th>
<th>Person A</th>
<th>Person B</th>
<th>Person C</th>
<th>Person D</th>
<th>Person E</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identify project leader</td>
<td>A</td>
<td>R, C</td>
<td>I</td>
<td></td>
<td>I</td>
</tr>
<tr>
<td>Generate team</td>
<td>A</td>
<td>R, C</td>
<td>I</td>
<td>I</td>
<td></td>
</tr>
<tr>
<td>Set up kick-off meeting</td>
<td>A</td>
<td>R</td>
<td>C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Project timelines</td>
<td>A</td>
<td>R</td>
<td>C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Analyse samples</td>
<td>A</td>
<td>I</td>
<td></td>
<td>R</td>
<td></td>
</tr>
</tbody>
</table>

For this purpose **Task** is defined as: Part of an Activity.

**Warning**

Projects can fail for the following reasons:
- **Responsible** people don’t know or don’t have clear leadership from the **Accountable** person
- There is more than one **Accountable** person, leading to confusion and conflicting priorities
- Those who are **Consulted** think they are **Responsible**, leading to conflict
- Those who should be **Consulted** aren’t, leading to omissions
- Those who are **Informed** believe they are either **Accountable** or **Responsible**, leading to confusion and conflicting priorities
- Those who should be **Informed** not being, leading to mistrust of management and disempowerment
The importance of planning is paramount, but in order to work any plan must be realistic. It may be that the minute detail is not finalised but the main components should be in place and should be agreed with relevant stakeholders.

The plan will define the desired inputs and outputs, and management will provide the resources, i.e. the people, materials, equipment and facilities, to process the inputs to outputs. The plan will define tests, procedures, methods, etc to be used during the Activity. The standards to which the work is to be done should also be clear.

Although a plan should always be prepared at the start of an Activity it may not always be possible to complete it or follow it without deviation until the end. It is in the nature of the research process that unexpected events will happen. Unusual laboratory results will appear or subjects will show unpredicted reactions to treatment.

Principles of Planning

1. Every research and development Activity must have a plan
   The plan is essential to communicate the strategies and methods to be used and also to define the aims, objectives and intended outputs. Without aims, objectives and outputs it is not possible to determine the degree of success of the Activity.

   The plan must define a person who represents the single point of control for the Activity (the ‘Leader’). It must be understood, agreed and approved by the Leader.

2. Every plan should be designed to work
   The plan must be realistic, so planning should involve all the stakeholders, achieving a consensus as to how to proceed. There should be a check back against objectives to ensure that the Activity is required, and will deliver against the objectives.

   The scope and timelines of the Activity must be realistic, and the resources and skills required will need to be available.

3. The content of the plan must reflect the degree of certainty relating to the Activity
   The plan needs to take account of the degree of variability associated with the Activity.

   For example, the plan to develop a new methodology may be couched in rather general terms about the approach and desired outcomes, whereas the later plan to validate the resultant method and show that it is accurate, precise, reproducible, etc will be very specific.

   Understanding the risks associated with the plan, and the Activities in the plan, is essential to its successful application. This means that the planner needs to understand what can go wrong, how likely it is to happen, how serious it is if it does, how likely are you to find out about it and what has already been done to mitigate the risk.

   You have already used a simple tool to help with risk management in Exercise 3.

4. The plan must be kept under continuous review
   The frequency of review will reflect the degree of uncertainty associated with the Activity. Predictable Activities will need less frequent review than unpredictable Activities.

   Particularly, the plan must be reviewed whenever there is a decision point. In the example of the method development, the plan may instruct a particular approach following which the method is tested to see if it has achieved the criteria for success set out in the plan. If not, the plan will require to be amended (see overleaf) to modify or replace the previous approach.
5. Amendments and deviations must be controlled
This is about change management. The impact of changes to the plan should be gauged as part of the control process.

There must be a simple, transparent and effective system for ensuring that the Activity remains under control during periods of planned change ‘amendment’ or unplanned change (deviation).

Amendments must be approved by the Leader. Deviations must be notified to the Leader who will assess their impact and take further actions, if necessary, to ensure that the Activity remains under control and is being conducted according to the plan and its amendments.

6. There must be evidence of continuous, effective planning
The plan, amendments, deviations and all other actions impacting on the management of the Activity must be documented so that there can be reconstruction of all the planning actions and decisions.

Warning

Activities can fail for the following reasons:
- Lack of planning
- Unrealistic or over-optimistic estimates
- Not involving those who have pertinent knowledge or vital input
- Divergence away from the plan
**How can you plan effectively?**

**Exercise 5**

What is under your control?
*That might be, for example, particular physical locations, or areas of responsibility.*

What can’t you change?

Circles of influence – think about the things you have control or influence over, and where you will need to enlist help.

How will you ensure that the other stakeholders will be involved in the planning stage?

- Theoretically?

- Practically?

As a stakeholder or planner, have you ever had a surprise? Have you been asked to provide services without appropriate notice or resources? Have you been asked to achieve a result in an unrealistic timescale? Have providers let you down in some way? Think about some examples and try to understand where the surprise came from.

With that hindsight, what steps would you put in place so that it didn’t happen next time?

Is it clear where any plan you are involved in stops? What is the output?
How do you demonstrate the plan was followed, or not?

What sort of changes might occur in your Activities?
* e.g. New Principal Investigator, change to software of an analyser, reagent unavailable, human error

Of your examples, which should be planned, and which would be unplanned?

How will you find out about changes?

Is there any assessment undertaken of the impact that change might have?
* Make sure you consider severity and all stakeholders

Who do you tell?

What should happen next?
* e.g. documentation, corrective action, preventive action. Make sure you consider who is responsible for any actions and when they should be completed

Is there a review process to see how the change went, or to try and stop unplanned changes happening again?

* Having completed Exercise 5 you have the tools you need to create a plan and manage changes to it.
**Tools and Tips**

**Stakeholder map**
An example stakeholder map.

SMART – a mnemonic to use when agreeing objectives – it helps to give clarity and something to measure against.

- **S** Specific – ensure it is very clear exactly what you are trying to achieve
- **M** Measurable – ensure you have some means of measuring whether it has been achieved or not – think about the output
- **A** Attainable – ensure the Activity is realistically achievable under the actual conditions and with the resources available
- **R** Relevant – ensure that what you are trying to achieve is pertinent to the organisation’s objectives and is not going off on a tangent or is unnecessary at that time
- **T** Timebound – ensure timelines are set and are clearly communicated

**Project planning software**
There are many types of software commercially available e.g. Microsoft Project or Prince 2. They are not by any means compulsory but they can be useful for dealing with the complexity of large projects. However, do be on guard against the software and process becoming more important than the principles and objectives of planning. There may be simpler ways to achieve the same outcome.
<table>
<thead>
<tr>
<th>Question</th>
</tr>
</thead>
<tbody>
<tr>
<td>What are we intending to change and why?</td>
</tr>
<tr>
<td>Who and what will that change affect?</td>
</tr>
<tr>
<td>What do those responsible for those areas have to say about it?</td>
</tr>
<tr>
<td>Is it still a valid change to make?</td>
</tr>
<tr>
<td>What do we need to do to make the change happen in a controlled manner so no adverse effects occur?</td>
</tr>
<tr>
<td>When can this be achieved and who is going to be responsible for it?</td>
</tr>
<tr>
<td>After the change, review how it went – what would you do differently, if anything?</td>
</tr>
</tbody>
</table>
Delivery starts when the plan and the resources meet. In order to ensure success, everyone involved in delivering the Activity needs to be clear about the role they will play and the tasks they need to perform. This is where procedures and standards come in.

Procedures and Standards

The procedures and standards need to be defined and communicated to everyone involved in delivering the Activity. Individuals need to understand what is required of them and be trained in these requirements. As a consequence, standards need to be expressly stated and procedures need to be available for use. All written instructions must be controlled appropriately so that the correct version is used.

Different approaches are possible but the key thing is that organisational management must define the standard approach to be used within their facility. This will ensure that each time a procedure is carried out, it is performed in the same way thus avoiding the possible variability that can be introduced by performing the same procedure in different ways. Such variability may be from the same individual performing the same procedure in different ways on separate occasions or by many individuals performing the same procedure differently.

Processes that happen regularly need a documented procedure. If it’s not done regularly then it is not a standard procedure, but should still be documented in an appropriate place.

Exercise 6a

Pick a procedure within your own organisation that happens regularly, i.e. is a standard procedure.

What is your process trying to achieve/what is the output?

* e.g. Dispensing the right drug to the right person, analysis of a sample

Draw a flow diagram of the process.

*Think about who is involved, what equipment or materials are needed and where the process starts and stops*

We will come back to your example procedure later on in this section.

*Having completed Exercise 6a you have started recording a process.*
Standardising procedures

For the standard approach to work it must be approved by Management and communicated to everyone involved in delivering the Activity. Management in this context is the individual who is accountable for ensuring the process is performed and able to ensure that appropriate resource is available.

For individual processes this is frequently done by publication of Standard Operating Procedures (SOPs) but alternative methods may meet the same aims. This may include, for example, standard methods, controlled forms, work instructions. These may be hard copy or electronic documents, templates, pro-formae, flow charts, videos or anything else that is used to define and communicate standards to be employed.

Whatever method is adopted the principle is that the procedures must always be under control. By control we mean that procedures should be available to those that need them and, crucially, that only one correct version is accessible. This is hugely important as it is impossible to ensure that everyone performs the same procedure in the same way if individuals can access different versions of the same procedure. Control also includes providing evidence that the procedures are kept up-to-date. See exercise 8.

The frequency of review should reflect the likelihood of ‘drift’ in the procedure. Drift is the concept that gradually over time people change the way they do things. The new way may be better than the old but it will be different to what is documented and what other individuals are doing, so it is important to ensure uncontrolled drift does not occur. A common review period is two years although there may be benefit in undertaking the first review six months after the first issue of the standard procedure since this is when change is most likely.

**Exercise 6b**

Remember your example procedure from earlier – how likely is it that drift will occur?

What sort of drift might occur?

Think about the individuals involved, the number of times and places the procedure is used and the likelihood of materials or equipment being changed. How often do you think it should be reviewed?
Process flow

The classic model is that inputs are transformed to outputs by processes.

Inputs can include materials, equipment, staff and facilities.

Processes involve the application of methods to the inputs.

Outputs are data, records, reports and specimens.

Valid inputs

Valid outputs require valid inputs. An uncertainty associated with an input will be associated with an equal or greater uncertainty in the output. If it is a biological system such as an animal, cell culture or bacterial strain it is essential that characteristics are defined in order to determine that you have the correct system in the correct condition and there should be evidence to support this. For example, if the process requires tissue samples to be stored at -80°C +/- 10%, then there should be evidence to prove that the samples have been stored appropriately e.g. temperature logs. Equally, if processes don’t require tissues to be stored within such tight temperatures then don’t specify limits within the process.

People, facilities, equipment and materials must be demonstrably fit for purpose

‘Fit for Purpose’ basically means that all inputs (whether they’re people, materials, facilities or equipment) should be suitable for the specific intended purpose. Logically, therefore, there needs to be a clear understanding of what ‘Fit for Purpose’ actually means in each circumstance and there must be evidence to demonstrate compliance.

Examples of ‘Fit For Purpose’ include:

- **People**  
  Training, experience, knowledge, method specific, skills

- **Materials**  
  Identity, purity, stability, concentration / titre, (earliest) expiry date

- **Facilities**  
  Size, design, construction, maintenance

- **Equipment**  
  Capacity, performance standards, calibration, maintenance

Valid processes

The processes involved in the study also need to be demonstrably fit for purpose.

A process will always have a start point and an end point. Sometimes it can be appropriate to split large, complex processes down into smaller sub-processes, particularly when communicating them to others.

Be aware of things that aren’t processes, such as policies or records. These will not have a route to follow. They may be a statement of intent, but will not provide detail of what an individual should actually do. For example ‘the organisation will ensure all staff have training records’ is a policy. The associated process will actually describe what documentation may be completed at each stage of the individual’s career, including an indication of any annual reviews by the employee and employer, with the responsibilities of each task defined.

**Warning**

*If you can’t draw a flow diagram of your process easily, then it may not be a process at all – it may be a policy or a record or something else other than a process.*

*If its 25 pages long it’s not likely to be a standard procedure. It cannot be easily followed. Consider cutting down complex processes into several shorter procedures.*
Sometimes processes may have an intrinsic variability (for example cell culture), in which case definitions of characteristics alone may not be sufficient. In such cases there may be a need to incorporate positive and negative controls which give predictable effects or results and can be used to demonstrate that the system is operating properly at the time of use. This is not about competency of the operator, which we will look at later, but is about variability of methods or test systems.

The same principles apply to biological, physical and chemical systems. The methods used in these systems need to be validated against clearly-defined performance characteristics such as accuracy, precision, reliability, sensitivity, etc.

Any such controls should be described in the procedural documents, including what the acceptance criteria should be.

**Valid outputs**

Often the only evidence of the outcomes of the process (or, indeed, the details of the process itself) are the data and records. The end-user will generally use a report generated from the data (e.g. clinical trial report, signed consent form, blood test result, published paper) but they may sometimes use the data directly. It is important to remember that there may be raw data lying behind the final report that the end-user sees, or that the end-user could go on to manipulate or analyse the data further once it has been released. The Quality System must therefore ensure the continuous credibility of the data and reports must be seen to be complete and transparent.

Data recording standards should be set to maximise the credibility of the data. Generally these will require recording directly (as ‘original’ or ‘raw’ data), promptly, accurately and with safeguards against undetectable changes (e.g. avoidance of using erasable media like pencil to make records, or overwriting of electronic data). Computer systems are discussed separately, on page 27.

Changes to data should be transparent, which means that the original value should not be obliterated and there should be clear evidence of who made the changes, when and why. In practice this can be done on hard copy by drawing a single line through the original value and signing/dating changes. Similar systems must be in place to track changes made to electronic original/raw data.

Reports should contain a signed statement attesting to their completeness and accuracy. They should reflect any degree of uncertainty regarding the results and conclusions. This may be from the intrinsic variability associated with inputs and processes or because of excursions from the requirements of the quality management system, such as the need to use a substitute reagent or piece of equipment.
Exercise 6c

Now, pull out the key points of your flow diagram from exercise 6a. These are the main points of your process. Identify the input[s] and output[s] of your process.

Are there any control steps/tests that need to be included? If so, what are their expected results, so you can determine if the procedure has worked?

Now you need to add in responsibilities – who does what?

To start building this into a documented standard procedure a little more detail is required about who should be aware of and/or using the procedure, and what to do at the end. Examples of headers/sections to use might include:

- Scope
- Responsibilities
- Materials/equipment required and their storage
- Process steps
- Records and their storage
- History of changes (Procedures will change over time and this should be in a template)

What would you include under these sorts of headings for your example procedure?

There may be resistance to implementing written procedures. What are the risks of not documenting the procedure?

Ultimately the “National Lottery” test is a good mental exercise. What would happen if a syndicate of staff won the lottery and all left work immediately? Would you have everything written down? How would someone having to take over their work know what to do?

Having completed Exercise 8 you have drafted a standard operating procedure – an SOP.
Computer systems

Computer systems are, ultimately, just pieces of equipment and the same principle of ‘demonstrably fit for purpose’ applies i.e. computer systems should be suitable for their intended purpose.

There needs to be a clear understanding of the definition of ‘original data’ and whether or not the ‘original data’ will be maintained electronically or printed out. If the ‘original data’ are electronic then special procedures are necessary to ensure they remain secure and are accurate for legal and patent purposes. Consideration also needs to be given to ensuring that electronic data remains accessible over time. Electronic media are advancing technologically all the time, so planning for change is advised. If in doubt, IT specialists might be consulted.

Computer systems may perform measurements and should be treated in the same way as other measurement equipment, i.e. be calibrated to demonstrate that the measurements are accurate within acceptable limits.

Computer systems may also store, transform or transmit data. They should be validated to ensure that they also perform these tasks accurately.

If the computer systems within your organisation are selected, installed and maintained by a separate IT group, it is advisable to discuss the requirements of your Quality System with someone in that group. You may even find it useful to conduct a gap analysis with your IT colleague (see Exercise 2), comparing what you need in terms of security, accessibility, updates, audit trails, etc. with what the computer system is capable of providing. That way you will find out whether the computer system is fit for your purpose, and your IT colleague may be able to advise on ways of overcoming potential difficulties.

**Exercise 7**

What is the data used for?

What is the worst that could happen – data loss, leaks, overwritten?

What about verification and validation? Can you prove that your computer systems are actually doing what you think they are?

What is the system for computer back up in your organisation?

Have you actually tried to retrieve lost data from the back up?

*Having completed Exercise 7 you have started to consider the validity of computer systems and the safety of electronic data.*
Document control

**Exercise 8**

How do you control documents in your organisation?

Can an old version of the documents be used?

What about results – are they version controlled?

Is it easy to access any version of a document? What is the accessibility like to key documents when you are working?

Go back to your draft SOP. As the first version you should number it v1, and also give it some document identifier, e.g. SOP 001 v1. Then when you update/amend it in 6-24 months’ time it would be SOP 001 v2.

Think about and write down how you will ensure that the old version [v1] is removed from circulation and how the new one [v2] will be communicated to everyone who needs it.

You should ensure that one master copy of old versions is retained so that the process (as it was at the time of the work) can be reconstructed from the records if needed.

*Having completed Exercise 8 you have started to design competency assessments, and would be able to demonstrate competency though training records.*
Is a procedure enough?

What about competency and training? Although having standardised procedures which are well documented and version controlled is an aim of the Quality System, this does not infer that the person undertaking these tasks will be suitably qualified and able to do so. You will also need to ensure that the person assigned the task has the appropriate competency by attending appropriate training or by demonstrating the technique to an experienced member of staff. They could also be shadowed for X number of measurements to ensure that these were taken accurately.

For example, in the measurement of skin fold thickness example, it would be very easy to concentrate on the calliper and calibration of equipment but, rather than the equipment itself, by far the most risky component of this measurement is human error and using the calliper incorrectly, either by measuring more than just subcutaneous fat (i.e. measuring subcutaneous fat and muscle) or measuring the wrong point of the body.

Exercise 9

What about those involved in your processes? Have they read and understood the procedure?

Do you think that reading the procedure is sufficient to demonstrate competence?

How do you measure competence at the moment?

- How could you improve on this?

Can you prove that individuals have been trained and are competent?

- Do you have training records?

Take your example procedure from exercise 6 and think about competency criteria for that process.

- What critical points are there that you would want to ensure the operator got right before you would let them do it on their own?

- What would you include in a record to indicate an individual was the right person to be doing that job?

Having completed Exercise 9 you have started to design competency assessments, and be able to demonstrate competency though training records.
Tools and Tips

Decision trees
These are visual aids to help show the process when there are different options in a process. They indicate what to do at each decision point.

A simplified example for expedited reporting of spontaneous adverse events is shown in Figure 4 below.

Figure 4

Adverse Event or follow-up information

Serious?

Yes

Related?

No

Don’t expeditedly report

Expedited report to National Competent Authority

Don’t expeditedly report

Report via periodic reports

Expected?

No

Yes

Related?

No

Don’t expeditedly report

Expedited report to National Competent Authority

No

Report via periodic reports

Expected?

Yes

Expected?

Related?

 Serious?

Yes

No

Expected?

Related?
Measuring is about determining success. It is the final part of the Quality Cycle and checks that the process has – or has not – met the expected standards.

Research, by its very nature has unpredictable outcomes. If the outcomes were predictable, then the research itself would be unnecessary. Therefore, any checking of quality in research must be about the way in which the process has been conducted rather than the results of the research.

Measuring in a Quality System can be illustrated as a triangle:

```
/\         /\          /\        /\     \
 /  \       /  \        /  \      /  \    \\
/    \      /    \      /    \    /    \   \
```

The measurement process involves the following to varying degrees, as appropriate:

**Quality Control (QC)**

- Quality Control is a pivotal part of the Quality Management System
- The quality of the process depends directly on Quality Control
- Quality Control is undertaken by those performing, managing or supervising the process to ensure that the required standards have been met
- Quality Control comprises routine procedures by the personnel undertaking a process, or others, to check and ensure that the process meets defined requirements. These checking, inspection and surveillance Activities form part of the Quality Management System.
- Quality Control may also involve external quality control systems and inter-laboratory testing to demonstrate that processes are providing comparable results between organisations.

Every Quality Management System should have clearly-defined and appropriate quality control systems. The output from quality control Activities should be reviewed to indicate the degree of adequacy of performance and also to monitor trends where there is improvement or deterioration.

**Quality Assurance (QA)**

- Procedures by defined personnel to independently assure that the defined requirements for the process have been followed
- Quality Assurance may use similar techniques to Quality Control but the fundamental difference is that Quality Assurance is independent of the Activities that are being audited
- One tool is an independent assessment of a procedure called an audit. Audit is a sampling process looking for independent confirmation that standards have been met, so it provides a snap shot of the scene rather than continuous footage
- The quality of the process or its outputs must not depend on audit
Inspection

- Official review by regulatory authorities of all documents, records and facilities related to the processes. When developing a Quality System it is important to note that an inspection may take place outside of your control, but it should not be the over-riding concern in the implementation of your system.

Feedback

- Information received – actively or passively – about the degree of satisfaction with the process and its outcomes

What comes next?

For continuous Quality Control Activities such as inclusion of analytical positive and negative controls, or checking of labelling Activities or transcription of results, a longitudinal approach should be taken. Regular review of results or data checks can be performed to identify any areas of concern.

For specific Quality Control and Quality Assurance events, such as monitoring visits or audits, a report should be made which details areas of non-compliance (also known as findings) with any of the processes reviewed. Depending on the organisation, the report may be given to the Leader of the section responsible for the processes, or to the staff engaged in the processes themselves. The key point is that someone in a position to authorise change sees the report and leads a process to address the issues identified.

The most common way to do this is to undertake a Corrective and Preventive Action (CAPA) plan with the aim of correcting all areas of non-compliance and determining how to prevent these issues from arising in the future. Corrective Action (according to ISO 9000) means ‘an action to eliminate the cause of a detected nonconformity or other undesirable situation’, i.e. not just correcting the problem but removing the cause of the problem. Preventive Action, on the other hand, means ‘an action to eliminate the cause of a potential nonconformity or other undesirable potential situation’. The difference is that with Preventive Action the problem has never occurred (it’s a potential problem) – you are taking pro-active steps to foresee any issues and stop them from ever occurring.

The main steps when implementing CAPA are shown in Figure 5 below:

*Figure 5*
Recording the steps taken for any CAPA is helpful to ensure transparency, and to assist with continuing management buy-in. It also builds the bigger quality picture, and allows review for trends or particular problem areas.

As we work through measuring the Activities and processes either through Quality Control or Quality Assurance, we should always be looking to improve the system wherever possible. For example, if we look at a data management system, is it possible to add checks into the database to minimise transcription errors? Solutions might be high tech programming changes, or more low tech manual double checking of data entry. Any solutions will need to be tailored to your organisation, but it is important to assess the impact of changes before making them, and then review their effectiveness after they have been implemented.

The outcome of measuring the Quality System can result in:
- Improvements to all processes within the system
- Allocation of resources to critical areas
- Training of personnel
- Revision of organisation policies

**Management review**

Senior management in your organisation should have a formal, overarching responsibility in the measurement of the Quality System and review it on a defined periodic basis, which should include:
- Measurement of achievement of the Quality System’s objectives. Has the system provided management with the appropriate means to reassure them of compliance?
- Assessment of performance indicators to monitor the effectiveness of processes. Do we need to add anything or change anything in the Quality System to achieve these objectives?

Depending on your organisation’s management policies, they may want to review or at least have access to the Quality Assurance/Quality Control reports and may want to comment on the CAPA plan in case it impacts, or even improves, another part of the organisation.

All of these quality processes will produce outputs of some kind – for example a report or Quality Control data points (for example number of failed runs of an assay). These can be used as sources of information to assess the effectiveness of the process and the Quality Management System. Objective measures are very helpful in evaluating performance providing they are meaningful and proportionate. They are invaluable in identifying areas for improvement. The classic example looks at the number of observations made during a Quality Assurance or monitoring visit, the categorisation of these observations (e.g. critical, major or minor), as well as the numbers of observations in different categories and puts them together so it is possible to look at trends and what areas would be the priority to improve immediately.

These measurements are often known as quality metrics.
How can you assure quality?

**Exercise 10**

Have you got any examples of QC steps in your Activities?

*This might be on a process basis, or in your departmental or project functions*

If audits or monitoring occurs, who gets told about the outcome?

Then what happens?

What would you audit to assure yourself the requirements for your Activity have been met?

*Remember, audit gives a snap shot of the situation, so think carefully about where to focus your Quality Assurance Activities*

Who can do this audit for you?

*Remember, they need to be independent of the processes being audited*

What could you measure to identify how well your Activities have been performed?
How can this be a constructive process?

How would improvement opportunities be followed up?

Do you identify and share best practice?

Having completed Exercise 10 you have looked at who in your organisation is able to help with Quality Control/Quality Assurance processes, and how to go about improving your processes after Quality Control/Quality Assurance.

Tools and Tips

Examples of Quality Control opportunities in hospitals, research labs, start up companies:

- Without dedicated Quality Control staff, a self-assessment process can be used to check the clinical trial site file, ensuring that the most current version of the documents are in use. Staff can check each other’s files for completeness. Checklists can be used to facilitate this.
- Data transcription checks of clinical trial data: raw data is written up by a technician and is then transcribed into a report form. A senior technician independently checks both the raw data and the report form to confirm that there are no errors.
- In labs, if it is important to ensure samples are stored at -80°C ± 10%, having a temperature log and monitoring this to ensure temperature does not fall outside this range.
- There might be an Information Officer whose role it is to ensure the data held by the Research & Development office is complete and valid e.g. running monthly reports to identify missing data, etc.
- Regular meetings to review data. This can help identify outliers related to individual staff members, e.g. consistently high skin fold measurements from one individual, or higher rates of assay failures from one individual.

Examples of CAPA that have little money or resource required:

- Knowledge sharing
- Template sharing
- Training
- Using different coloured tubes to store samples and avoid species mix up
- Equipment maintenance – ensuring that equipment is kept clean and ready for use
- Regular meetings with staff or students to review progress against plans, and agree next steps
**SUMMARY**

**Congratulations!**
We hope that by following this workbook we have helped you to understand, develop and implement an improved Quality System within your organisation.

By focusing on the four principles you should have:
- A good understanding of the system you started with
- Knowledge of the requirements (rules, regulations and issues), and therefore standards that you need to apply
- A gap analysis against those requirements
- A Risk Assessment of where your priorities are, to make changes
- The tools you need to create a Quality System
- The tools you need to implement the system
- The tools you need to measure and evaluate the changes that you have made

**Now the good news and the bad...**
Organisations and their requirements change over time. The Quality System needs to adjust to those changes and just because you’ve been successful in tackling the high risk issues doesn’t mean you can rest on your laurels. Alternatively, if you haven’t been successful that’s no reason to give up! It is an opportunity to review why you have not been successful. Were you being unrealistic in your goals, or have you had a change in resources?

Either way, what this means is that you have to start again.

The same process applies but you need to remember to stop the Quality System taking over the organisation and keep it being of value.

**Quality cycle diagram**

*Figure 6*

Finally, please remember that you are not alone. Every organisation that needs a Quality System goes through this process and there is help available at every stage. There may be colleagues within your own organisation or neighbouring facilities that can help.

The RQA website has information and links to regulations and other professional bodies. You can also contact the Committees and Working Parties (through the website or individual details available in Quasar magazine) who are there to help answer any questions that you may have.

**Good luck!**
GLOSSARY

Activity
Any organised piece of work such as a study, project or testing campaign.

Activity Leaders
An Activity Leader is responsible for overseeing the management of the Activity.

Adverse effects
Results from a process which are not what was intended.

Amendment
A planned change to anything, e.g. a protocol, SOP, project plan.

Approver
The person (Leader) who is ultimately responsible for the correct and thorough delivery of the task.

Audit
A sampling process looking for independent confirmation that standards have been met. Audit provides a snapshot of the scene rather than continuous footage.

CAPA
Corrective and Preventive Action. A plan with the aim of correcting all areas of non-compliance and determining how to prevent these issues or new issues from arising in the future.

Certificate of analysis
Formal statement of an item’s characteristics. Normally found in Good Marketing Practice or production environments, confirming the quality of a product.

Change control
The process used to ensure changes to a product or system are introduced in a controlled and coordinated manner.

Compliance
Adherence to all the Activity-related requirements, including all Standard Operating Procedures. Evidence is normally required to substantiate compliance.

Data validation
The checking of data for correctness, or the determination of compliance with applicable standards, rules, and conventions.

Decision point
The natural points during a process when decisions have to be made on which action to take next.

Degree of success
The extent to which the aims and objectives for an Activity have been met.

Degree of certainty
How likely something is to happen.

Degree of variability
How much inherent variation there is in a system, process or methodology.

Deviation
An unplanned change to anything, e.g. a protocol, SOP, project plan.

Document Control
A consistent method of controlling documents. Includes version numbering, dating, issuing and withdrawing as control procedures.

Drift
Drift is the concept that gradually over time people change the way they do things. The new way may be better than the old but it will be different to what is documented and what other individuals are doing, so it is important to ensure uncontrolled drift does not occur.

Effectiveness review
A review of the level to which a system or process, and any changes made to it, have been effective or have achieved the objectives.
**Feedback**
Information received – actively or passively – about the degree of satisfaction with the process and its outcomes.

**Fit for purpose**
Fit for purpose means suitable for the specific intended purpose.

**GxP**
The Good Practice Standards (i.e. GCP (Good Clinical Practice), GLP (Good Laboratory Practice), GCLP (Good Clinical Laboratory Practice), GMP (Good Manufacturing Practice), GDP (Good Distribution Practice) - collectively known as GxPs).

**HTA**
Human Tissue Act.

**Impact (risk)**
Impact gives a measure to the possible outcome(s) of the risk.

**Inputs**
Inputs are transformed to outputs by processes and can include materials, equipment, staff and facilities.

**Intrinsic variability**
The inbuilt variability of a system or process. Biological systems, such as tissue culture methods, by their very nature, have a much greater intrinsic variability than other systems, such as electronic data capture or a chemical assay.

**ISO 9000, ISO 9001 & ISO 9004**
International standards for quality management systems.

**Likelihood (risk)**
Likelihood is a measure of the chance a particular risk will result in a particular level of impact.

**Negative control**
Inclusion of a known sample/standard/item to illustrate that a system is working correctly.

**Objective metrics**
Outputs from the system/processes which are helpful in evaluating performance, providing they are meaningful and proportionate.

**Original data / Raw data**
The very first recording of a piece of data.

**Outputs**
Outputs are data, records, reports, specimens or anything that is the result of performing a process.

**Performance characteristics**
Known features of an item or system, which can be used to demonstrate whether the system or process is working correctly, or to assure that the correct item is in use.

**Positive control**
Inclusion of a known sample/standard/item to illustrate that a system is working correctly.

**Processes**
Processes are the actions which are performed, transforming inputs, into outputs.

**Quality**
The degree to which a set of inherent properties of a product, system or process fulfil requirements.

**Quality Assurance**
All those planned and systematic actions that are established to ensure that the Activity is performed and the data are generated, documented (recorded), and reported in compliance with stated SOPs. This includes a systematic and independent examination of Activity related Activities and documents to determine whether the evaluated related Activities were conducted, and the data were recorded, analysed and accurately reported according to the standards defined.
Quality control
The operational techniques and Activities undertaken within the Quality System to verify that the requirements for quality of the Activities have been fulfilled. This includes overseeing the progress of an Activity, and of ensuring that it is conducted, recorded, and reported in accordance with the standards defined.

Quality cycle
See page 36.

Quality Management System
A Quality System sets out the standards that you are working to, and how you are going to meet them. The system should define what people, actions and documents are going to be employed in order to carry out the work in a consistent manner, leaving evidence of what has happened.

Regulatory /Competent Authority
A public authority or government agency responsible for exercising autonomous authority in a regulatory or supervisory capacity. In the UK this is the MHRA. In the USA it is the FDA.

Risk assessment
The identification, evaluation and estimation of the levels of risks involved in a situation, their comparison against benchmarks or standards and determination of an acceptable level of risk.

Risk management
A systematic process for the assessment, control, communication and review of risks to the quality of the activity/product across its entire lifecycle.

Single point of control
Each specific Activity should have a single point of control such as an Activity Leader.

SMART
A way of setting objectives to ensure that they are clear and unambiguous. This is in the interests of all concerned.

Stakeholders
Any person or organisation (internal or external) involved in the project/process who may have an influence on, interest in, or who can be positively or negatively impacted by the actions of a company or organisation. This includes stakeholders for individual Activities of the company or organisation.

State of control
A condition in which the set of controls consistently provides assurance of continued process performance and product quality.

Version control
This ensures that only the current version of a document is in use and that everyone is trained to use it.

Some quality standards you may hear about
For people involved in Research and Development there are two types of “Quality Systems” – the Good Practice (i.e. GCP, GLP, GMP, GDP - collectively known as GxP) Standards and specific Accreditation Standards such as ISO 17025, ISO 15189, and Clinical Pathology Association (CPA).

There is also the fundamental Quality Management standard – ISO 9001 – which can be applied to any Quality System but is little known or used in Research and Development.

The GxP standards are principles and do not generally set out specific performance requirements that have to be achieved. The interpretation of the principles is down to the individual establishment. They are applicable over wide areas of clinical research (GCP), laboratory work (GLP) or manufacture and distribution of materials (GMP and GDP).

Accreditation standards are quite specific to certain areas and accreditation is usually against a clearly-defined range of tests or procedures and cannot be applied outside this range.