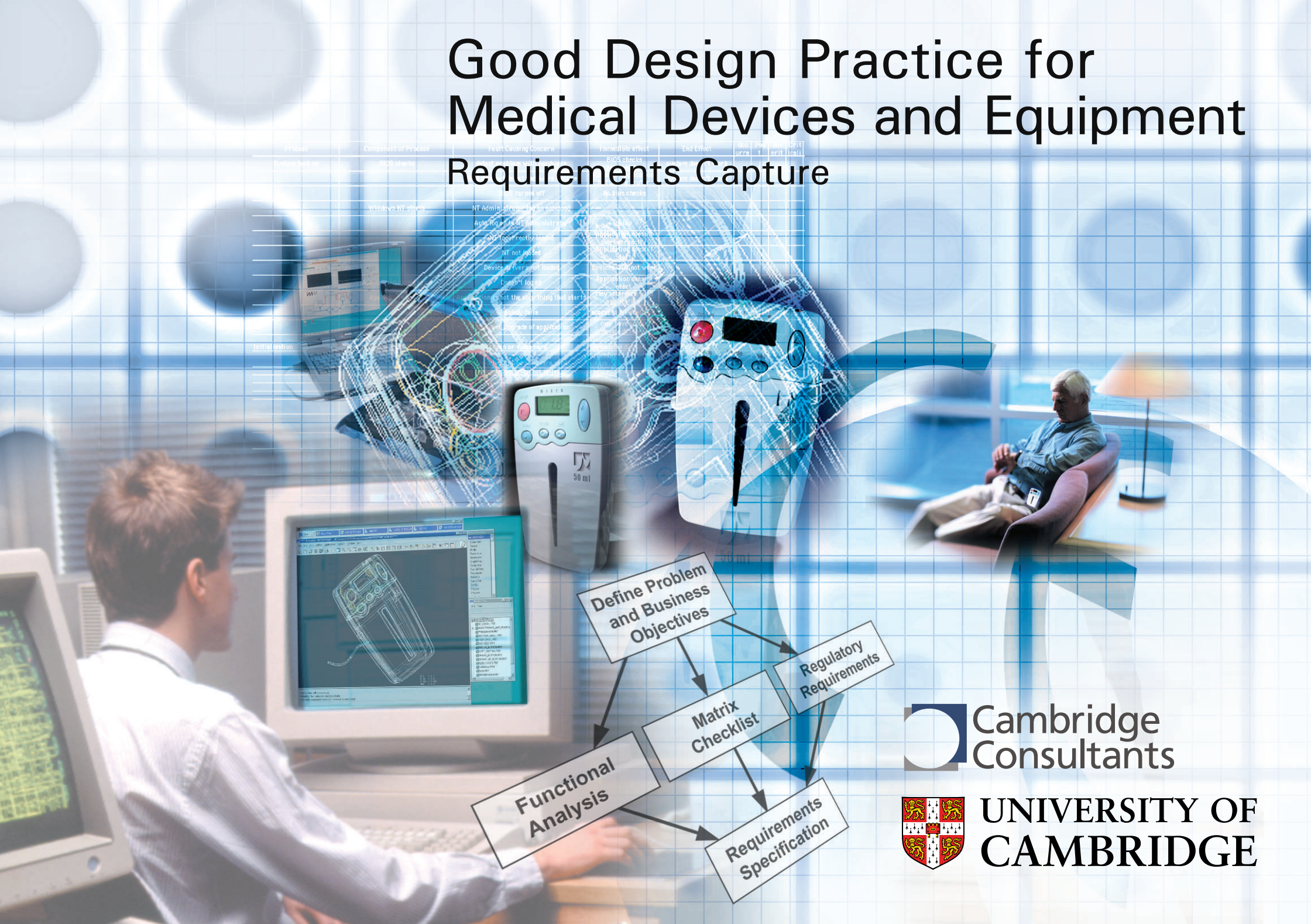
Good Design Practice for Medical Devices and Equipment

Requirements Capture



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GOOD DESIGN PRACTICE FOR MEDICAL DEVICES AND EQUIPMENT – REQUIREMENTS CAPTURE

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GOOD DESIGN PRACTICE FOR MEDICAL DEVICES AND EQUIPMENT – A FRAMEWORK

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*The Institute for Manufacturing is also based within the Department of Engineering and includes experts in technology management, international manufacturing, strategy, economic and business performance. It publishes a range of workbooks (see back cover).

" When I say a word, " Humpty Dumpty said in a rather scornful tone, " it means just what I choose it to mean - nothing more, nothing less. "

Alice in Wonderland, Lewis Carroll

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INTRODUCTION

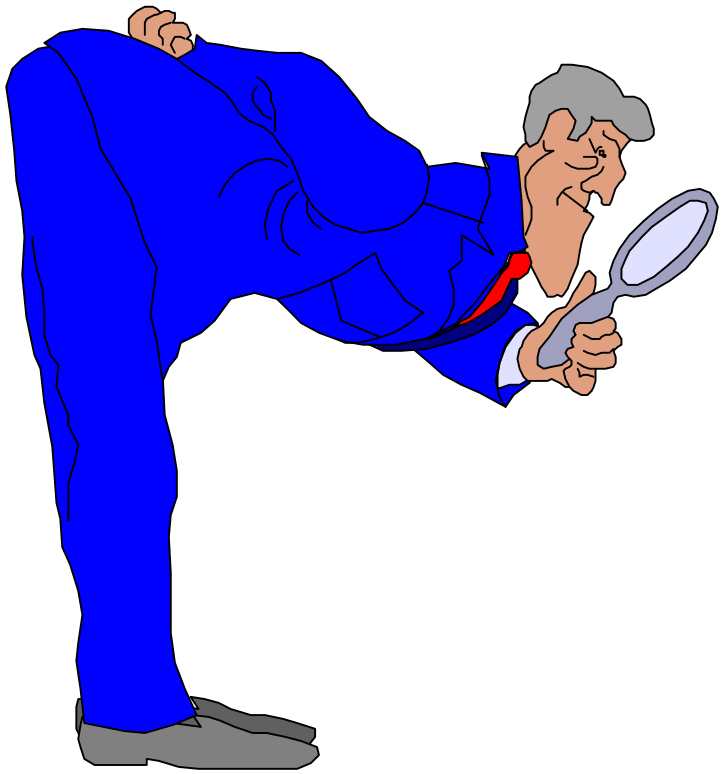
Medical device technology brings together the fields of engineering and medicine to provide technical solutions to medical problems.

The Food and Drug Administration (FDA) in the U.S. defines a medical device as a healthcare product that is intended to diagnose, treat, cure, or prevent a disease or other health condition. It may affect the structure or function of the body, but it does not achieve its primary effects through chemical or metabolic activity.

There are over 100,000 different medical devices on the market today, and the industry is growing every year. Due to the direct health and safety effects they have on the users, medical devices are subject to many regulations and must undergo extensive validation procedures, composed of checks, tests, analysis and reviews before they are allowed on the market. Requirements formulation is one of the most important aspects of the design process because it lays the foundation for the rest of the design.

WHO IS THIS WORKBOOK FOR?

This workbook is intended to be used by medical device designers, engineers, project managers, and procurement personnel. Previous experience in writing specifications is not necessary, but experience in medical device design is likely to be helpful.



Requirements

WHAT DOES IT CONTAIN?

This workbook explains a method for capturing requirements. It does not provide information on how to gather information and perform background research. Rather, it details how to organise information that has already been gathered into a requirements specification. The method involves three phases:

- defining the problem and the business requirements,
- determining and detailing the functions required to satisfy the problem,
- documenting the results in a requirements specification.

Three tools are provided to facilitate the above process:

- Functional Analysis - for determining functional and performance characteristics,
- Matrix Checklist – which covers a wide range of requirements including reliability, safety, and documentation,
- Regulatory Guidelines – information on regulations and standards.

HOW TO USE THIS BOOK

It is intended that the method be used in its entirety to produce a complete and comprehensive requirements specification. However, the method is modular to allow the independent use of particular parts.

OVERVIEW OF DESIGN AND REQUIREMENTS CAPTURE

" Design is the prolonged checking, pondering, and compromising on requirements which are often quite contradictory until there appears - as the end product of numerous associations of ideas, a network of ideas - the design."

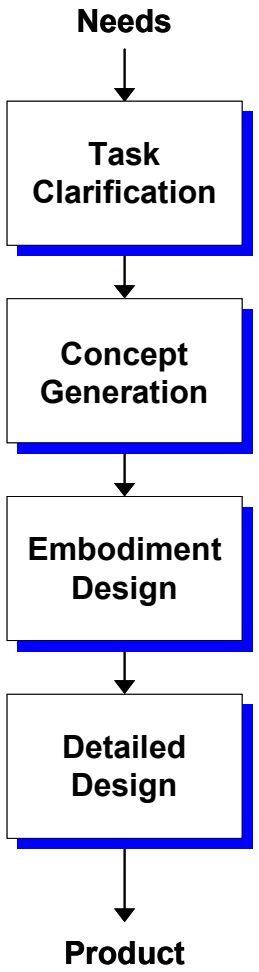
Engineering Design, I. R. Matousek

WHAT IS THE DESIGN PROCESS?

The design process describes the steps a designer takes to find a solution to a problem and is usually divided into four steps:

- **task clarification** - defines the problem, identifies the needs, and establishes the requirements,
- **concept generation** - identifies and evaluates possible solutions,
- **embodiment design** - elaborates the selected solution and determines the layout and structure,
- **detailed design** - finalises the details including dimensions and materials,

Iterations, checks, and reviews occur between these steps as the design develops.



Verification:

"Are we building the thing right?"

Validation:

"Are we building the right thing?"

VERIFICATION AND VALIDATION

Verification and validation are checks and balances in the design process that identify deficiencies and discrepancies in the design before the device is produced. Verification and validation are particularly important in medical device design.

Verification: Verification ensures the output of each phase of the design process meets the requirements derived from the previous phase. It answers the question, "Are we building the thing right?" Verification activities include:

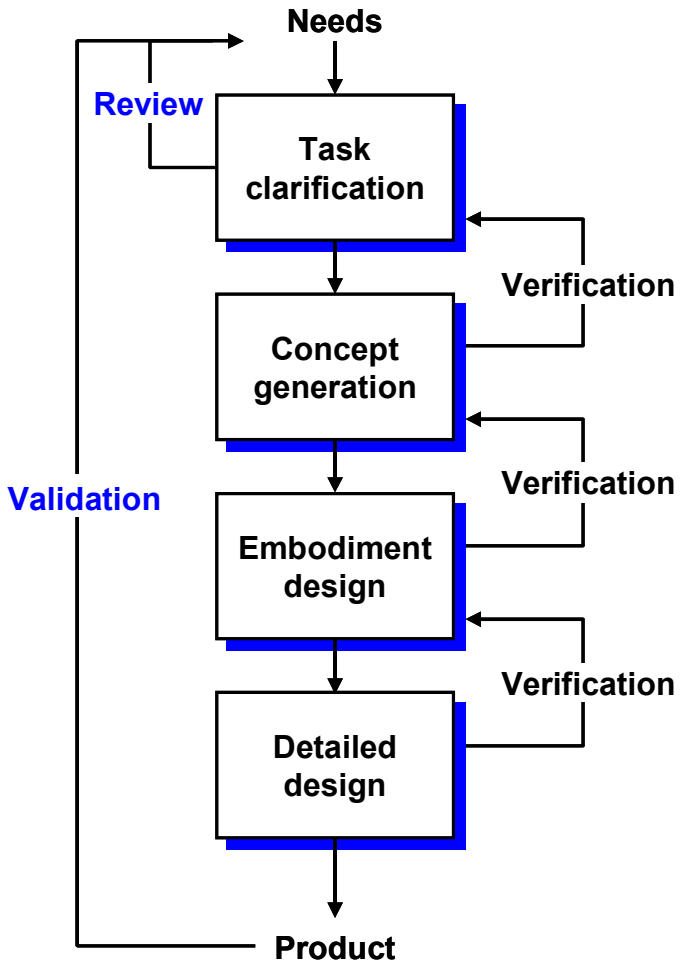
- worst case analysis,
- Fault Tree Analysis,
- Failure Mode and Effects Analysis,
- inspection,
- testing.

Validation: Validation encompasses all activities that demonstrate that the product meets user needs. It answers the question, "Are we building the right thing?" Validation activities are carried out during design to provide assurance that design and specifications are consistent with the user needs.

Verification tests the output from each step against the previous step.

Validation ensures that the product meets the user's needs.

In medical device design, verification and validation must be done in order to obtain approval of the device.

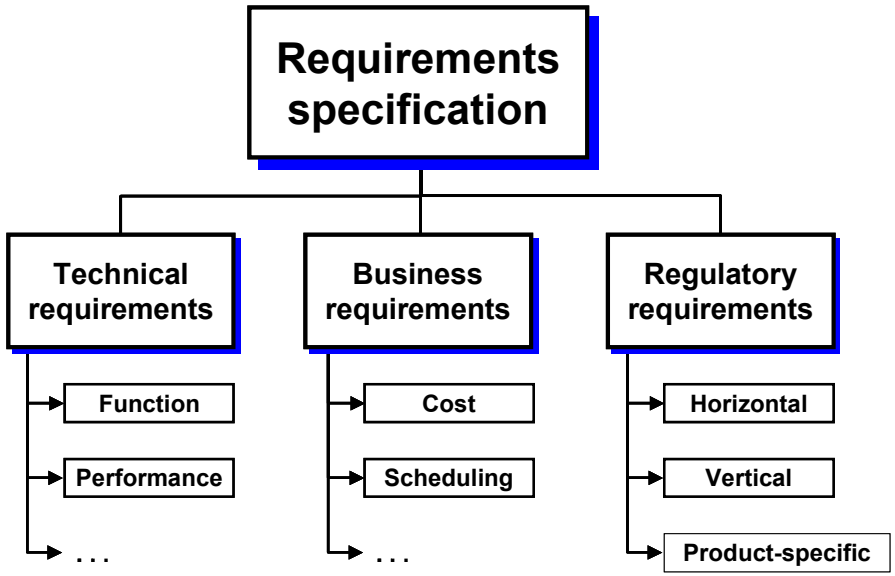


WHAT IS THE ROLE OF REQUIREMENTS IN THE DESIGN PROCESS?

The requirements specification begins the design process by defining what is needed. It is used later as a yardstick against which solutions are measured. Because people refer to the requirements specification throughout the design, development, and manufacturing processes, it is essential that it is correct. It is important, therefore, to review the requirements specification and that the designer's understanding of the requirements, that is the output of task clarification, does satisfy the need.

The benefits of a good requirements specification are:

- a thorough understanding of the problem,
- decreased time and cost of the design process,
- enhanced communication among project team members,
- easier compliance with regulations,
- a quality product.



WHAT ARE REQUIREMENTS?

The requirements specification is an elaboration, expansion, and translation of the need into engineering terms. It provides a means of communication between marketers and engineers, clients and consultants, engineers in different disciplines, and the project team.

The requirements specification defines *what* is to be achieved, but not *how* it is to be achieved.

There are three types of requirements:

- ***technical requirements*** - the functional and performance requirements of the product,
- ***business requirements*** - cost, scheduling, and other managerial requirements,
- ***regulatory requirements*** - governmental laws, industrial standards, or product regulations. These are particularly important in medical device design. The three types of regulations are:
  - horizontal, which apply to all medical devices,
  - vertical, which apply to a specific type of medical devices,
  - product specific, which apply to a particular medical device.

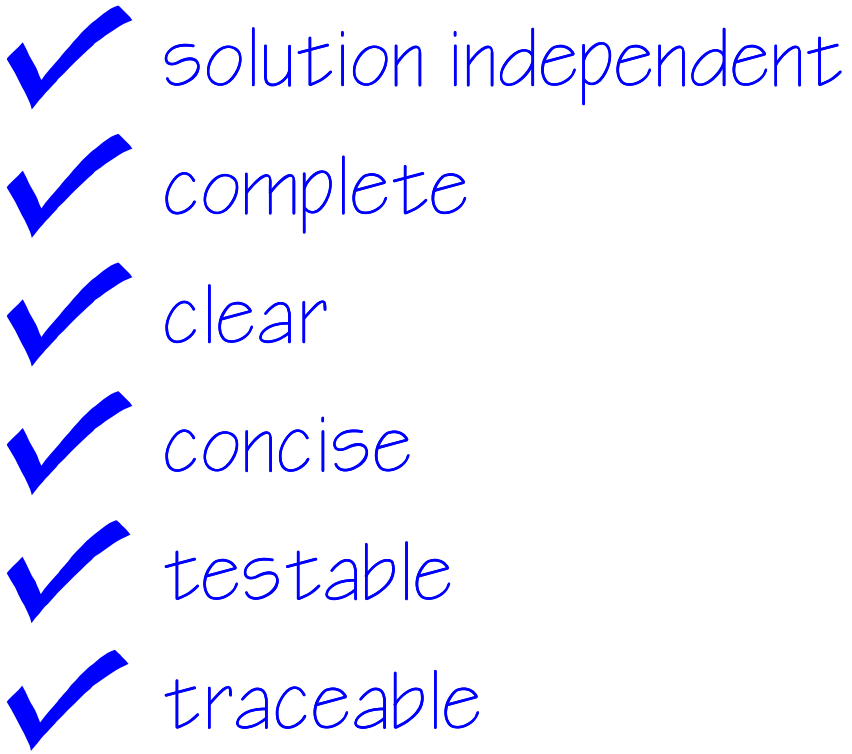
These are discussed in more detail later.

DESIRED CHARACTERISTICS OF REQUIREMENTS

There are certain characteristics that requirements should have in order to be effective. Writing the requirements well is as important as determining the right requirements.

Requirements should be:

- **solution independent** - requirements should not specify a solution to the problem - they should specify *what* needs to be done, but not *how* it will be done,
- **complete** - the requirements must include all areas of concern, including all phases of the product life cycle,
- **clear** - requirements should not leave anyone guessing what is required,
- **concise** - unnecessary requirements should be omitted - the wording of requirements should be concise - do not bury the requirement in unneeded text,
- **testable** - quantitative (numerical) limits, tolerances, ranges, and intended values should be indicated when possible - testable requirements can be measured in order to determine if the design goal is met,
- **traceable** - a requirement should be able to be traced back to the rationale from which it was derived and forward to its implementation in the design.



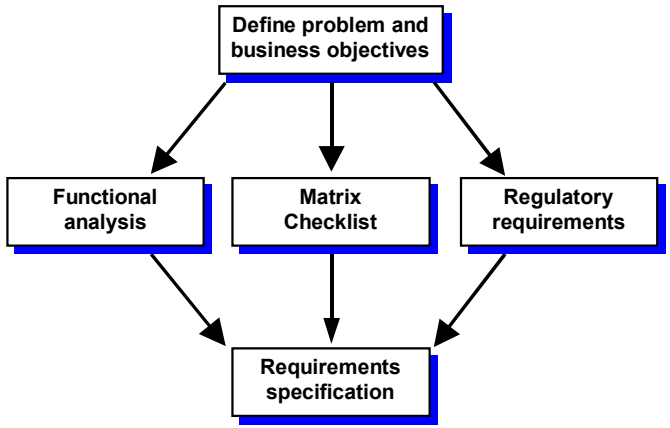
THE REQUIREMENTS SPECIFICATION PROCESS

The process is as illustrated. There are three main phases:

Phase 1 – Set objectives

Phase 2 – Analyse and detail functions

Phase 3 – Document requirements



Phase 1

The problem and the business objectives are defined

Phase 2

The functions that must be performed by the product, if it is to satisfy the perceived problem, are detailed. This involves understanding all aspects of how and in what circumstances the product is going to be used, maintained and ultimately taken out of service. The applicable regulatory requirements also need to be addressed.

Three tools, described later, are provided to help designers carry out this phase:

- functional analysis,
- the matrix checklist,
- regulatory requirements guidelines.

Phase 3

The outcomes of phases 1 and 2 are methodically documented

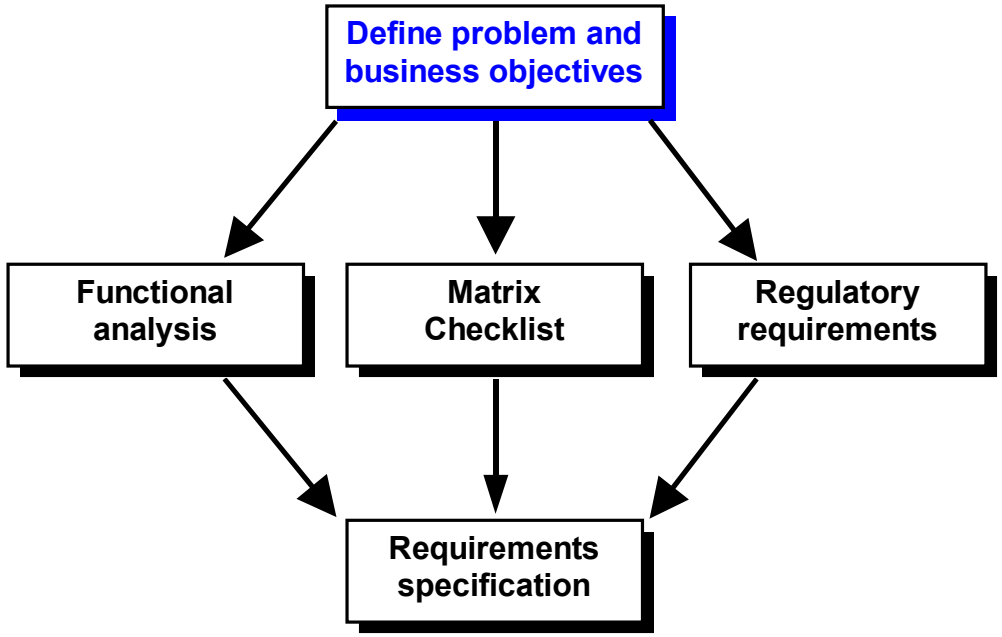
In practice, Phases 2 and 3 overlap and the requirements specification is often built up as Phase 2 activities are carried out.

Requirements Capture Phase 1: Define Problem and Business Objectives

Phase 1 – Set objectives

Phase 2 – Analyse and detail functions

Phase 3 – Document requirements



1 DETERMINE THE PROBLEM TO BE SOLVED.

The information used to define the problem comes from many different sources.

After gathering this information, write down:

WHO? Who will be using the product?
Who will be affected by the product?

WHAT? What must the product do?
What needs must it serve?

WHY? Why will the product be used?

WHERE? Where will the product be used?

WHEN? When will the product be used?

For example, a syringe injector may have the following problem definition:

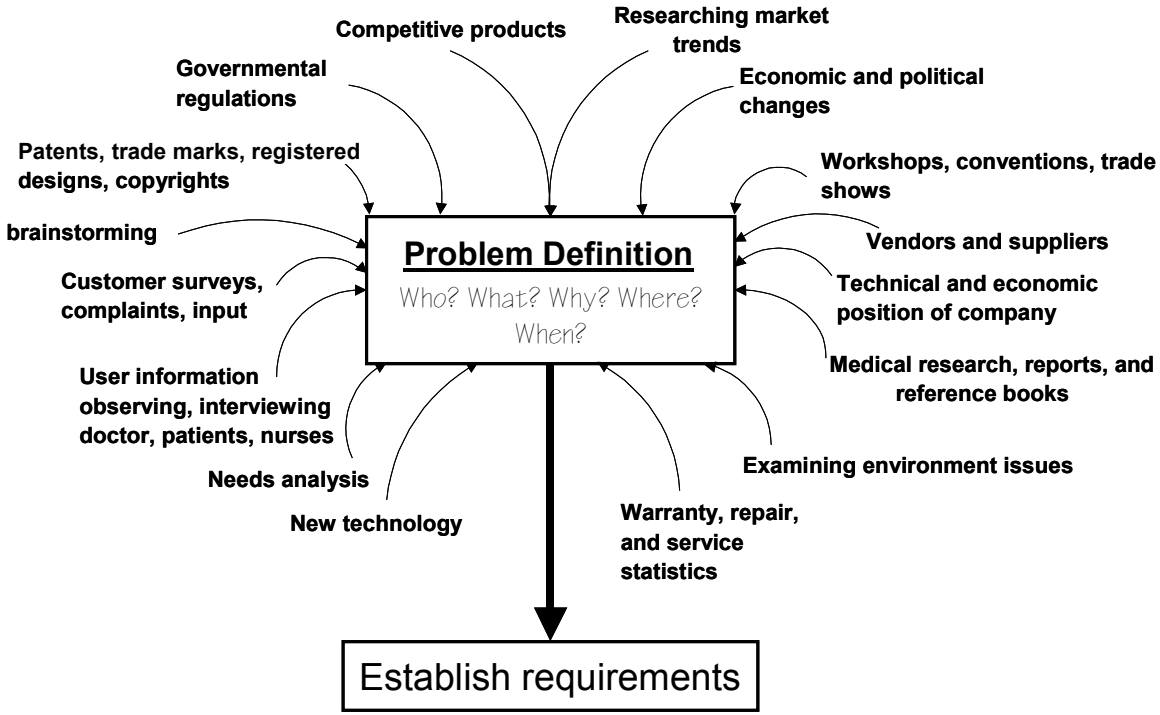
WHO? nurses, doctors, and patients,

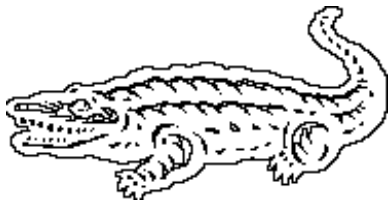
WHAT? drug delivery syringe that is low cost, transportable, and accurate,

WHY? delivery of a drug through single injection,

WHERE? in the home, doctor's office, or hospital,

WHEN? when venous delivery of a drug is required.





2 DETERMINE BUSINESS REQUIREMENTS.

For most new product developments, commercial or business objectives must also be met, for example:

- pay back development costs within a specified time period,
- increase market share within a defined segment,
- extend product life through cost reduction or introduction of new features,
- enhance product range by adding new variants.

A first assessment of how a new product can meet business objectives typically needs to be done before any significant development or investment takes place. It will then be refined as the requirements become clearer and the product definition is evolved. The assessment will need to address factors such as:

- who the users are and what their needs are (see step 1),
- how the new product might expand or change the users' needs and perceptions,
- how this product will be more attractive to users than others available,
- how big the market is and how it is changing,
- the prime causes of change,
- who the competitors are and how they are likely to react to a new product introduction,
- how and when the product will be launched and how long it is likely to be competitive.

3 REVIEWING WHAT IS ACHIEVABLE

Management review of the initial business assessment is vitally important. If a project is not viable, it should be stopped there and then. If a project is marginal, management may decide that it should be re-evaluated.

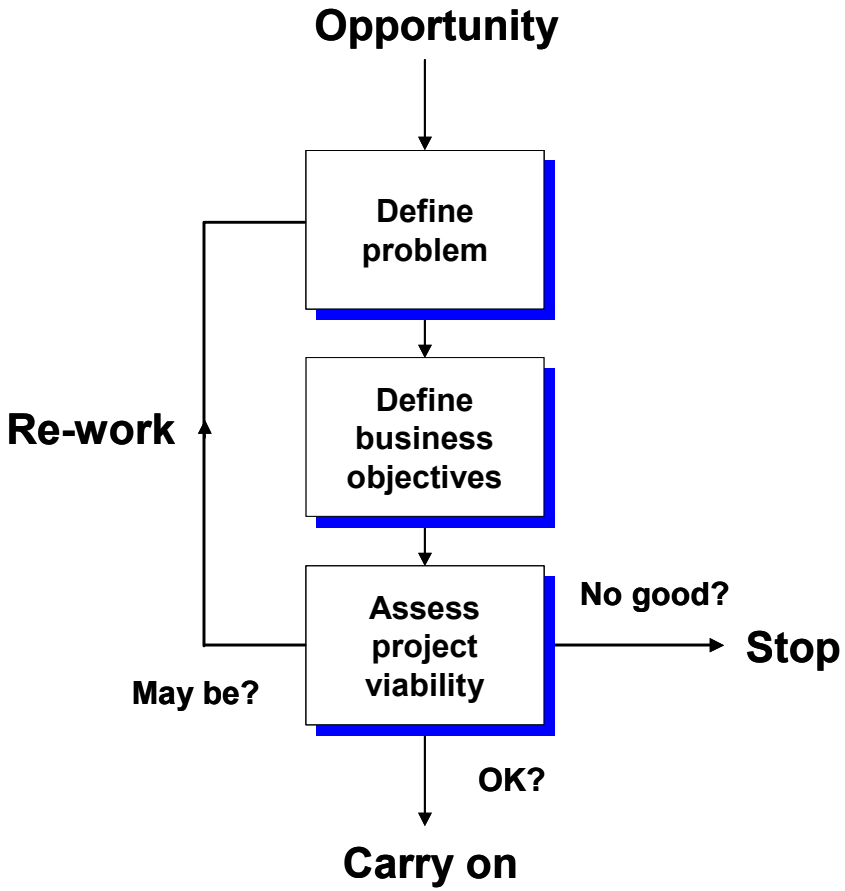
Normally, development programmes include reviews held at appropriate milestones to update the assessment in the light of the evolving product concept. These reviews enable trade-offs to be made where necessary between what is desirable and what is achievable. It is often also appropriate for management to review whether continuing investment in the development is justified.

4 ACQUIRING INFORMATION

Much of the information needed to describe the above factors can be gathered by literature searching or through user research. For products that are essentially 'evolutionary' in nature (such as a product range extension or a product re-engineered to reduce cost) this will often be sufficient. For new products that are more 'revolutionary', either through the use of new technology or through addressing user needs in an innovative way, other approaches need to be used.

These approaches will include seeking expert opinion, using creative techniques to explore unmet user needs, and the use of scenarios to illustrate and explore a range of future possibilities.

Consideration of these factors will help to ensure that product requirements are matched to business requirements and that the product when launched will meet its commercial objectives.

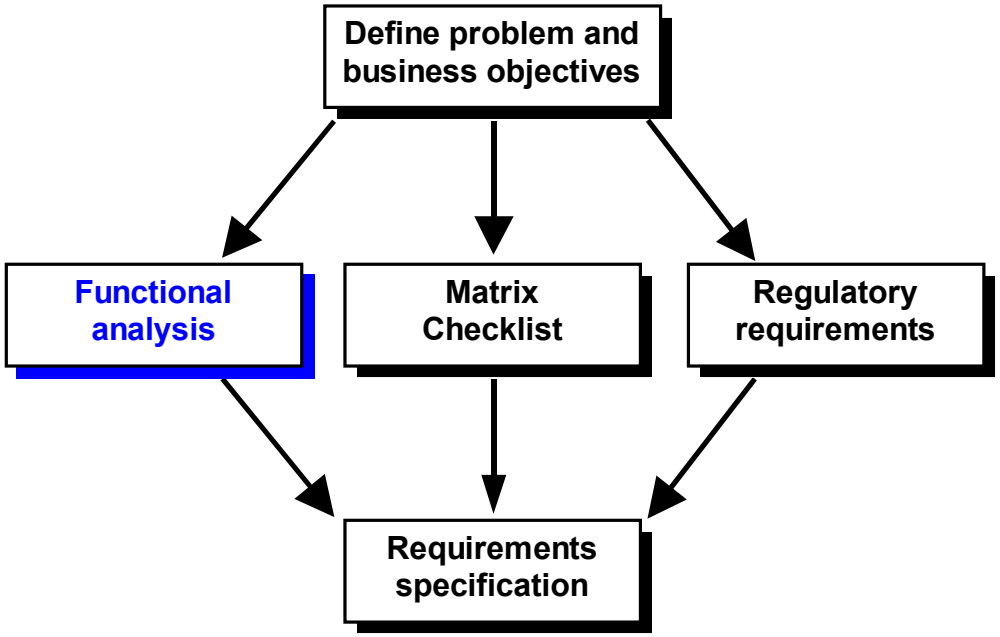


REQUIREMENTS CAPTURE PHASE 2: FUNCTIONAL ANALYSIS

Phase 1 – Set objectives

Phase 2 – Analyse and detail functions

Phase 3 – Document requirements



WHY FUNCTIONAL ANALYSIS?

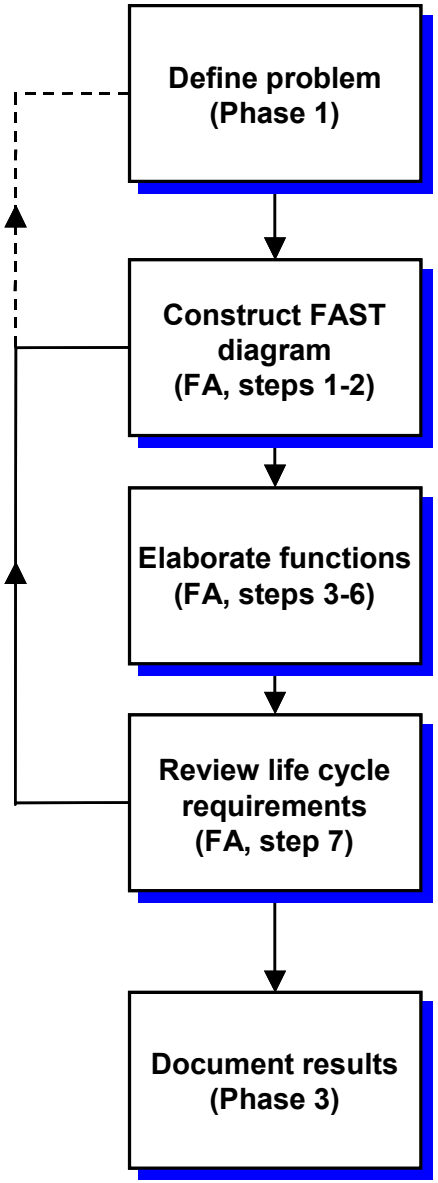
The second phase of the requirements capture method involves use of the functional analysis tool (that is, stating the problem in terms of functions) and is intended to identify functional and performance requirements.

Functional analysis is often done during the concept generation stage of the design in order to help designers generate possible solutions. In this method it is moved one stage earlier, into the task clarification stage. There are many reasons for performing functional analysis at this stage.

Functional analysis:

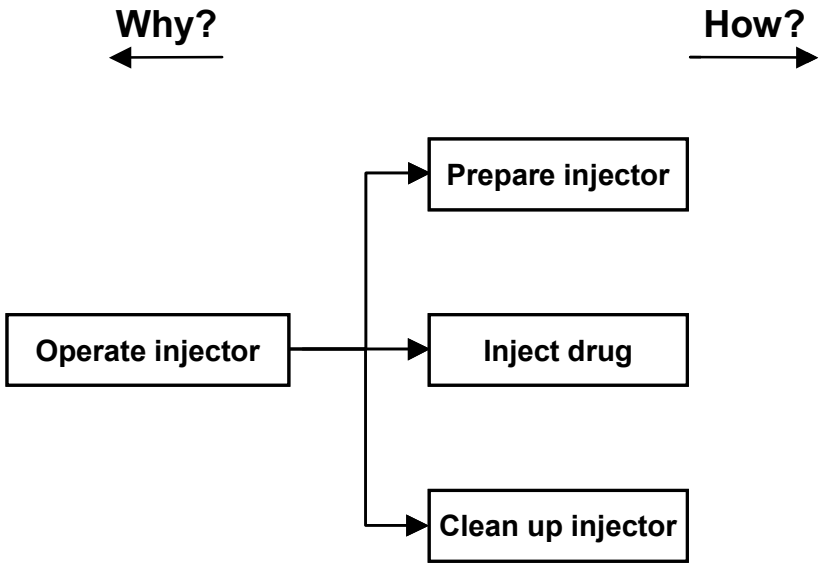
- provides a means for expressing the problem without specifying a particular solution,
- provides a graphical way to view the functional requirements,
- encourages the designer to trace through each function of the product, making it more likely that all the requirements will be captured,
- can be used in other stages of the design process.

The following procedure provides step-by-step instructions for doing functional analysis using the functional analysis system technique (FAST)[1].



[1] Fox, J. (1993) Quality *through design.* London: McGraw-Hill Book Company.

Example: Pen Injector (Syringe)



CONSTRUCT THE FAST DIAGRAM

1 **Determine the main function that needs to be accomplished.**

The main function consists of a verb/noun pair that summarises the problem. The main function is usually very general, for example:

"operate dialysis machine" or "operate inhaler."

Put the main function in a box on the far left side of a piece of paper.

2 **Break down the main function into sub-functions.**

The main function is composed of sub-functions that must be done in order to accomplish the main function.

For each function ask, "*How* will this be accomplished?" Put the answer (or set of answers) to the right of the main function. If there is more than one task that must be accomplished, put them in chronological order from top to bottom. Continue breaking down the sub-functions.

The question "How?" is answered as you move from left to right across the diagram; the question "Why?" is answered as you move from right to left.

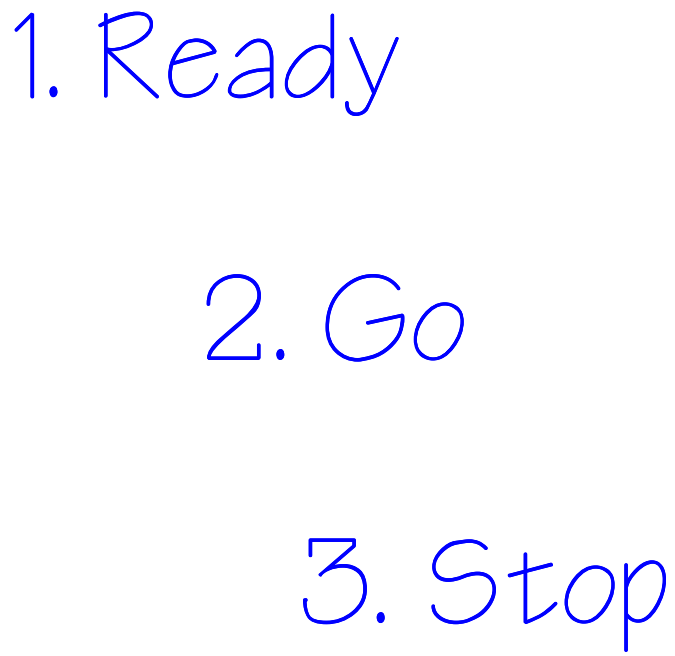
If you keep asking "How?" you will eventually start generating solutions, which begins the conceptual design stage. For requirements specification, it is important to stop asking "How" before you start generating solutions.

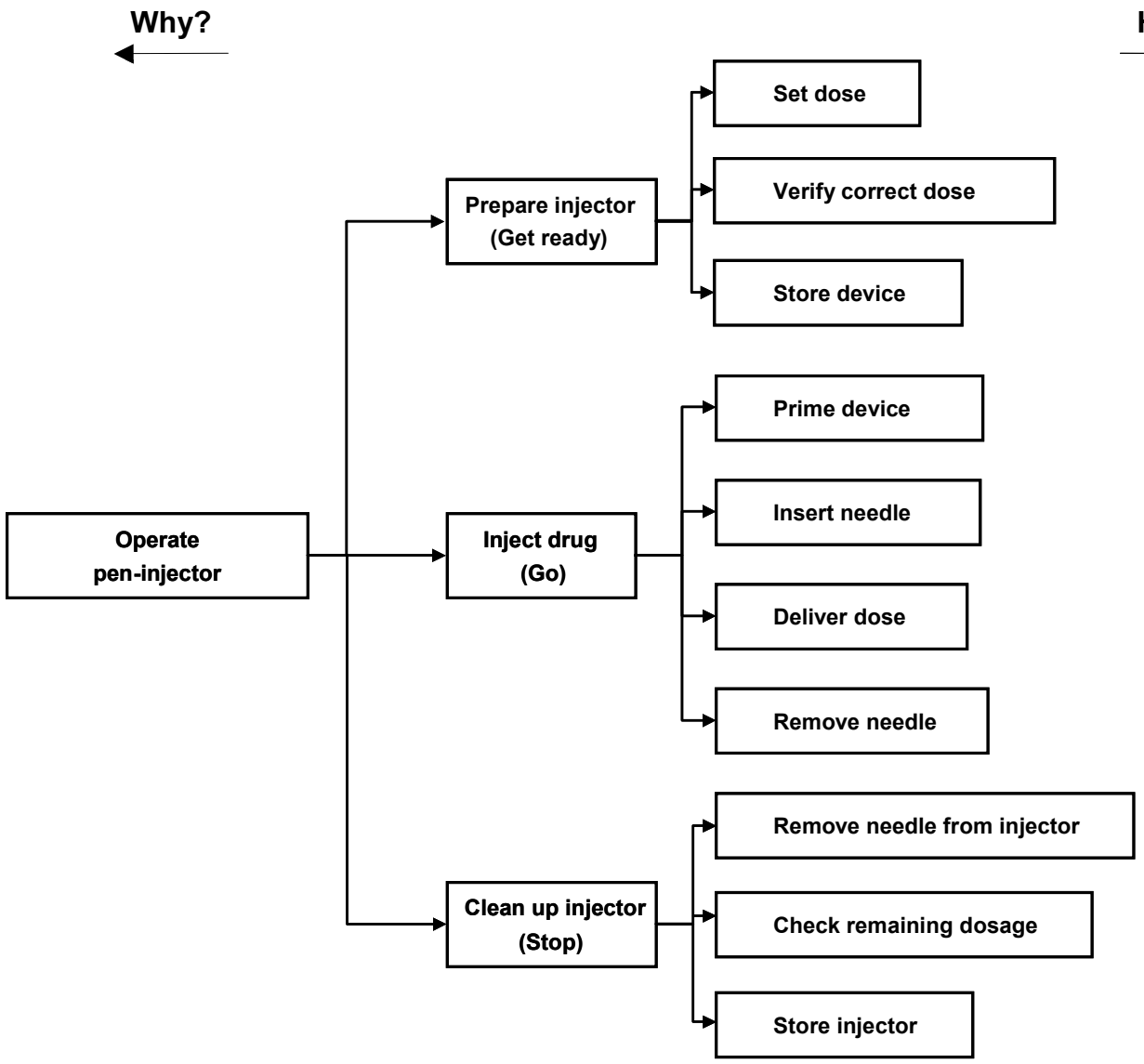
The operation of most devices and processes divides readily into “ready-go-stop” functions:

function	sub function
1. Ready	prepare, set, initialise
2. Go	operate, start, steps of operation
3. Stop	clean up, dispose, save data

Tips for making the FAST diagram:

- start with general functions and get more specific as you keep asking “How?”,
- each function should be a verb and a noun (keep it as simple as possible),
- chronologically trace through each function that must be accomplished - if it is done step by step, you are less likely to miss out on requirements,
- be sure to include all special modes of operation such as stand-by, run and cleaning - functions that are not part of the normal operation are as important as the others,
- avoid specifying form, structure or solutions - the functions should describe behaviour, not embodiment,
- customise the FAST diagram - the more information that can be visualised, the more helpful it is.





This example illustrates a FAST diagram for a pen injector.

The main function, "Operate pen-injector" is broken down into:

1. Get ready - preparing the injector
2. Go - injecting the drug
3. Stop - cleaning up after the injection.

ELABORATE THE FUNCTIONS

3 **Mark the important functions.**

There will be some functions on the right side of the diagram that need to be elaborated or defined in more detail. These functions are usually critical in using the device or accomplishing the task than other functions.

To identify the important functions ask:

- Is this function critical to the operation of the device?
- If this function is taken to the extreme, will it cause harm or damage?
- If this function fails is there potential danger to the user?

Important Function:

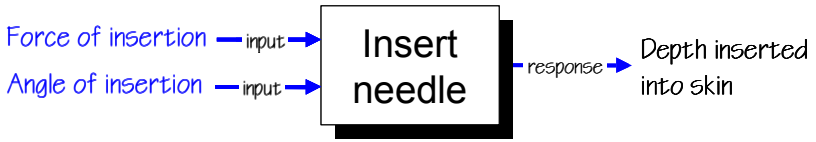
- harms patient if extreme
- injection will not be effective if fails

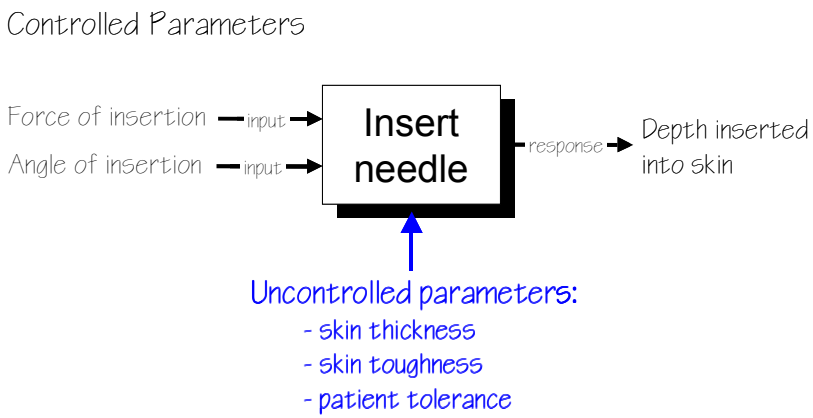
4 **Identify the inputs and responses of the important functions.**

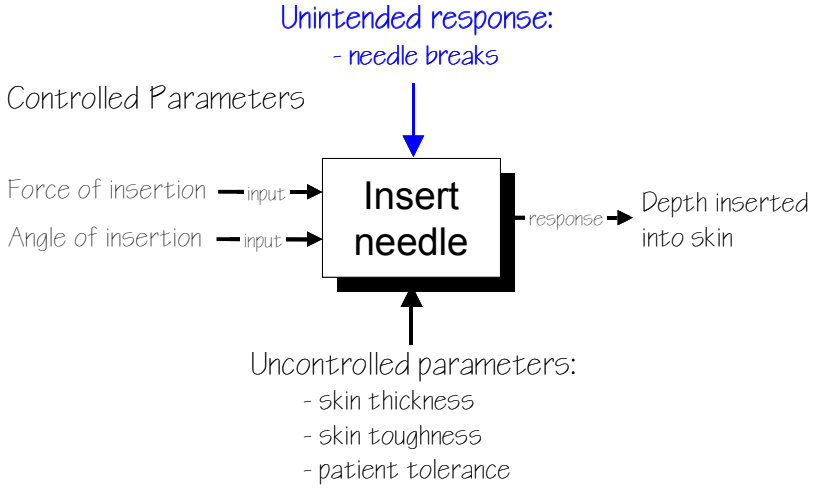
Functions have inputs, which are the parameters, actions, conditions, or signals needed for the function to happen. The inputs the designer can specify in the design are **controlled parameters**.

The input elicits a response from the function. There may be multiple inputs and responses for a single function.

Controlled Parameters







5 Determine the uncontrolled parameters.

An **uncontrolled parameter** is an input to a function that the designer cannot control. Uncontrolled parameters may include:

- environmental conditions,
- irregularities,
- misplacements,
- storage conditions,
- differences between users,
- differences between patients.

6 Identify any unintended responses.

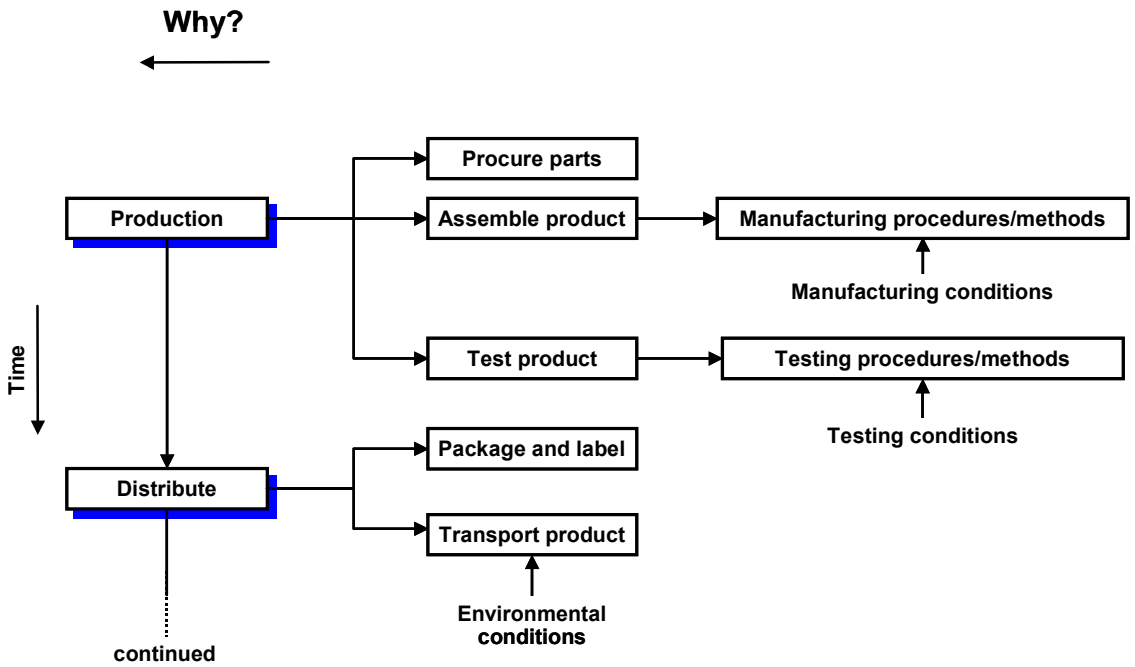
The unintended responses of the system may be in addition to or instead of the intended response. It is a result of the critical parameters and noise affecting the function in some way other than intended.

7 Consider functional requirements throughout the entire life cycle of the product.

It is important to consider the life cycle of the product, not just its use. This includes, manufacture, distribution, support, and disposal.

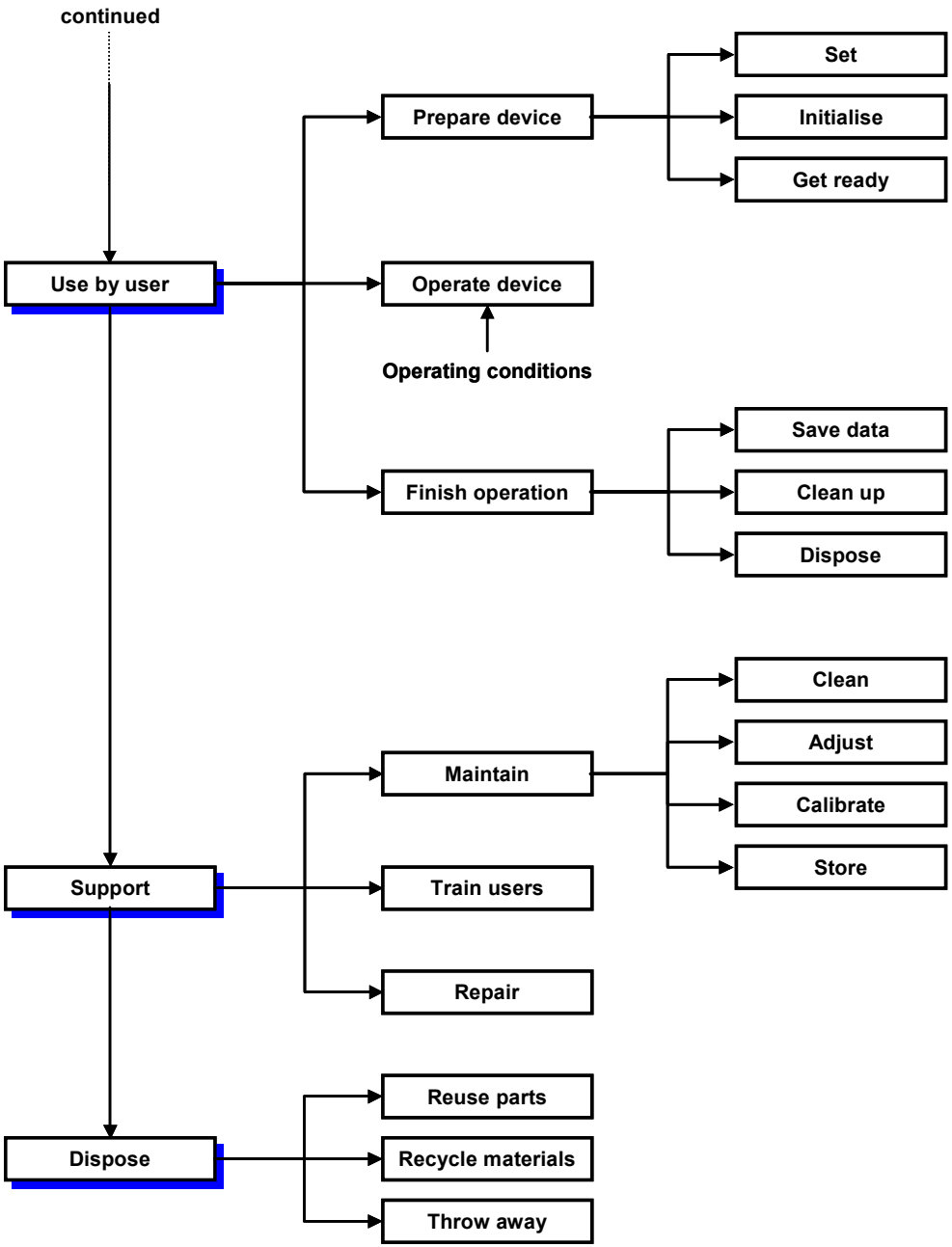
Trace through the following life cycle FAST diagram to identify additional functional and performance requirements.

If certain functions are not defined, then steps 1-6 need to be repeated. It might also to necessary to revisit phase 1 if overall functionality need to be compromised.



How well?	Quality
How often?	Production rate
How fast?	Cycle time
How safe?	Safety precautions
How much?	Costs
How soon?	Schedule
How recorded?	Documentation

How safe?	Safety packaging, transporting
How much?	Transport costs
How soon?	Delivery date
How recorded?	Transport records



How well?	Quality of performance
How long?	Product life span
How fast?	Capable run time
How safe?	Features, interlocks, standards
How much?	Unit cost
How soon?	Market date, life
How recorded?	User instructions, manuals

How long?	Support period
How fast?	Maintenance time
How safe?	Maintenance safety
How much?	Maintenance/inspection costs
How soon?	Servicing/inspection interval
How recorded?	Installation/maintenance instructions, training manuals

How safe?	Environmental compatibility
How much?	Recycling
How soon?	Dispose after how long?
How recorded?	Disposal records

DOCUMENTING THE RESULTS OF FUNCTIONAL ANALYSIS

All requirements should be organised into a requirements specification document. This is achieved by using the template format provided for Phase 3.

Most of the requirements will fall under the category "Functional Performance" (Section 3.3 of the template).

It is convenient to organise the functional performance in terms of function. Each function becomes a separate sub-section in the specification template. The pen injector example is shown on the sample specification.

Requirements Specification

1. Introduction

A pen injector is a drug delivery syringe that doctors and nurses can use to administer a range of drugs. This specification identifies the requirements for a low cost, transportable, accurate pen injector.

2 Functional Properties

2.1 Functional Performance

2.1.1 Dosage Setting

The injector shall have a means for setting the dosage.

The user shall set the dose before every injection.

The injector shall be capable of dosages from 0-0.5 ml.

The injector should be capable of dosage from 0-1 ml.

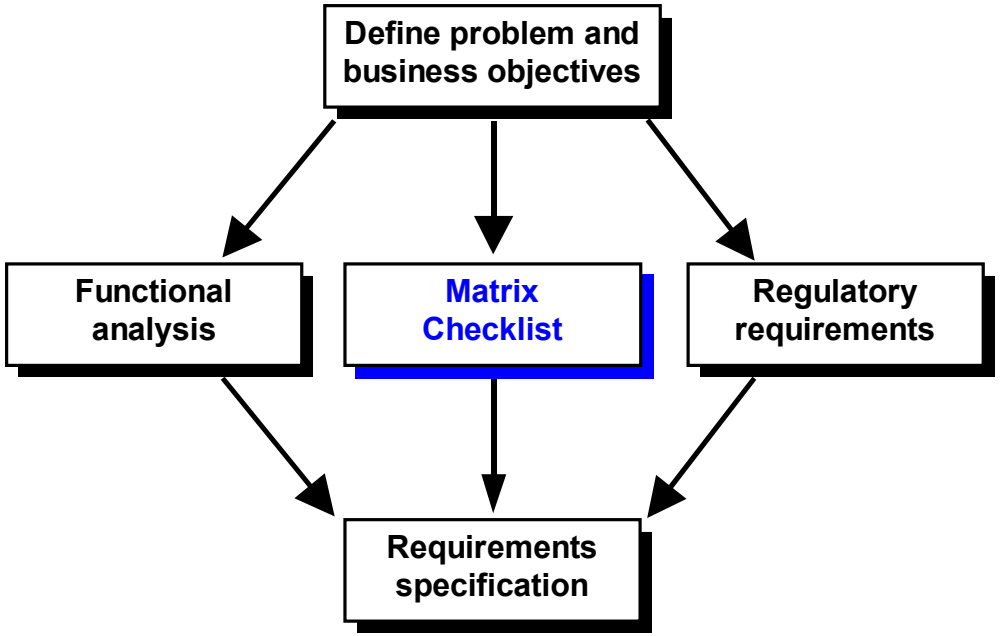
2.1.2 Verification of Dosage Setting

REQUIREMENTS CAPTURE PHASE 2: MATRIX CHECKLIST

Phase 1 – Set objectives

Phase 2 – Analyse and detail functions

Phase 3 – Document requirements



FORMAT OF THE MATRIX CHECKLIST

The purpose of the matrix checklist is to identify requirements not captured by functional analysis. Most of these requirements apply to the product as a whole, not to a particular function. The checklist is presented as a matrix. The rows of the matrix correspond to stages in the life cycle of the product and the columns address the general requirement areas. The matrix is intended to focus the designer's attention on how the product is going to be used (Operation process - top row, left-hand column) and how it should perform in use (Operation performance). Other 'product in use' requirements are captured under Maintenance process, Maintenance performance, Disposal process and Disposal performance.

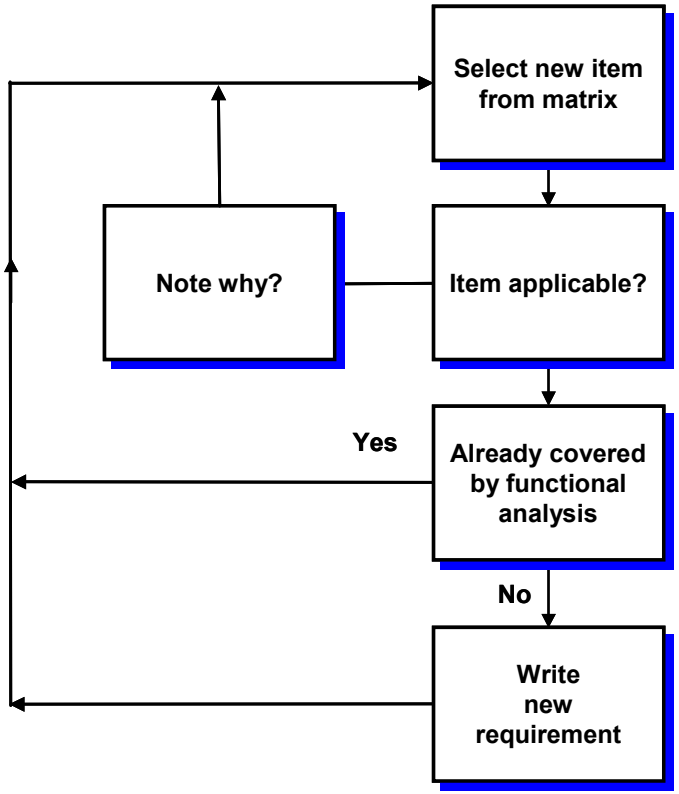
This matrix is intended to be computer-based, whereby clicking on a box in the matrix will bring up the associated checklist. The items of the checklist have also been listed in Appendix 1 of this workbook.

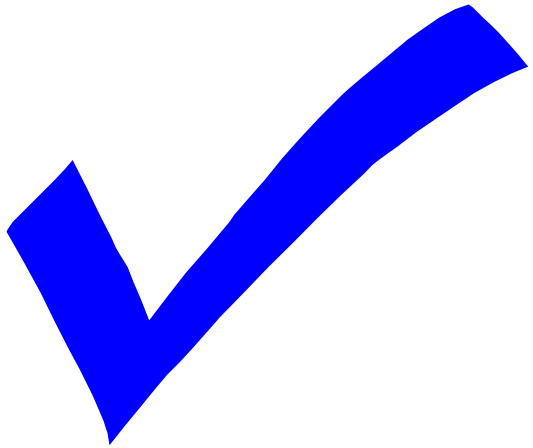
HOW TO USE THE CHECKLIST

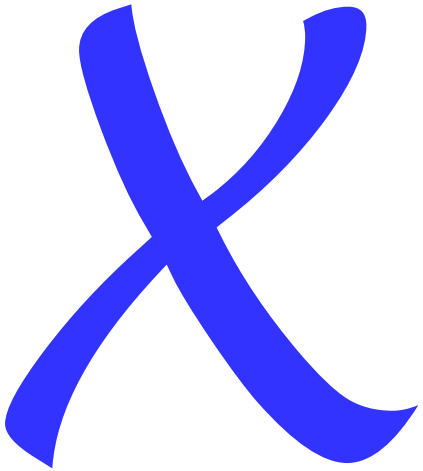
This matrix may be used in parts or in its entirety. It is impossible for a checklist covering a broad area such as medical device design to be fully comprehensive. However, this checklist should trigger ideas to consider.

To use the checklist:

1. Decide if the item is applicable to the product.
2. If it is applicable, determine if there is already a requirement that covers it (identified in the functional analysis).
3. If there is not a requirement already, write one and put it in the appropriate place in the template.
4. If the item is not applicable, you may also wish to note why this is so.







COLUMNS OF THE MATRIX CHECKLIST:

Process - requirements of methods, modes and uses. Many of these items will also be captured in functional analysis. Scheduling, including timelines, dates, and milestones. References to regulations where appropriate.

Performance - usability, availability, reliability, and other general performance requirements. Compatibility with existing products and future product improvements. Characterisation of the environment for each stage of the life cycle. References to regulations where appropriate.

Safety - features, standards, and issues concerning the product throughout its entire life cycle.

Cost - target costs and sources of cost for each stage.

Documentation - appropriate records, logs, and documents to be produced.

See Appendix 1 for the items of the checklist.

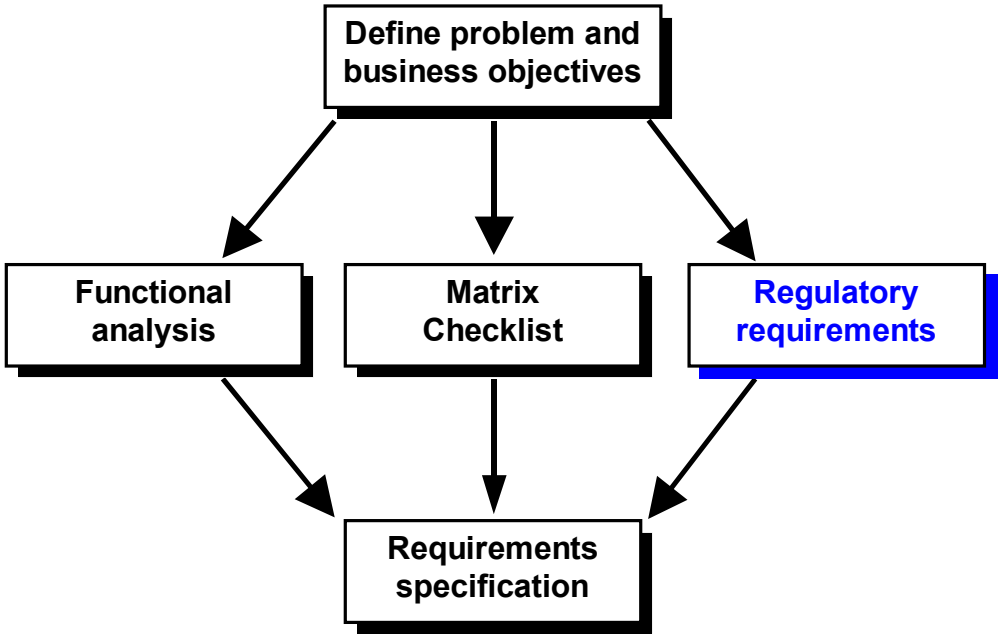
MATRIX CHECKLIST

		Process	Performance	Safety	Cost	Documentation
Product in Use	**Operation**	Operation Process	Operation Performance	Operation Safety	Operation Cost	Operation Documentation
	Maintenance	Maintenance Process	Maintenance Performance	Maintenance Safety	Maintenance Cost	Maintenance Documentation
	Disposal	Disposal Process	Disposal Performance	Disposal Safety	Disposal Cost	Disposal Documentation
Product Design/ Manufacture/ Supply	**Design**	Design Process	Design Performance	Design Safety	Design Cost	Design Documentation
	Manufacture	Manufacturing Process	Manufacturing Performance	Manufacturing Safety	Manufacturing Cost	Manufacturing Documentation
	Distribution	Distribution Process	Distribution Performance	Distribution Safety	Distribution Cost	Distribution Documentation
	Installation	Installation Process	Installation Performance	Installation Safety	Installation Cost	Installation Documentation

Phase 1 – Set objectives

Phase 2 – Analyse and detail functions

Phase 3 – Document requirements



REGULATORY REQUIREMENTS

All medical devices must be approved before they are released to market.

Devices fall into certain type categories. Broadly speaking, for each market area and for each type of device there are internationally and nationally agreed requirements with which the device must be designed to conform. Moves are afoot through the work of the Global Harmonization Task Force (GHTF) to minimise the differences in regional requirements. The GHTF web site is at www.ghtf.org

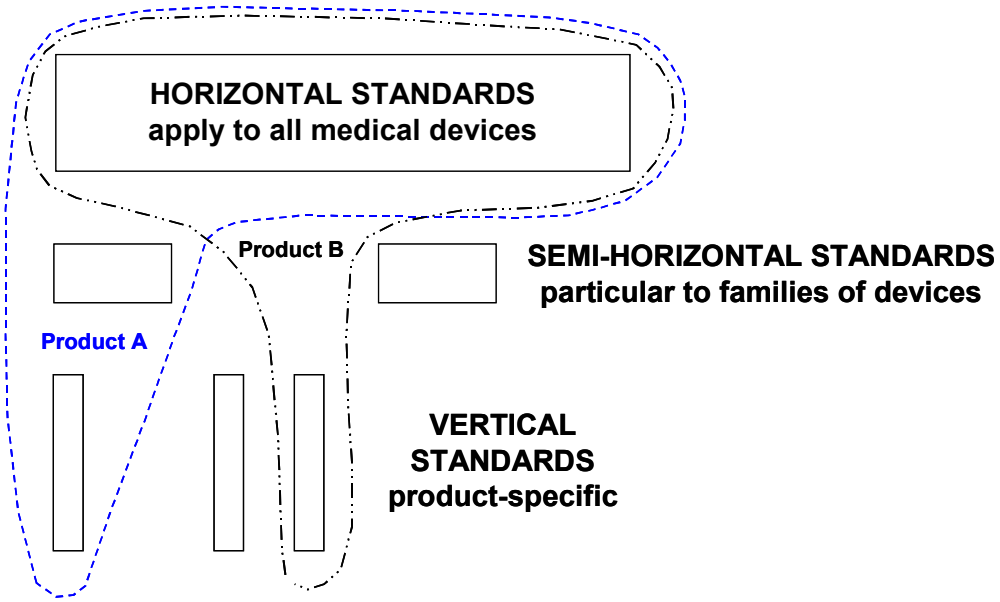
All devices need to be classified, the classification being dependent upon the amount of risk they pose to the user and/or the patient. The classification determines the approval routes that are possible.

This section provides a brief introduction to requirements, device classification and the regulatory environments in Europe and the USA. Appendix 2 contains more detailed guidance on determining the classification of a device and the effects this has on possible approval routes.

IDENTIFYING REQUIREMENTS

At the onset of design, advice should be sought from the relevant Regulatory Authority, Conformity Assessment Body or other authorised third party, or through official publications, on the requirements and standards that are recognised by the Regulation Authority. Not all of the recognised standards are mandatory but the approvals process might well be accelerated if the relevant standards, which represent a consensus of current good practice, are referenced and followed.

A useful perspective on the role and recognition of requirements standards may be found in document GHTF-SG1-N012R10 issued by the GHTF (www.ghtf.org).



Product A must conform to generally applicable standards, family standards and product-specific standards

Product B must conform to generally applicable standards and product-specific standards only

Ultimately, the adoption of international standards will lead to harmonised regulatory processes to assure the safety, quality and performance of medical devices.

There are three types of regulatory requirements standards:

1. **Horizontal standards** - general regulations that apply to all medical devices sold and used in a particular market area.

   Examples for Europe:

   Medical Device Directive (93/42/EEC),

   EN ISO 9000 Quality Management Systems Standards,

   EN ISO 14971 Application of risk management to medical devices.

   In the USA, the Code of Federal Regulations is the master reference source for regulatory information.

2. **Semi-horizontal standards** - particular to a family of devices, such as electrical devices, and regulating certain aspects of the devices such as toxicity, material, or safety.

   Example: BS EN 60601-1 Medical electrical equipment - General requirements for safety

3. **Product-specific or vertical standards** - apply to a particular device or piece of equipment.

   Examples: Rehabilitation Engineering and Assistive Technology Society of North America (RESNA) standard WC93-1991 sets maximum wheel chair dimensions,

   BS EN 60601-2-16 specifies particular requirements for the safety of haemodialysis equipment.

Appendix 3 references the sources for standards information.

CLASSIFICATION OF DEVICES

Medical devices are classified into groups by their potential risk and the dangers they pose to users and/or patients. The classification of the device determines the level of intervention by the relevant regulatory authorities in controlling the design and production of the device.

Class 1 - low risk healthcare devices, for example, spectacles, hospital beds and tongue depressors

Class 2 - medium risk devices

The EU regulatory system splits Class 2 devices further into 2a and 2b, with the latter being higher risk.

Class 2a covers short-term invasive devices, for example, endoscopes and hypodermic needles.

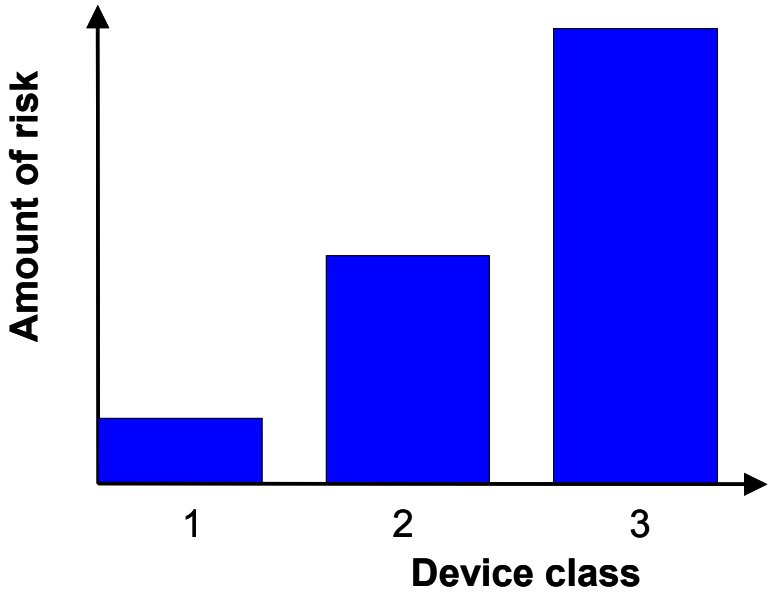
Class 2b covers devices that impart energy in a potentially hazardous way, for example, X-ray machines.

Class 3 - high-risk devices

This relates to long term invasive devices that come into contact with the central nervous system or the circulatory system.

Examples of long-term invasive devices are heart valves, pacemakers and aortic balloons. Class 3 also covers devices that contain medicines or substances derived from animals, for example, heparin-coated catheters or antibiotic-coated wound dressings.

The classification of a device is often, but not necessarily, the same between the EU and US systems. You must confirm the classification in each system as this usually has an impact upon the amount and type of work required to design and evaluate the device (How to classify your device is explained in Appendix 2).



	EU	US
Regulatory Authority	Competent Authorities, usually the Ministry of Health of each of the member states. They delegate responsibility for performing assessments to Notified Bodies (usually private companies).	Government (FDA)
Risk-based classification	Class 1, 2a, 2b, 3 Manufacturer decides classification.	Class 1, 2, 3 FDA decides classification
Approval routes	1. Full quality assessment 2. Type examination with partial quality assessment 3. Testing by Notified Bodies	1. Pre-market notification 2. Pre-market approval
Objectives	Device is safe and *performs as manufacturer intended.*	Device is safe and *effective* (benefit to user).

DIFFERENCES BETWEEN EU AND US REGULATIONS

The European Union and the United States are attempting to harmonise, but there are still some major differences in the approval processes and regulations. A device must meet both EU and US regulatory requirements if it is to be sold in both markets.

- In the EU, regulatory assessments are performed by the Notified Bodies, which are usually private companies. These are appointed and monitored at the national level by a Competent Authority, such as the Medical Devices Agency in the UK. In the US, the government maintains regulatory control through the Food and Drug Administration (FDA).

- Both the EU and US use risk-based classification systems. In the EU the manufacturer decides the classification; in the US the FDA does.

- Both systems have approval routes that depend on the classification of the device.

- The objectives of the regulatory control are different between the two systems:

  EU: ensure the device is safe and *performs as the manufacturer intended,*

  US: ensure the device is safe and *effective.*

This means that devices both in the EU and the US must be proven to be safe and demonstrate benefit to the user, often through clinical evaluations. This extends the time to market.

EUROPEAN REGULATIONS

The European regulations are encapsulated in the three European Union Medical Device Directives:

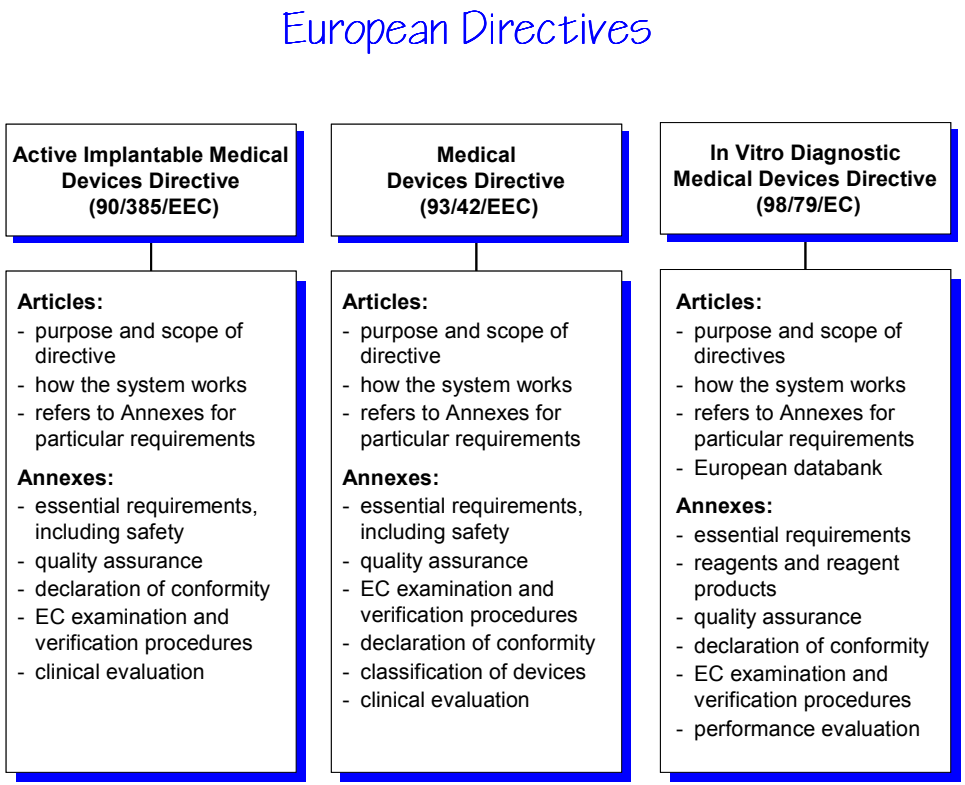
- Active Implantable Medical Devices Directive (90/385/EEC), published in June 1990,
- Medical Device Directive (93/42/EEC), published in July 1993,
- In Vitro Diagnostic Medical Devices Directive (98/79/EC), published in December 1998.

The contents of the Directives are summarised on the right.

The purposes of the Directives are:

1. to ensure devices are safe,
2. to ensure devices perform as the manufacturer intended,
3. to harmonise standards throughout Europe.

All devices that meet the directives are labelled with the CE mark and can be sold in the EU.



www.mueller-lierheim.com/regaff/reg_affs_europe.htm

Quality requirements and guidance

Scope of activity	Product design, manufacture, test, delivery and support	Product manufacture, test, delivery and support
Quality requirements	EN ISO 9001:1994 EN ISO 13485:1996	EN ISO 9002:1994 EN ISO 13488:1996
Non-active device guidance	EN 724:1994	EN 724:1994
In vitro diagnostic device guidance	EN 928:1995	EN 928:1995
Active device guidance	EN 50103:1996	EN 50103:1996

Use of the international quality (ISO) standards for general products, is the most common way to comply with the EU Directives requirements for quality assurance.

The European version of the ISO quality management standard is EN ISO 9001:1994 Quality systems – Model for quality assurance in design, development, production, installation and servicing. It sets out the requirements and controls that the management system must satisfy in order to assure the quality of the product delivered to the customer. For organisations only involved in production, installation and servicing, EN ISO 9002:1994 is applicable.

Supporting standards EN ISO 13485:1996 and EN ISO 13488:1996, which have replaced EN 46001 and EN 46002 respectively, define the special requirements for the application of EN ISO 9001:1994 and EN ISO 9002:1994 to medical devices.

Other guidance may be extracted from EN 724:1994 for non-active medical devices, EN 928:1995 for in vitro diagnostic medical devices and EN 50103:1996 for active medical devices.

The latest version of the quality standard, EN ISO 9001:2000 is significantly different from the 1994 version and has still to be adopted in EU regulations. When this happens, the related guidance standards will also require to be updated.

The British versions of the European standards have 'BS' as a prefix to the 'EN' number. The date of issue may, however, differ, for example, BS EN ISO 13485:2001 contains the same text as EN ISO 13485:1996. It is always worth checking the title of the standard and its origins, if possible.

US REGULATIONS

The following US laws define the government regulatory control:

Medical Device Amendment of 1976 ensures safety and effectiveness of medical devices through:

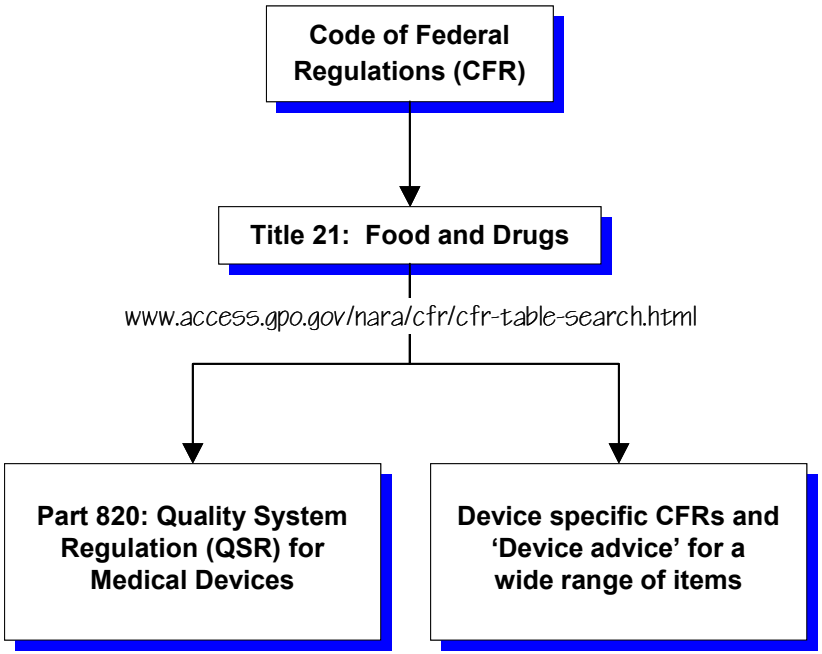
- pre-market approval - FDA must approve the medical device before it is released to market,
- compliance with Quality System Regulation (QSR) to ensure the introduction to market of products of consistent quality,
- post market surveillance to monitor the performance of the device after being released to market.

Safe Medical Device Act (SMDA) of 1990 and the Medical Device Amendments of 1992 require:

- pre-production design controls,
- data analysis of recalled devices,
- harmonisation of USA regulatory requirements with international regulations, especially ISO 9001.

The web sites for the Code of Federal Regulations (CFR) (www.access.gpo.gov/nara/cfr) and the FDA Center for Devices and Radiological Health (CDRH) (www.fda.gov/cdrh/index.html) contain the latest regulatory information.

Title 21 CFR Part 820 - Quality System Regulation (1996) is similar to EN ISO 9001:1994 (see next page) but it also includes detailed regulations on validation, labelling, and complaint handling. The relationship between Title 21 CFR Part 820 and EN ISO 9001:2000 is shown on page 36.



The following table summarises the quality requirements covered by Title 21 CFR Part 820 (CGMP) and EN ISO 9001:1994. The first two columns are the references to the appropriate sections in the respective documents.

CGMP	ISO	Stage in Life Cycle	Summary of Requirement
820.30	4.4	design and development	Write a design plan.
820.30	4.4	design input	Make sure design requirements are appropriate and address intended use and needs of user.
820.30	4.4	design output	Identify acceptable criteria for output so that device functions properly.
820.30	4.4	design verification	Make sure device meets requirements.
820.30		design validation	Make sure device meets user needs.
820.30	4.4	design changes	Establish a way to record design changes.
820.30		design history file (DHF)	Prove that design plan was followed.
820.40	4.5	document control	Establish procedures to control documents (approval, distribution, changes).
820.50	4.6	purchasing controls	Make sure anything purchased meets requirements.
820.60	4.7	identification	Have a way to identify the product through all stages of its life cycle.
820.65	4.8	traceability	If there is risk of injury while using device, make sure the device can be traced to a lot or batch. (Makes corrective action easier)
820.70	4.9	production controls	Make sure product is produced to specifications. (Includes making sure the environment, personnel, and equipment are correctly maintained, inspected, and adjusted.)
820.72	4.10	inspection and testing	Make sure inspection, measuring and testing equipment is suitable.
820.75		process validation	Make sure the manufacturing equipment makes what it is supposed to.
820.80	4.11	acceptance activities	Establish tests, inspections, and verifications to show that product meets the criteria,
820.86	4.12		Have a way to show if a product was accepted or rejected.
820.90	4.13	nonconforming products	Decide what to do with products that are not accepted.
820.100	4.14	corrective action	Figure out why the product does not work and take corrective action to prevent more failures.
820.120		labelling	Label the product correctly.
820.130-160	4.15	handling	Handle, store, pack, and deliver product without damaging
820.170		installation	Write installation instructions if necessary.
820.180	4.16	records	Maintain all records to show the quality plan was followed.
820.181		documentation	Device Master Record (DMR) shall include documentation for all of the above procedures.
820.184		documentation	Device History Record (DHR) shall record the date of manufacture, the quantity manufactured, and the test results for each batch, lot, or unit.
820.186		documentation	Quality system record shall document the quality system procedures.
820.198		complaint handling	Complaints should be processed, acted on, and filed.
	4.17	training	Make sure proper training is provided.
820.200	4.19	servicing	Provide instructions for servicing and maintain service reports when necessary.

The following table compares the scope of Title 21 CFR Part 820 (QSR) with that of EN ISO 9001:2000. The first two columns are the references to the appropriate sections in the respective documents. It can be seen that QSR contains specific documentation requirements.

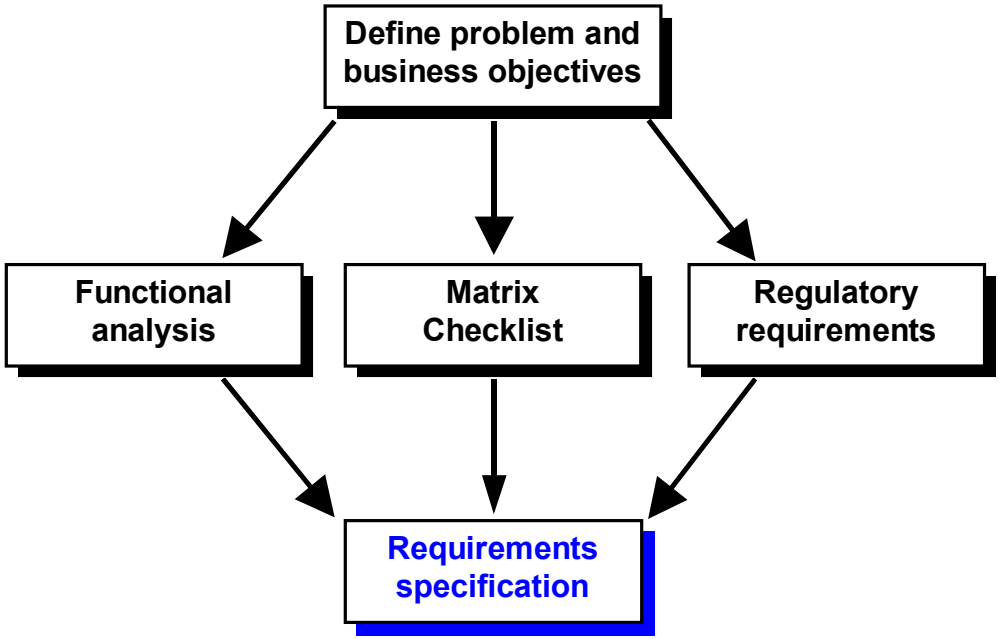
QSR	ISO	Stage in Life Cycle	Summary of Requirement
820.20	5.1-5.5		Management is responsible for establishing quality policy and objectives, organisation structure, responsibilities and authorities, quality planning and quality system procedures
820.22	5.6		Establish procedures for quality audits.
820.25	6.2		Provide trained and appropriately experienced personnel.
820.30	7.1, 7.3.1	design and development planning	Write a design plan.
820.30	7.2, 7.3.2	design input	Ensure design requirements are appropriate and address intended use and needs of user.
820.30	7.3.3	design output	Identify acceptable criteria for output so that device functions properly.
820.30	7.3.4	design review	Plan and document reviews of design results at appropriate stages of design.
820.30	7.3.5	design verification	Ensure device meets requirements.
820.30	7.3.6	design validation	Ensure device meets user needs.
820.30	7.3.3	design transfer	Correctly translate design into production specifications.
820.30	7.3.7	design changes	Establish a way to record design changes.
820.30		design history file (DHF)	Prove that design plan was followed.
820.40	4.2.3	document controls	Establish procedures to control documents (approval, distribution, changes).
820.50	7.4	purchasing controls	Ensure all purchased goods and services meet specified requirements.
820.60	7.5.3	identification and traceability	Identify the product through all stages of its life cycle. If there is risk of injury while using device, make sure the device can be traced to a lot or batch. (Makes corrective action easier.)
820.70	7.5.1	production and process controls	Ensure product is produced to specifications. (Includes making sure the environment, personnel, and equipment are correctly maintained, inspected, and adjusted.)
820.72	7.6	inspection, measuring and test equipment	Ensure inspection, measuring and test equipment is suitable and calibrated.
820.75	7.5.2, 8.2.3	process validation	Ensure the manufacturing equipment makes what it is supposed to.
820.80	8.2.4	acceptance activities	Establish tests, inspections, and verifications to show that product meets the criteria,
820.86	7.1, 8.2.4	acceptance status	Identify product to show whether it has been accepted or rejected.
820.90	8.3	nonconforming products	Decide what to do with products that are not accepted.
820.100	8.5.2	corrective and preventive action	Ascertain why the product does not work and take action to prevent more failures.
820.120	7.5.5	labelling	Label the product correctly.
820.130-160	7.5.5	packing, handling, storage and distribution	Pack, handle, store, and deliver product without damaging it.
820.170	7.5.1	installation	Write installation, inspection and test instructions if required and ensure product is installed in accordance with these.
820.180	4.2.4	records	Maintain all records to show the quality plan was followed.
820.181		documentation	Device Master Record (DMR) shall include documentation for all of the above procedures.
820.184		documentation	Device History Record (DHR) shall record the date of manufacture, the quantity manufactured, and the test results for each batch, lot, or unit.
820.186	4.2.1	documentation	Quality system record shall document the quality system procedures.
820.198	7.2.3, 8.2.1	complaint handling	Complaints should be processed, acted on, and filed.
820.200	7.3.3, 7.5.1	servicing	Provide instructions for servicing and maintain service reports when necessary.

REQUIREMENTS CAPTURE PHASE 3: DOCUMENT REQUIREMENTS

Phase 1 – Set objectives

Phase 2 – Analyse and detail functions

Phase 3 – Document requirements



SPECIFICATION TEMPLATE

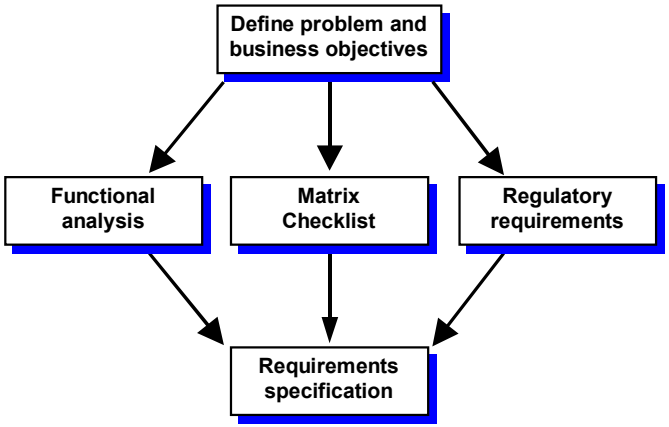
It is necessary to structure and organise the Phase 1 definitions and the requirements generated from the functional analysis, matrix checklist, and regulatory guidelines parts of Phase 2. This template provides a format for the requirements specification document. The template supplies the main headings and possible sub-headings of the specification and prompts you for the requirements to include under each heading.

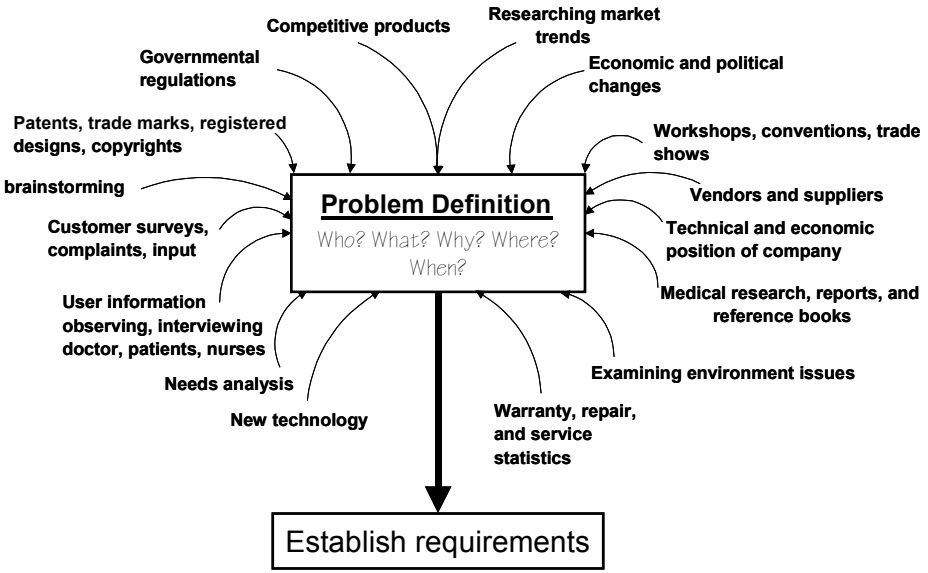
In order to fill in the specification template:

1. Use the definitions of the problem and the business objectives derived in Phase I.
2. Transfer all the requirements from the steps of functional analysis into the appropriate places in the template.
3. As you go through the matrix checklist, add requirements that are identified under the appropriate heading.
4. Complete the specification by including all relevant regulations and standards.

For each section in the template, an indication is given of from where most of the requirements in that section will come.

This is only a template and should be modified as necessary. It is however, useful to have a standard template in order to maintain consistency and clarity between requirements specifications.





SUGGESTED FORMAT

1. Introduction

Use the assessment data generated in Phase 1 and describe the general task to be accomplished by the medical device or equipment. Include the scope of the product/process and its intended use.

Identify issues pertinent to marketing, for example, where the product will be marketed, what other products it will be marketed with, anticipated sales quantities, distribution routes and patenting policy.

Summarise the financial objectives that are to be achieved.

2. Regulations and Standards

Identify the international, federal, and regional regulations that apply. Classify the product according to these regulations. Note the approval routes that are relevant, the likely extent of the approvals process and the requirements for technical documentation.

3. Functional Properties

3.1 Requirements derivation

It is necessary to translate the FAST/functional diagram derived during function analysis into document form for the requirements specification.

The requirements are derived from the lowest level functions, which are the functions furthest to the right of the FAST diagram. These are the elemental functions that are required of the product; functions at higher levels in the hierarchy are composed of these elemental functions.

Each identified requirement should be testable, quantitative when possible, solution independent, and have a rationale. A checklist of the properties that should be considered is tabulated on the left.

Requirements check list:

- **relationship?** - should relate directly to an elemental function
- **performance?** – review the 'how' questions associated with requirement (see next page)
- **testable?** - is requirement quantitative?
- **solution independent?** - does the requirement specify a solution?
- **safety?** - does the requirement have associated hazards or risks? (see section 3.5)
- **rationale?** - what is the rationale behind the requirement? This is particularly important for requirements specifying a particular solution

- How much?
- How soon?
- How often?
- How fast?
- How long?
- How many?
- How accurate?
- How will it be documented?
- How easy?

3.2 Performance

For each function, there could be several associated performance requirements, each of which may be determined by asking the 'How' questions.

Whereas functional requirements identify ***that*** something must be done, performance requirements identify ***how well*** it must be done.

For each performance requirement provide the nominal value, acceptable range, and tolerances when possible.

An example of the way in which these performance criteria may be applied whilst constructing the FAST diagram is shown on pages 20 and 21.

3.3 Documenting each requirement

Using again the example of the injector, for the function 'set dose', the requirements would be listed as follows (the rationale for each is shown in brackets). For mechanisms, performance requirements might include, for example: speed of operation, capacity, load handling, accuracy, repeat-ability, response time, quietness and expected lifetime.

It is tempting when writing functional requirements to include how it will be achieve, but this should be avoided. ***The requirement should not identify a solution.***

For example, the function 'set dose' generates a functional requirement:

> 'The injector shall have a means for setting dosage.'

not,

> 'The dosage shall be set by twisting a dial.'

Use ***shall*** to indicate requirements that are demands that must be met.

Use ***should*** to indicate requirements that are wishes that should be met if possible.

Function: Set Dose

The injector **shall** have a means for setting dosage (injector will be used for variable dosage).

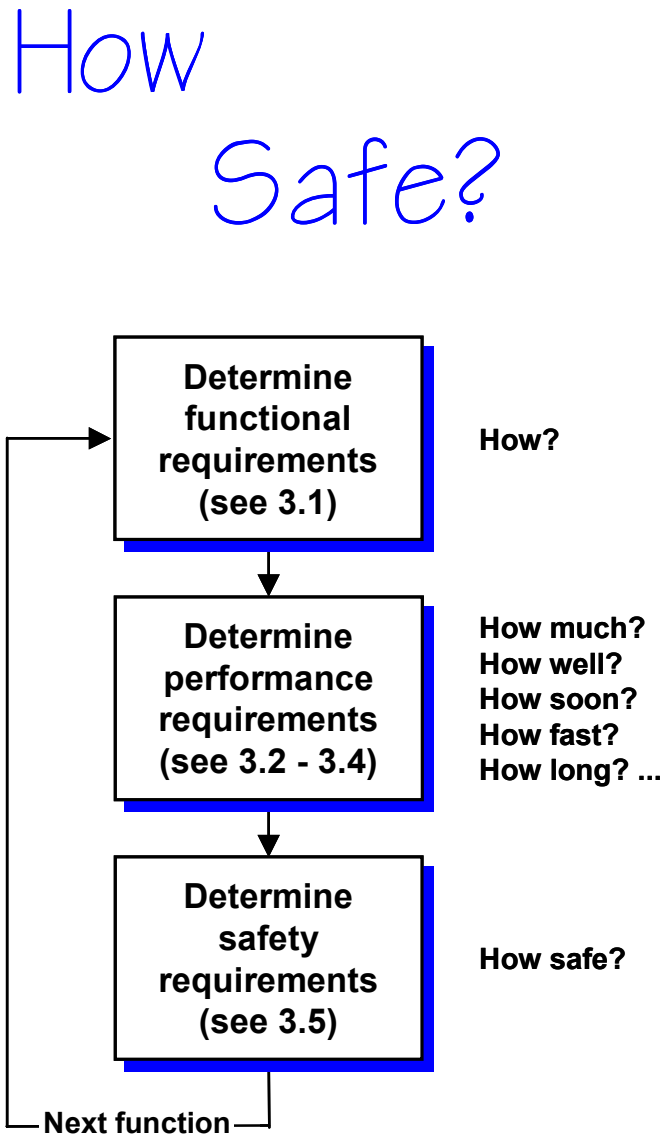
The user **shall** set the dose before every injection (ensure the proper dosage is given).

The injector **shall** be capable of dosages from 0 to 0.5 ml (the injector will be used with drugs requiring this range of dosage).

The injector **should** be capable of dosages from 0.5 to 1ml (0.5-1 ml is not necessary, therefore indicated as a wish).

Shall = Demand

Should = Wish



3.4 Testability

Indicate if the requirement is testable and solution independent and record the rationale behind the requirement.

For each performance requirement provide the nominal value, acceptable range, and tolerances when possible.

3.5 Identify safety requirements and precautions.

If the function is an important function as identified in steps 3 and 4 of Part 1 functional analysis, determine if there is a need for safety requirements to protect the user from danger in case of failure.

These safety requirements may include:

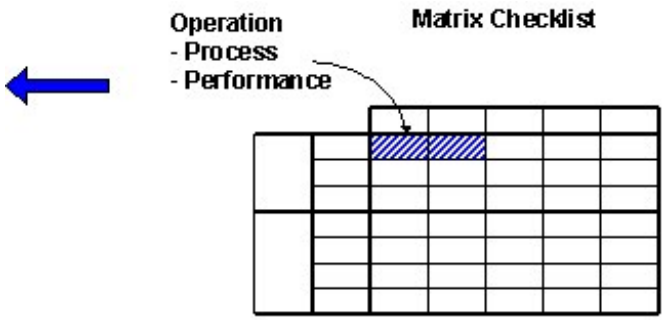
- safety features,
- interlocks,
- warnings and alarms,
- fail safe mechanisms,
- fault handling hierarchy,
- detection systems,
- means of recovery from failure.

If a safety is an issue, include the appropriate requirements.

3.6 Completing the functional properties

Continue to build up the requirements specification for the rest of the functions starting at the top right of the FAST diagram and continuing down the right side.

Use the Matrix Checklist as a further check to ensure that all requirements have been considered.



3.7 Modes of Operation/Use

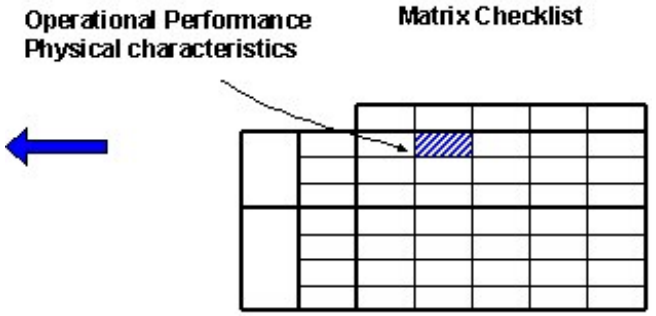
Indicate all modes of operation or ways of using the device, for example, on, off, run, stand-by, save, failure modes, future use, non-use (storage).

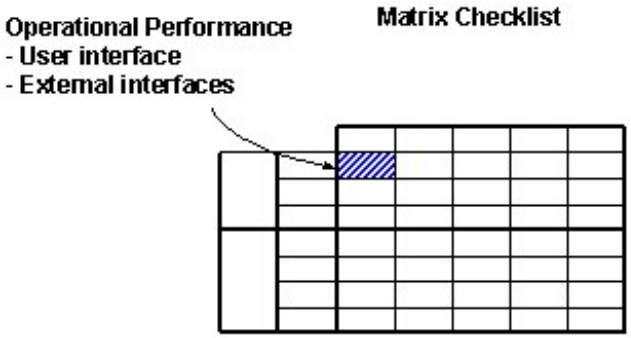
Indicate how the modes are related, and what functions occur in each mode.

4. Physical Properties

Determine the physical characteristics that are required.

Include, for example, weight, size, colour, biocompatibility requirements and material.

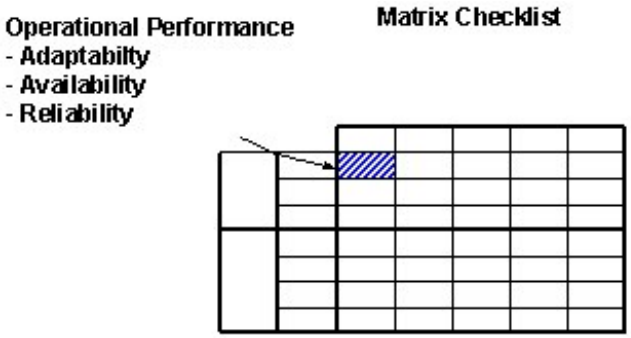




5. Interface Requirements

Determine the information that must be supplied to and supplied by the product.

Include interaction with the user, information required for each operation, signals, indicators and ease of use. Include how each interface interacts. Indicate, when necessary, particular interface technologies.



6. Additional Performance Requirements

6.1 Adaptability

Identify any previous products or equipment with which the system should be compatible. Specify any additional functions that may be considered in the future.

6.2 Availability

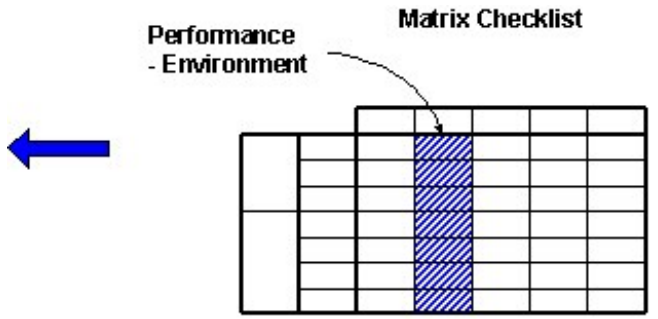
Determine the level of downtime that can be accepted whilst the product is in use, that is the mean availability and the mean time between failures (MTBF).

6.3 Reliability

Establish the reliability required of the device including: mean time to failure, mean time to repair, robustness, drop test, and diagnostic methods for detecting failure.

7. Environmental Conditions

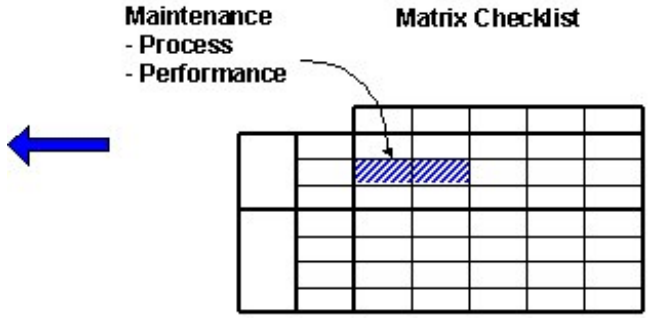
Indicate the environmental conditions in which the device/equipment must function, for example, temperature, pressure, humidity, clean room or other con-trolled environment, manufacturing conditions, storage conditions and transporting conditions (shock, vibrations).



8. Maintenance

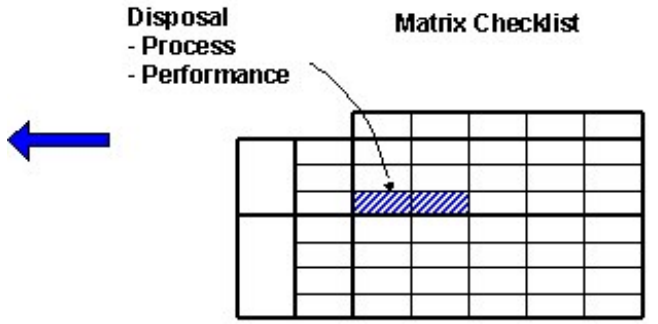
Establish requirements for upkeep of the device or equipment, for ex-ample, test and calibration equipment needs, how often the device must be cleaned, calibrated, or maintained, the cleanability of parts, sterilisation if necessary and inspection interval.

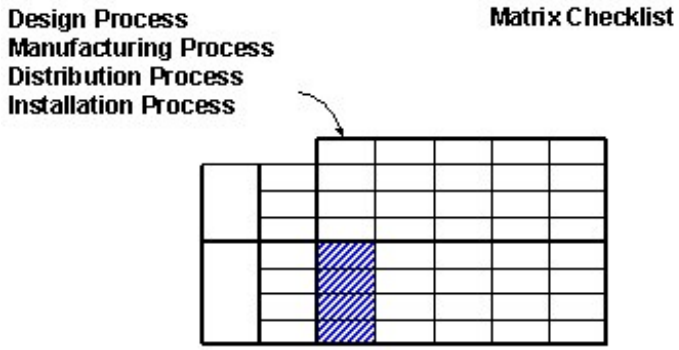
Identify the maintenance philosophy required to meet user's requirements for mean time to repair, on-line support, etc.



9. Disposal

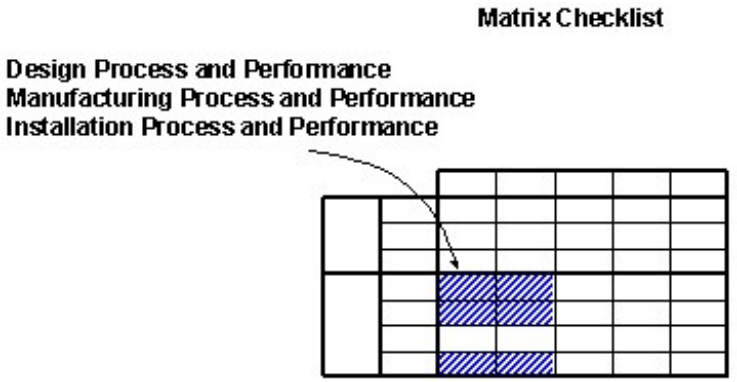
Define requirements for disposal of the device or equipment. These include specialised dismantling equipment, the policy to be followed regarding the disposal of dismantled equipment and materials, and the potential for recycling.





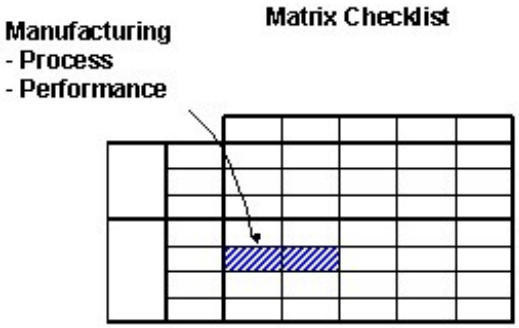
10. Schedule

Establish the project plan or timeline to indicate when certain stages of the design must be completed. Evaluate the time required to set up manufacturing, distribution and installation (if required).



11. Validation

Review the functional requirements and the way in which each of these should be tested. Thence, establish what requirements and aspects of verification and validation should be covered by simulations, models and prototypes during product development and how final verification and validation is to be performed by means of clinical trials and/or user acceptance tests.

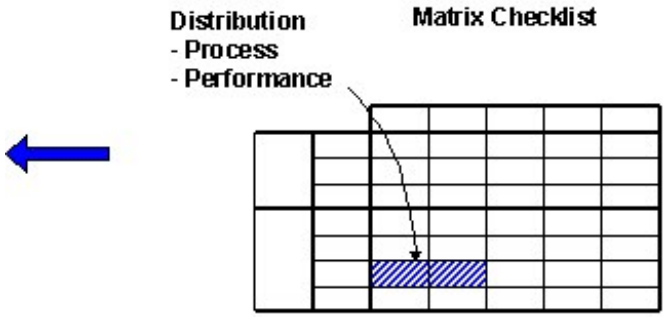


12. Manufacturability

Identify requirements relating to the manufacturing of the device such as referred methods of production, factory limitations, production quantity and product testing requirements.

13. Distribution and Storage Requirements

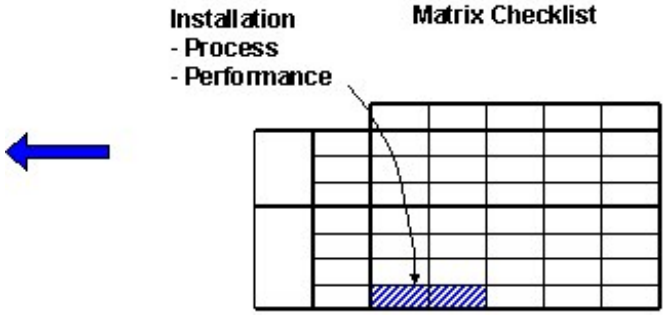
Identify the preferred means of distributing and storing the product, including labelling needs and shelf life.



14. Installation

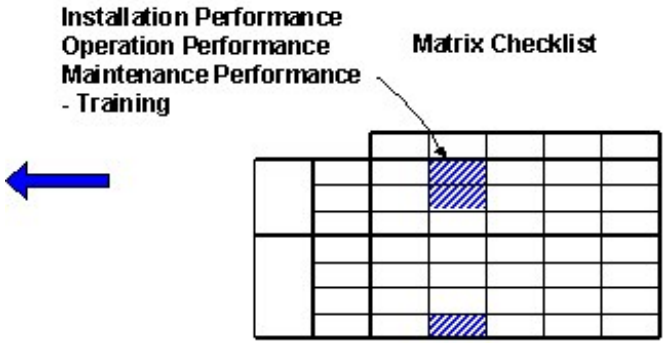
Determine what site preparation and equipment is required to install the product and what mains supplies and other infrastructure items are required for product operation. Include electrical, chemical, computer or other equipment required to use the device and data networking and telecommunications facilities.

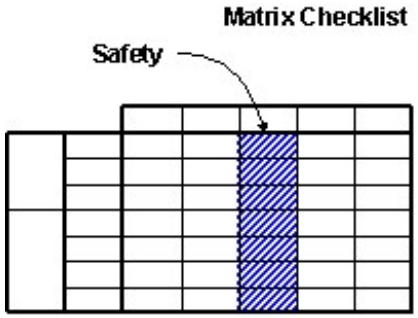
Also, define how the correct operation of the product will be validated once installation is complete.



15. Training of personnel

Usually, personnel will need to be trained to safely install, operate and maintain the product. Personnel will need to be trained throughout the operational lifetime of the product.

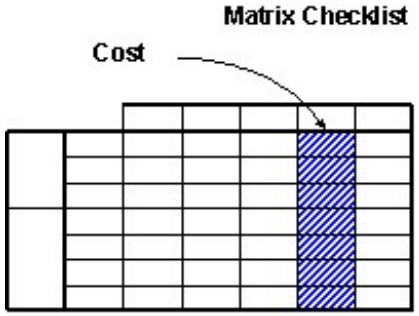




16. Safety

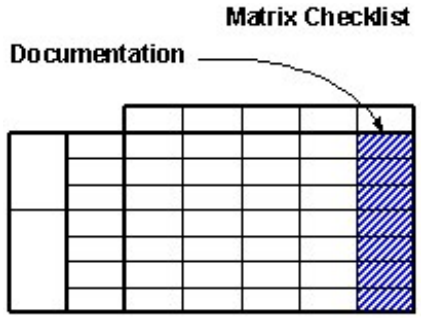
Determine what safety procedures, interlocks, features are required for safe use of the product in operation, maintenance and disposal. Include relevant safety standards and regulations.

Also, determine what safety procedures are required during manufacture distribution and installation. Include relevant safety standards and regulations.



17. Cost

Determine the intended consumer price and the net selling price that can be achieved. Determine manufacturing and distribution costs and attributable overhead costs, including product development and marketing. Where appropriate, the costs of ownership of the product should also be assessed – this includes operating and maintenance costs.



18. Documentation

Identify all the documentation that is required such as risk analysis, the quality plan, the design history file, test and validation criteria, manufacturing instructions, installation instructions, user instructions, training manuals and maintenance instructions. Additional technical documents may be required to demonstrate conformity with the relevant regulatory requirements.

SUMMARY

The requirements capture method presented in this workbook aids the capture and documentation of requirements for medical device design.

The three phases of the method are:

- defining the problem and the business requirements,
- determining and detailing the functions required to satisfy the problem,
- documenting the results in a requirements specification.

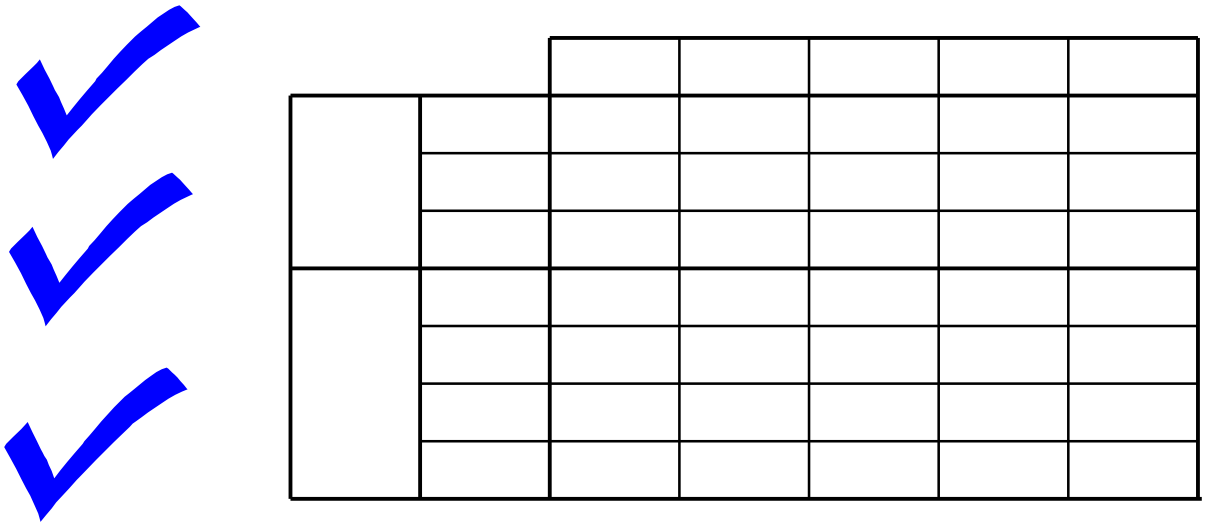
The requirements thus generated are compiled and organised in the requirements specification template to produce the requirements specification document.

There are other parts of the requirements process that should be done during the design process, but are not covered in this workbook. These include:

- gathering information to determine the needs,
- validating the requirements against the user needs using prototypes, models, and simulations.

This method should be modified and adapted to meet your specific needs. Include more items in the checklist, write more links to helpful sites with regulatory guideline, etc. Customise it to provide the maximum benefit.

APPENDIX 1: MATRIX CHECKLIST



Operation Process

Identify what functions occur in each Type and Mode of Use:

Types of Use

- ☐ intended use
- ☐ special use
- ☐ non-use (storage)
- ☐ misuse (abuse)

Modes of Use

- ☐ automatic
- ☐ manual
- ☐ on/off
- ☐ standby
- ☐ start-up/shut down
- ☐ normal operating
- ☐ saving
- ☐ failure
  - ☐ recovery from failure
  - ☐ signals/warnings/fault alarms
  - ☐ operation in event of power loss
- ☐ maintenance

Identify infrastructure requirements:

- ☐ energy (electricity, gas, hydraulic power, compressed air)
- ☐ water and sewerage
- ☐ cooling
- ☐ communications (data, telecoms)

Operational Performance

Physical characteristics:

- ☐ geometry
  - ☐ shape
  - ☐ size (height, breadth, length, volume, diameter)
  - ☐ space requirement
  - ☐ maximum dimensions
- ☐ weight
- ☐ operating temperature range
- ☐ operating pressure range
- ☐ forces (magnitude, direction, frequency, resonance effects)
- ☐ aesthetics
  - ☐ appearance
  - ☐ finish
  - ☐ colour
  - ☐ texture
- ☐ materials
  - ☐ prescribed materials
  - ☐ corrosion resistance
  - ☐ physical and chemical properties
  - ☐ coating requirements
  - ☐ chemical compatibility (cleaning agents)
  - ☐ bio-compatibility
  - ☐ sterilisation needed

Performance parameters:

- ☐ speed of operation
- ☐ cycle time/run time
- ☐ capacity
- ☐ load handling
- ☐ accuracy
- ☐ repeatability
- ☐ response time
- ☐ quietness
- ☐ expected lifetime
  - ☐ working life – number of operations or hours of operation
  - ☐ shelf life
  - ☐ total life span
- ☐ *for manufacturing:* production rate
- ☐ *for manufacturing:* scrap rate

User Interface:

- ☐ man-machine relationship
- ☐ operator skill/training requirements
- ☐ clarity of interface
  - ☐ operator input
  - ☐ product output
  - ☐ visual displays in all lighting conditions
  - ☐ visual instructions
  - ☐ guidance/prompting for user
  - ☐ feedback to user
  - ☐ display language
- ☐ ergonomics
  - ☐ height and reach
  - ☐ lighting
  - ☐ posture of operator
  - ☐ operator fatigue

User Interface (continued):

- ☐ access levels to controls
- ☐ maintenance
- ☐ system development (programming)

Guidance:

AAMI HE48 Human factors engineering guidelines and preferred practices for the design of medical devices

External Interfaces:

- ☐ signals (sensors, control equipment, displays)
- ☐ type (electronic, pneumatic, hydraulic)
- ☐ transmission standards (analogue, digital, serial, parallel)
- ☐ audible signals
  - ☐ volume
  - ☐ option to mute

Adaptability:

- ☐ compatibility with existing equipment/previous products
- ☐ design features for future expansion
- ☐ capacity for future expansion
- ☐ likelihood of future enhancements
- ☐ ease of modification

Availability:

- ☐ acceptable downtime
- ☐ mean availability
- ☐ MTBF (operating time)

Reliability:

- ☐ level of reliability required
- ☐ MTTF (operations or hours of operation before failure)
- ☐ Mean elapsed time between failures
- ☐ possible failure mechanisms
  - ☐ inherent weakness
  - ☐ misuse
  - ☐ wear
  - ☐ corrosion
  - ☐ stress corrosion
  - ☐ ageing

Working environment:

- ☐ geographic locations
- ☐ ambient temperature range
- ☐ humidity range
- ☐ external pressure
- ☐ vibration and shock
- ☐ ventilation
- ☐ permitted noise level
- ☐ dust and dirt (IP rating)
- ☐ gases and vapours
- ☐ corrosion from fluids
- ☐ EMC

for machinery:

- ☐ clean room requirements
- ☐ environmental monitoring during use
- ☐ microbiological controls during use
- ☐ effluent measurement and disposal

Operational Safety

Check that product conforms with relevant safety regulations – see Appendix 3 for details:

- ☐ Medical Device Directives
- ☐ Machinery Directive for moving parts
- ☐ Electrical Device Safety Standards and Requirements
- ☐ Machinery Safety Regulations

Product safety:

- ☐ safety hazards in use
- ☐ safety factors
- ☐ preventive measures to safeguard against hazards
- ☐ warning labels
- ☐ fault alarms/warnings
- ☐ fault hierarchy

Environmental impact – lifetime considerations:

- ☐ energy consumption
- ☐ consumables used
- ☐ effluent disposal
- ☐ cleaning/sterilisation

Operating Costs

- ☐ initial costs
  - ☐ product (target consumer price, selling discounts)
  - ☐ delivery/distribution
  - ☐ installation
  - ☐ acceptance tests
  - ☐ operator and support personnel training
- ☐ running costs
  - ☐ operating and support personnel wages
  - ☐ energy
  - ☐ communications infrastructure
  - ☐ other services
  - ☐ depreciation
  - ☐ on-going operator and support personnel training

Operating documentation

- ☐ user manuals
- ☐ operating instructions
- ☐ safety instructions
- ☐ drawings
- ☐ specifications
- ☐ risk analysis for hazards in use

Maintenance Process

- ☐ customer (distributor) support
  - ☐ help desk
  - ☐ support staff (distributor staff) training
- ☐ maintenance policy
  - ☐ diagnostic methods
  - ☐ schedule
  - ☐ MTTR
  - ☐ resources (spares, trained people)
- ☐ maintenance operations
  - ☐ procedures
  - ☐ calibration
  - ☐ exchange of parts
  - ☐ repair
  - ☐ cleaning/sterilisation
  - ☐ painting

Maintenance Performance

Product maintainability

- ☐ accessibility
- ☐ modularity
- ☐ status indications
- ☐ test and diagnostic facilities (need for special test equipment?)
- ☐ fault isolation facilities
- ☐ documentation
- ☐ expected service life

Performance parameters

- ☐ warranty/support period
- ☐ inspection interval
- ☐ calibration interval
- ☐ service interval
- ☐ response/repair time
- ☐ user maintenance
- ☐ training requirements

Maintenance Safety

- ☐ safety during maintenance operations
  - ☐ product users
  - ☐ maintenance staff
  - ☐ associated plant and equipment

Maintenance Costs

- ☐ cost if relevant of planned and unplanned downtime
- ☐ maintenance staff
  - ☐ wages
  - ☐ training
  - ☐ travel and subsistence
- ☐ maintenance materials
  - ☐ replacement parts
  - ☐ consumables

Support and maintenance documentation

- ☐ manuals
  - ☐ installation
  - ☐ calibration
  - ☐ maintenance
  - ☐ training
- ☐ records/logs
- ☐ risk analysis for service hazards

Disposal Process

- ☐ disposal policy
- ☐ dismantling requirements
- ☐ schedule (lifetime issues)
- ☐ country of disposal
- ☐ availability of recycling facilities
- ☐ components to be returned to manufacturer

Disposal Performance

- ☐ amount of product recyclable
- ☐ product re-usability

Disposal Safety

- ☐ safety of dismantling and disposal machinery
- ☐ safety aspects of dismantling procedures
- ☐ safety of disposal method
- ☐ environmental impact

Disposal Costs

- ☐ dismantling
- ☐ waste materials (transportation and disposal)
- ☐ re-cycling (may reduce overall costs)

Disposal Documentation

- ☐ disposal records

Design Process

Design Planning:

- ☐ target marketing date
- ☐ design methods to use
  - ☐ 'V' model
  - ☐ prototyping
  - ☐ simulation
- ☐ design tools
  - ☐ CASE (computer-aided systems engineering) tools to use and relevant constraints
  - ☐ programming language to use and relevant constraints
- ☐ test requirements
  - ☐ trials, (clinical, pre-market)
  - ☐ product qualification testing
- ☐ definition of project responsibilities
- ☐ criteria for make/buy decisions
- ☐ design review, verification and validation activities

Risk Management:

- ☐ identify potential causes of delay
  - ☐ misunderstanding of requirements
  - ☐ inadequate design infrastructure
  - ☐ use of new technology
  - ☐ skills limitations
  - ☐ product complexity
- ☐ use appropriate risk management method (see also Product Safety)
- ☐ identify risk assessment criteria
- ☐ define levels of risk acceptability
- ☐ progress monitoring/reporting and risk re-evaluation

Design Schedule:

- ☐ identify main steps and milestones
- ☐ set achievable schedules
- ☐ agree availability dates for deliverables (components, products, documentation)

Economic Considerations:

- ☐ cost of delay in product launch
  - ☐ lost sales opportunity
  - ☐ additional design costs
  - ☐ cost of other resources not being utilised
- ☐ protection afforded by patenting designs
- ☐ costs related to infringement of IPR
- ☐ identify those economic hazards that require risk management

Design Performance

Design Quality:

- ☐ requirements validation
- ☐ design verification
- ☐ design validation
  - ☐ how?
  - ☐ by whom?
  - ☐ validation criteria?
  - ☐ validation environment?
  - ☐ service environment?
- ☐ control of design changes and re-validation

Guidance:

CFR Title 21 - Food and Drugs, Part 820 - Quality System Regulation – Design Controls

BS EN ISO 9001:2000 Quality management systems – Requirements: Clause 7.3 Design and development

Design Safety

Design personnel:

- ☐ exposure to dangerous environments
- ☐ exposure to dangerous materials
- ☐ exposure to dangerous processes
- ☐ protection when testing prototype products and processes

Product safety:

- ☐ identify areas of potential safety hazard
- ☐ use appropriate risk management method
  - ☐ FMEA (Failure Mode Effect Analysis)
  - ☐ FTA (Fault Tree Analysis)
  - ☐ ETA (Event Tree Analysis)
  - ☐ HACCP (Hazard analysis critical control point)
  - ☐ HAZOP (Hazard and operability study – especially for safety)
- ☐ appropriate design planning and risk management (see Design Process)

Design Cost

Manpower:

- ☐ internal staff
- ☐ subcontract staff
- ☐ design consultants

Materials:

- ☐ cost of prototyping materials
- ☐ cost of prototype tooling

Infrastructure:

- ☐ use of design tools
- ☐ laboratory use
- ☐ simulation costs

Trials (Clinical Investigations):

- ☐ manpower
- ☐ materials
- ☐ test equipment
- ☐ subsistence and travel
- ☐ results evaluation

Industrial engineering:

- ☐ process design
- ☐ tool design

Product qualification testing:

- ☐ EMC testing
- ☐ noise emissions
- ☐ quality certification

Regulations:

BS EN 30993, Biological evaluation of medical devices

Part 1:1992, Guidance on selection of tests
Part 3:1992 Tests for genotoxicity, carcino-genicity, and reproductive toxicity

BS EN ISO 10993-2 Biological evaluation of medical devices - Animal welfare requirements

Design Documentation

- ☐ specifications
  - ☐ agreed requirements
  - ☐ EHSRs (Essential Health and Safety Requirements)
- ☐ risk analysis for the design hazards
- ☐ verification and validation plan
- ☐ records of design changes
- ☐ drawings
- ☐ the technical documents required to demonstrate conformity with the relevant regulatory requirements

  (FDA requires the design history file to prove the design plan was followed and the device master record, which documents all design and development procedures)

Manufacturing Process

Preferred methods:

- ☐ available processes and related design constraints
- ☐ processes available via subcontractors
- ☐ technology options
- ☐ manufacturing philosophy (batch, semi-batch, dedicated line, JIT)

Means of production:

- ☐ production outputs
  - ☐ products
  - ☐ parts
  - ☐ documentation
- ☐ availability of supplies
  - ☐ raw materials
  - ☐ components
- ☐ availability/limitations of resources
  - ☐ equipment
  - ☐ competent staff

Product testing:

- ☐ definition of properties to be tested (dimensions, performance, colour)
- ☐ define acceptance criteria
- ☐ type of test
  - ☐ pass/fail
  - ☐ correct or repair
  - ☐ destructive/non-destructive
  - ☐ drop test (height, surface, number of times)
- ☐ amount of product to be tested
  - ☐ one-off
  - ☐ 100%
  - ☐ none (customer can exchange defective product)
  - ☐ sample basis (batch size, percentage, modality)
  - ☐ destructive/non-destructive
- ☐ availability of competent test personnel
- ☐ direct labour regime

Packaging:

- ☐ need for particular processes, for example, vacuum packaging, product sterilisation
- ☐ labelling requirements
  - ☐ label size
  - ☐ label content (product characteristics, warnings)

Regulations:

BS EN 980:1997, Graphical symbols for use in the labelling of medical devices

IEC/TR 60878:1988, Graphical symbols for electrical equipment in medical practice

CFR Title 21 - Food and Drugs, Part 801 Labelling, Subpart A - General labelling provisions Subpart H - Special requirements for specific devices

CFR Title 21 - Food and Drugs, Part 809 In vitro diagnostic products for human use, Subpart B--Labelling

- ☐ access requirements (through doors)
- ☐ lifting facilities

Manufacturing schedule:

- ☐ lead time required
- ☐ set-up time
- ☐ ramp up procedure and time
- ☐ ramp down procedure and time
- ☐ finish date

Economic Considerations:

- ☐ cost of delay in manufacturing start-up
  - ☐ lost sales opportunity
  - ☐ additional start-up costs
  - ☐ cost of resources not being utilised
- ☐ likelihood of operator error
- ☐ confidentiality, particularly where novel processes are being employed
- ☐ identify those economic hazards that require risk management

Manufacturing Performance

Adaptability:

- ☐ use of existing product lines
- ☐ need for new manufacturing lines
  - ☐ equipment
  - ☐ space
  - ☐ tooling
  - ☐ potential new capacity for other products
- ☐ ability to manufacture future product variants or different products

Quality:

- ☐ qualification of manufacturing processes
  - ☐ obtainable tolerances
  - ☐ acceptable standard deviations
  - ☐ production rate
  - ☐ scrap rate
  - ☐ production quantity
- ☐ adequacy of product testing facilities and test criteria
- ☐ disposal of non-conforming product

Manufacturing/packaging environment:

- ☐ geographic location
- ☐ temperature range
- ☐ humidity range
- ☐ external pressure
- ☐ vibration (direction, duration, profile, profile characteristics)
- ☐ shock(direction, peak acceleration, pulse duration, number)
- ☐ noise level
- ☐ dust and dirt (IP rating)
- ☐ gases and vapours
- ☐ ventilation
- ☐ corrosion from fluids
- ☐ magnetic fields
- ☐ electrostatic controls
- ☐ class of manufacturing area (100,000, 10,000, etc. US Standard 209c)
- ☐ environmental monitoring
- ☐ microbiological controls (allowable count)

Packaging issues:

- ☐ packing configuration
- ☐ adequacy
  - ☐ protection afforded fragile components
  - ☐ functionality
  - ☐ aesthetics
- ☐ style/promotional requirements
- ☐ packed size
- ☐ packed weight
- ☐ lifting facilities (handles)

Manufacturing Safety

Machinery used must comply with the provisions of the EC Machinery Directive 89/392/EEC

Process Regulations:

- ☐ PD 5304 (British Standards) Safe use of machinery
- ☐ UK Health and Safety - The Supply of Machinery (Safety) Regulations 1992
- ☐ IEC 60204-1 Safety of machinery – Electrical equipment of machines - General requirements
- ☐ IEC 61140 Protection against electric shock - Common aspects for installation and equipment

Safety provisions-personnel:

- ☐ use of warning signs
- ☐ interlocks
- ☐ adequacy and deployment of safety procedures and instructions for workers and cleaners
- ☐ safety training
- ☐ first aid provisions

Handling provisions:

- ☐ machinery
- ☐ components
- ☐ material/component movements
- ☐ material/component storage

Safety-related environmental issues:

- ☐ use of dangerous materials
- ☐ collection of process waste (shavings, scrap, dust)
- ☐ disposal of process waste
- ☐ working conditions (toxic substances, heat, cold)
- ☐ energy emissions (radiation)
- ☐ noise
- ☐ visual impact of production facility (proximity to housing)

Manufacturing Cost

In-house manufactured parts:

- ☐ maximum permissible manufacturing cost
- ☐ raw material costs
- ☐ direct labour costs, including assembly
- ☐ machine utilisation costs
- ☐ economic batch size
- ☐ tooling and assembly jig costs (amortisation policy)
- ☐ energy costs
- ☐ consumables costs
- ☐ scrap rates

Bought-in parts:

- ☐ price/volume sensitivity
- ☐ stocking policy (storage requirements and costs, Kanbans)

Other factors:

- ☐ packaging costs
- ☐ manufacturing licence costs
- ☐ warranty provisions

Manufacturing Documentation

- ☐ specifications
- ☐ drawings
- ☐ standards to be followed
- ☐ assembly and dissembly instructions
- ☐ risk analysis - potential manufacturing hazards (BS EN 414, BS EN 1050)
- ☐ quality plan
- ☐ process qualification plan
- ☐ Certificate of Conformity
- ☐ test results
- ☐ build status/traceability of components and product

Distribution Process

- ☐ means of transport
- ☐ means and procedures to load and unload
- ☐ means and procedures for storage
  - ☐ in plant
  - ☐ wholesaler's warehouse
  - ☐ on display
- ☐ labelling for transport
- ☐ distribution schedule
  - ☐ target delivery date
  - ☐ mean storage time
  - ☐ expiry date
- ☐ economic hazards
  - ☐ distribution delay
  - ☐ storage delay
  - ☐ waste of space during storage
  - ☐ human errors
  - ☐ identify those economic hazards that require risk management

Distribution Performance

- ☐ transportation
  - ☐ use of existing transport facilities
  - ☐ need for new transport facilities
- ☐ distribution and storage environment
  - ☐ location
  - ☐ temperature range
  - ☐ humidity range
  - ☐ external pressure
  - ☐ vibration and shock (direction, duration, profile, profile characteristics)

Distribution Safety

- ☐ safety of transportation equipment
- ☐ safety of machinery used for storage, loading and unloading
- ☐ safety procedures for storage, loading and unloading
- ☐ safety in storage
- ☐ environmental safety, for example, emissions from transportation equipment

Distribution Costs

- ☐ transport and shipping costs
- ☐ distribution and storage environment
  - ☐ warehouse rent and running costs
  - ☐ warehouse labour costs

Distribution Documentation

- ☐ shipment records (product codes, batch data, date and time, etc)
- ☐ delivery instructions
- ☐ delivery acceptance records

Installation Process

- preparation
  - buildings
  - foundations and mountings
  - mains supplies (electricity, gas, hydraulic power, compressed air, water, sewerage)
  - telecommunications facilities
  - data network connections
  - staff training
- product validation in its operating environment
  - test conditions
  - validation procedure
  - fault correction
- economic factors
  - cost of process delays (process unavailability to user, additional resource requirements)

Installation Performance

- ease of installation
  - modularity of equipment to be installed
  - lifting equipment requirements
  - interconnections (mechanical, electrical and piping)
  - set-up and calibration

Installation Safety

- safety protection for installation personnel
- safety of lifting gear and other installation equipment
- safety of working environment

Installation Costs

- installation equipment and materials
- installation staff time
- staff travel and subsistence
- staff training

Installation Documentation

- installation specifications
- drawings
- installation instructions
- set-up and calibration procedures
- verification and validation plan
- validation criteria
- acceptance records

APPENDIX 2: DEVICE CLASSIFICATION AND APPROVAL ROUTES

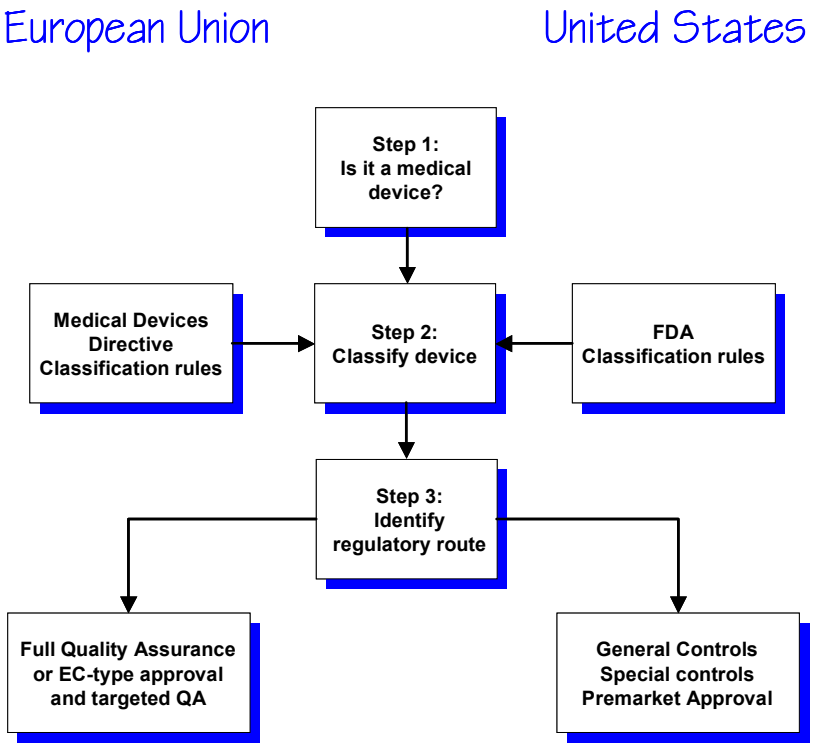
SUMMARY OF REGULATIONS

- Medical devices that fall within the device classification rules must be designed and manufactured in conformance with regulations before they are released to market.
- The amount of risk they pose to the user determines the classification of the device.
- The classification determines the approval routes that are possible.
- Most approval routes require a quality system.

  ISO 9001 is commonly used, but is not mandated by the EU.

  Quality System Regulation (QSR) is the mandated quality system in the US.
- Quality systems ensure that the following are controlled:
  - design,
  - manufacture,
  - packaging,
  - labelling,
  - transportation.
- Other standards may apply to specific devices and must be adhered to in order for the device to be approved.

The following steps are intended to help determine the device classification, possible approval routes, and what these approval routes require. Resources for additional information for each step are indicated in the HELP boxes.



HELP:

www.medical-devices.gov.uk/reg-guid.htm
Directives Bulletin 17 - Medical Devices and Medicinal Products

www.fda.gov/cdrh/consumer/index.shtml
A good starting place for general information on medical products and advice as to whether your product should be classified as a medical device.

STEPS FOR APPLYING THE REGULATIONS

1 Is it a medical device?

The EU Medical Device Directive defines a medical device as:

'Any instrument, apparatus, appliance, material, or other article, whether used alone or in combination, including the software necessary for its proper application, intended by the manufacturer to be used for human beings for the purpose of:

- diagnosing, prevention, monitoring, treatment or alleviation of disease,
- diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap,
- investigation, replacement or modification of the anatomy or of a physiological process,
- control of conception;

and which does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means.'

The equivalent definition in the Federal Food, Drug and Cosmetic Act, Section 201 is:

'An instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar article that is intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment or prevention of disease.'

Medical devices can be anything from thermometers to artificial hearts to at-home pregnancy test kits.

2 Determine the device classification.

EU Regulations: Device classification is based on the rules in the Medical Device Directive 93/42/EEC.

There are four classes (1, 2a, 2b, and 3). The criteria for the classes are listed in Annex IX.

Rules 1-4	non-invasive devices - devices that do not penetrate the body
Rules 5-8	invasive devices - devices that penetrate inside the body
Rules 9-12	active devices - devices that depend on a source of energy to operate (other than gravity or human power)
Rules 13-18	special rules and exceptions

HELP:
www.mueller-lierheim.com/regaff/Guidancedoc.htm
MEDDEV 2.4/1 Version March 1996 - Guideline to the classification of medical devices (rev.5)

www.medical-devices.gov.uk/reg-guid.htm
Directives Bulletin 10 - The Classification Rules

HELP:
www.fda.gov/cdrh/devadvice
CDRH's self-service site for medical device and radiation emitting product information

www.fda.gov/cdrh/devadvice/313.html
Page 3.1.3 will lead you through the process of determining the classification of a medical device.

US Regulations: **Device classification is based on U.S. Food and Drug Administration (FDA) rules and guidance from the Center for Devices and Radiological Health (CDRH).**

The following text paraphrases information on the CDRH web site:

The FDA has established classifications for about 1,700 different generic types of devices and grouped them into 16 medical specialties referred to as panels. Each of these generic types of devices is assigned to one of three regulatory classes based on the level of control necessary to assure the safety and effectiveness of the device. 'General Controls' apply to all classes of device.

Class 1 devices are subject to the least regulatory control. They present minimal potential for harm to the user and are often simpler in design than Class 2 or Class 3 devices. Examples include elastic bandages, examination gloves, and hand-held surgical instruments.

Class 2 devices are those for which general controls alone are insufficient to assure safety and effectiveness, and existing methods are available to provide such assurances. In addition to complying with general controls, Class 2 devices are also subject to special controls. Examples include powered wheelchairs, infusion pumps, and surgical drapes.

Class 3 is the most stringent regulatory category for devices. Class 3 devices are those for which insufficient information exists to assure safety and effectiveness solely through general or special controls. Class 3 devices are usually those that support or sustain human life, are of substantial importance in preventing impairment of human health, or which present a potential, unreasonable risk of illness or injury. Examples include replacement heart valves, silicone gel-filled breast implants, and implanted cerebella stimulators.

3 *EU Regulations:* **Determine the appropriate quality assurance route.**

Whichever of the three EU Directives is applicable, the device manufacturer has to comply with the essential requirements in Annex 1 of that Directive. The manufacturer can then opt to carry out 'Full Quality Assurance' as prescribed in the relevant Directive or follow the requirements as detailed, for example for EC Type-Examination coupled with EC Verification (or Production or Product Quality Assurance where required) or EC Declaration of Conformity to Type (or Production or Product Quality Assurance where required).

Medical Device Directive 93/42/EEC

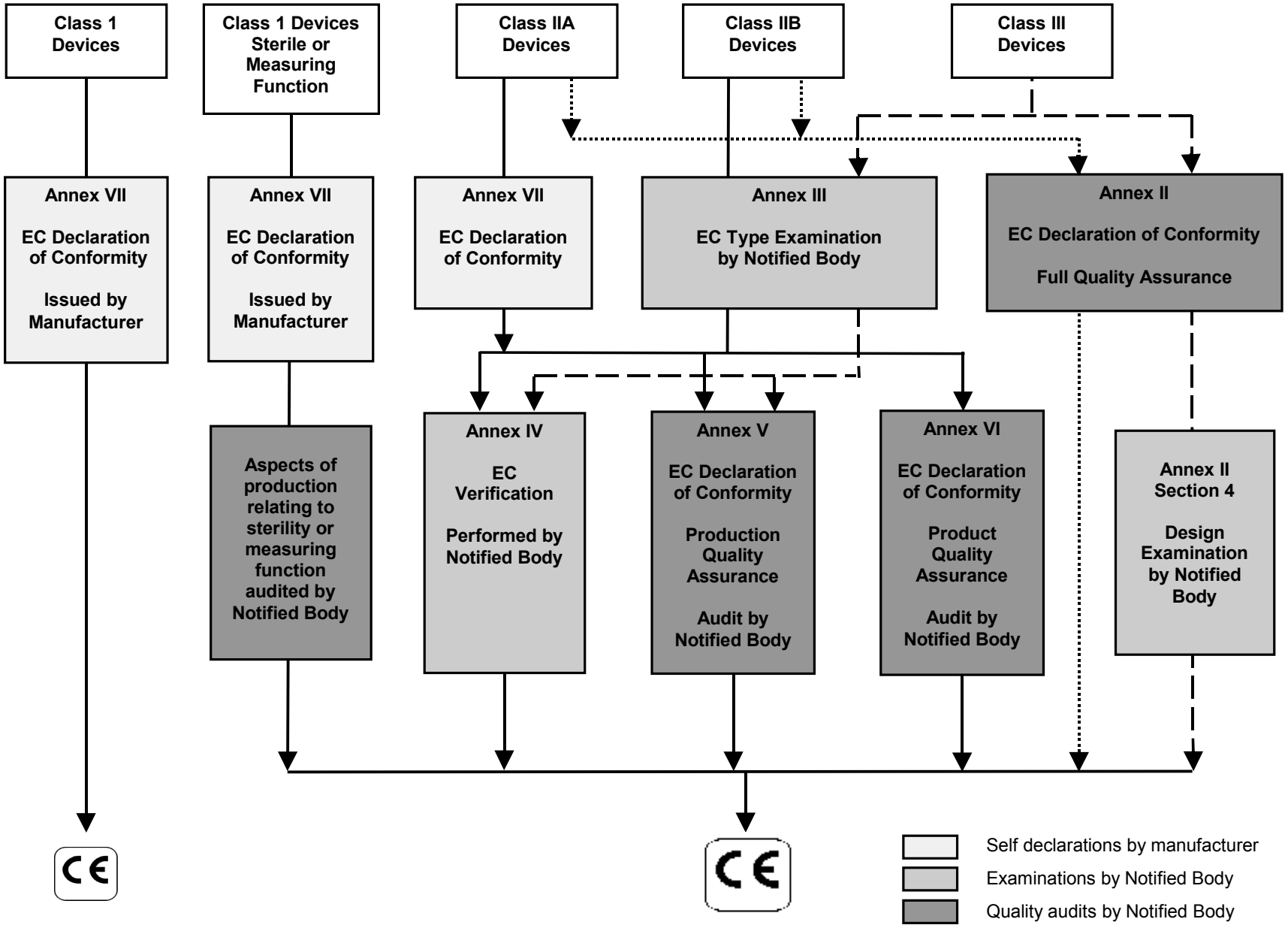
When this Directive is applicable, the conformity assessment routes and quality assurance options depend on device classification as shown in the diagram on page 67.

The Annexes cover the following topics:

Annex I: Essential Requirements

Requirements for all devices, regardless of class, to ensure that:

1. devices are safe,
2. devices perform as intended,
3. design and manufacturing standards are followed.



Medical Device Directive 93/42/EEC
Conformity Assessment Routes (Source: Anne Jury)

Annex II: Full Quality Assurance

The manufacturer may use this route for any class of device. For Full Quality Assurance, the manufacturer must demonstrate that there is a quality procedure for each stage of the design and production process. Full quality assurance is not performed for a particular product. Instead, the notified body inspects the quality system of the manufacturer and assumes all devices under the same quality system will be safe and perform as intended. This allows the manufacturer to put a CE mark on related devices without additional quality assessment by a notified body.

Annex III: Type Examination

The notified body certifies the device meets the essential requirements by testing prototypes and reviewing documentation. This is coupled with EC Verification, Production Quality Assurance and Product Quality Assurance, as prescribed for the device classification.

Annex IV: EC Verification

Involves every product or a sample from every batch being tested by the Notified Body. Only chosen usually for single high-value products or large batches of low-volume products.

Annex V: Production Quality Assurance

Review of the quality system for the production process. Assessment of the design process is excluded.

Annex VI: Product Quality Assurance

Review of the manufacturer’s inspection and testing processes for the final product.

HELP:
www.mueller-lierheim.com/regaff/Guidancedoc.htm
NB-MED/ 2.7/Rec1 1998 - Guidance on clinical trials

NB-MED/ 2.7/Rec3 1998 - Draft: Evaluation of Clinical Data

Annex VII: EC Declaration of Conformity

Declaration by the manufacturer that the device meets the Essential Requirements and with documentation to prove it.

Annex X: Clinical Evaluation

Class 3 and implantable or long-term invasive devices are required to undergo clinical investigations or trials. The objectives are to verify that, under normal conditions of use, device performance is in accordance with the manufacturer's specifications and there are no undesirable side effects arising from its use.

Medical Device Directives 90/385/EEC and 98/79/EC

The Active Implantable Medical Devices Directive (90/385/EEC) and the In Vitro Diagnostic Medical Devices Directive (98/79/EC) and their annexes are structured differently. For each Directive, a diagram similar to that shown on page 67 may be drawn to indicate the conformity assessment routes and quality assurance options. However, for active implantable devices, manufacturers always have to involve a Notified Body to obtain the necessary conformity assessment.

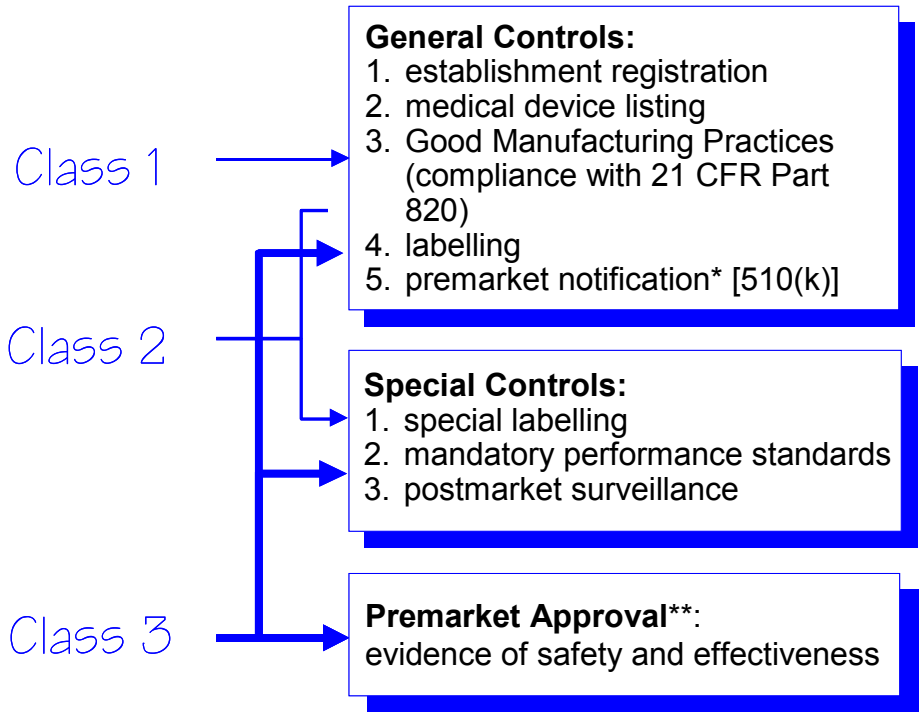
US Regulations: **Determine whether the device has to comply with General Controls, Special Controls, and Pre-market Approval.**

General Controls:

General Controls apply to all three classes of devices.

It should be noted that most Class 1 devices and a few Class 2 devices are exempt from the premarket notification [510(k)] requirements (for further details, refer to www.fda.gov/cdrh/devadvice/3133.html#contents), however these devices are not exempt from other general controls.

All medical devices must be manufactured under a quality assurance program, be suitable for the intended use, be adequately packaged and properly labelled, and have establishment registration and device listing forms on file with the FDA.



* most Class I devices and a few Class II devices are exempt from premarket notification
** some Class 3 devices can be marketed without Premarket Approval

HELP:

www.fda.gov/cdrh/devadvice/313.html
General Controls for Medical Devices

www.fda.gov/cdrh/devadvice/3132.html#contents
Describes the controls applicable to the three device classes

www.fda.gov/cdrh/devadvice/3133.html#contents)
Describes exemptions for various Class 1 and Class 2 devices

HELP:

www.fda.gov/cdrh/devadvice/341.html#contents
Details the FDA requirements for medical device establishment registration with link to Form 2891

HELP:

www.fda.gov/cdrh/devadvice/342.html#contents
Provides the FDA requirements for medical device listing with link to Form 2892

HELP:

www.fda.gov/cdrh/devadvice/32.html#contents
Provides information on the good manufacturing practice (GMP) requirements of the quality system (QS) regulation.

www.fda.gov/cdrh/humfac/frqsr.html
Medical Devices; Current Good Manufacturing Practice (CGMP) Final Rule; Quality System Regulation

www.fda.gov/cdrh/dsma/gmp_man.html
Medical Device Quality Systems Manual: A Small Entity Compliance Guide - guidance for interpreting CGMP.

www.fda.gov/cdrh/comp/designgd.pdf
Design Control Guidance for Medical Device Manufacturers - guidance for interpreting the design controls of CGMP.

The five main controls are as follows:

1. Establishment Registration: Form 2891

All companies involved in the preparation, manufacture, assembly, or processing of medical devices marketed in the US must register with the FDA. Distributors of medical devices are not required to register.

2. Medical device listing: Form 2892

All companies involved in the preparation, manufacture, assembly, or processing of medical devices marketed in the US or medical devices exported from the US are required to list with the FDA the generic type of device they have in the market.

3. Good Manufacturing Practices (GMP)

All manufacturers marketing medical devices in the US must have a quality system conformant with Quality System Regulation (QSR) 21 CFR Part 820 for the design, manufacture, packaging, labelling, storage, installation, and servicing of finished devices.

4. Labelling:

Medical devices must be labelled with certain information. If items are left off the label or the device is mislabelled the device will not be approved.

The relevant regulations are:

21 CFR Part 801 General Device Labelling

21 CFR Part 809 InVitro Device Labelling

HELP:

www.fda.gov/cdrh/devadvice/33.html#contents
Provides information on labelling requirements for medical devices, in vitro diagnostic devices, and radiation emitting products

www.fda.gov/cdrh/designlabel.html
Design and Labelling of Medical Devices

5. Pre-market Notification

Everyone intending to market Class 1, Class 2 and some Class 3 devices for use in the U.S. must submit a 510(k) to the FDA at least 90 days beforehand, unless the device is exempt from 510(k) requirements. This is to demonstrate that the device to be marketed is safe and effective.

The new 510(k) method embraces the 'Traditional 510(k) method' for Pre-market Notification, the Special 510(k) Device Modification option, which utilises certain aspects of the Quality System Regulation, and the Abbreviated 510(k) option, which relies on the use of guidance documents, special controls and recognised standards to facilitate 510(k) review. The details of these options may be found on the CDRH Premarket Notification web page.

HELP:

www.fda.gov/cdrh/devadvice/314.html
Premarket Notification [510(k)]

HELP:

www.access.gpo.gov/nara/cfr/cfr-table-search.html
To access this part of the CFR, select the latest data within Title 21 in the Table of Available CFR Titles, then select Parts 800-1299, then select part 801.

Special Controls:

1. Special labelling

Certain devices have special labelling requirements. Information may be found in 21 CFR 801.

2. Mandatory performance standards

Mandatory performance standards are applicable to certain Class 2 and Class 3 devices to provide reasonable assurance of their safety and effectiveness.

Notices of intentions to introduce, and notices of recognition, modification and withdrawal of mandatory performance standards are published in the Federal Register.

HELP:

www.fda.gov/cdrh/devadvice/352.html
Postmarket Surveillance Studies

www.fda.gov/cdrh/modact/critappr.pdf
Guidance on Criteria and Approaches for Postmarket Surveillance

3. Postmarket surveillance

Postmarket surveillance enables the performance of a device to be assessed after its introduction into the market and may be seen as a warning system for the early detection of potential problems.

Premarket Approval:

06A Premarket Approval (PMA) is an application submitted to the FDA to request clearance to market, or to continue marketing, a Class 3 medical device.

The regulations for premarket approval are in Title 21 Code of Federal Regulations Part 814 (21 CFR Part 814) – Premarket Approval of Medical Devices, which contains many subparts.

The PMA procedure is clearly described on CDRH web page:
www.fda.gov/cdrh/devadvice/316.html

The FDA process for reviewing a PMA after it has been submitted has 4 steps:

Step 1 - review of application content for completeness (filing review),

Step 2 - if step 1 is satisfactory, there follows an in-depth scientific, regulatory and GMP review to assess device safety and effectiveness,

Step 3 - review by the appropriate advisory panel,

Step 4 - notification of approval decision.

HELP:

www.fda.gov/cdrh/devadvice/316.html
Premarket Approval (PMA), the medical device marketing process for Class 3 devices

www.fda.gov/cdrh/manual/pmamanul.pdf
Premarket Approval Manual

www.access.gpo.gov/nara/cfr/cfr-table-search.html
To access this part of the CFR, select the latest data within Title 21 in the Table of Available CFR Titles, select Parts 800-1299, and then select part 814, which relates to Premarket Approval

www.fda.gov/cdrh/ode/pumasupp.pdf
Modifications To Devices Subject to Pre-market Approval - The PMA Supplement Decision Making Process

HELP:

www.fda.gov/cdrh/manual/idemanul.html
Investigational Device Exemptions Manual

www.fda.gov/cdrh/devadvice/ide/index.shtml
June 13, 2001 updates regarding IDE

www.access.gpo.gov/nara/cfr/cfr-table-search.html
To access this part of the CFR, select the latest data within Title 21 in the Table of Available CFR Titles, select Parts 800-1299, then select part 812, which relates to IDEs.

www.fda.gov/cdrh/devadvice/ide/print/ideall.pdf
IDE procedures

Clinical trials

When clinical trials involving people are required so as to evaluate a device before it is cleared for marketing by means of either the Premarket Notification or the Premarket Approval procedures, the manufacturer may apply to the FDA for Investigational Device Exemption (IDE).

The clinical trials may only proceed once the IDE application is approved. Detailed guidance on the IDE requirements can be found in the *Investigational Device Exemption Manua*l.

HELP:

www.fda.gov/cdrh/pdp/pdpguide.pdf
Contents of a Product Development Protocol

Product Development Protocol (PDP)

The Food, Drug, and Cosmetic Act provides an alternative to the IDE and PMA processes for class 3 devices which are subject to premarket approval. This alternative process, the product development protocol (PDP) is still being developed and has not yet been approved by the FDA. Published guidance on PDP is for information and comment only.

APPENDIX 3: STANDARDS AND REGULATION INFORMATION SOURCES

SOURCES OF STANDARDS INFORMATION

List of standards organisations	www.wssn.net
American National Standards Institute (ANSI) standards	www.ansi.org
International Electrotechnical Commission - IEC standards	www.iec.ch
International Organization for Standardization - ISO standards	www.iso.org
On-line catalogue of all British and related international standards	bsonline.techindex.co.uk
FDA approved standards database	www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm

SOURCES OF REGULATORY INFORMATION ON MEDICAL DEVICES

EU Regulations	www.mueller-lierheim.com - select 'MEDDEV Guidance'
UK Medical Devices Agency Guidance	www.medical-devices.gov.uk -select 'Publications', then 'Regulatory'
FDA Device Advice	www.fda.gov/cdrh/devadvice
Index of CDRH Web Documents	www.fda.gov/cdrh/consumer - select 'Topic Index'
CDRH Guidance Documents & Reports	www.fda.gov/cdrh/guidance.html
Good Guidance Practice (GGP) Database (This is a vital resource for obtaining current recommended good practice on a wide range of device topics, for example, provision of important information to the FDA for IDEs and PMAs, to detailed advice on aspects of clinical testing practice)	www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm

A SELECTION OF RELEVANT SAFETY STANDARDS

Materials:

Guidelines on Drug Master Files (DMF) www.fda.gov/cder/guidance/dmf.htm
FDA Tripartite Biocompatibility Guidance www.fda.gov/cdrh/g951.html
BS EN 30993, Biological evaluation of medical devices

Risk analysis and control:

IEC 60812 (1985), Analysis Techniques for System Reliability - Procedure for Failure Mode and Effects Analysis (FMEA)
BS 8444-3:1996 (IEC 60300-3-9:1995), Risk management - Guide to risk analysis of technological systems
BS EN ISO 14971:2001, Medical Devices – Application of risk management to medical devices
IEC 61025 (1990), Fault Tree Analysis (FTA)

Product Safety:

PD 6573:1994 (IEC TR 60513:1994), Fundamental aspects of safety standards for medical electrical equipment
BS EN 60601-1:1990 (BS 5724-1:1989) Medical electrical equipment - General requirements for safety
- BS EN 60601-1-1:2001 - Collateral standard: Safety requirements for medical electrical systems
- BS EN 60601-1-2:2002 - Collateral standard: Electromagnetic compatibility. Requirements and tests
- BS EN 60601-1-4:1997 - Collateral standard: General requirements for programmable electrical medical systems

BS EN 60601-2-X (IEC 60601-2- X), Medical electrical equipment - Particular requirements for safety - Specification for device X
BS EN 60601-3-Y (IEC 60601-3-Y), Medical electrical equipment - Particular requirements for performance - Specification for device Y
BS EN 475:1995, Medical devices - Electrically-generated alarm signals
FDA Guidelines for Software Controlled Medical Devices http://www.fda.gov/cdrh/guidance.html - follow 'Topic Index'/'Software'

User Interface:

AAMI HE48:1993 Human factors engineering guidelines and preferred practices for the design of medical devices

Manufacturing process:

PD 5304:2000 (British Standards) – Safe use of machinery
The Supply of Machinery (Safety) Regulations 1992, ISBN 0110257197 (www.legislation.hmso.gov.uk/si/si1992/Uksi_19923073_en_1.htm)
IEC 60204-1:2000 (Consolidated edition) - Safety of machinery - Electrical equipment of machines - General requirements
IEC 61140:2001, Protection against electric shock - Common aspects for installation and equipment
BS EN 414:2000, Safety of machinery - Rules for the drafting and presentation of safety standards
BS EN 1050:1997, Safety of machinery - Principles for risk assessment

Other workbooks obtainable from the Institute for Manufacturing

Manufacturing Mobility - a strategic guide to transferring manufacturing capability

Provides a guide to the total process of moving manufacturing capability to a new location. Senior managers who have strategic responsibility for the transfer of production technology will find the structured approach to planning a transfer invaluable in order to avoid the many pitfalls associated with such projects. The workbook describes the total transfer process from its initial conception as part of the business strategy right through to the point when the transferred technology is operating successfully in its new location.

Speeding new products to market - a practical workbook for achieving more successful new product development and introduction

For managers resolved to lead their companies to greater success in developing and introducing new products. This workbook describes a simple approach and specific tools, including staff and supply chain questionnaires, which can be used to reveal the strengths and weaknesses of current activities so that improvements can be soundly based. A software package is available for automatic processing of the surveys (Requires Windows 3.1 or later plus Microsoft Excel to perform full analysis).

Creating a winning business formula

A straightforward, structured approach to manufacturing strategy to help managers focus on long-term business planning and take a pro-active stance to managing their own business. This workbook builds on the introduction provided by "Competitive manufacturing" (see below). *"Without this process, I could have spent £100,000 on the wrong capital plant"* - MD of a pharmaceutical supply company.

Getting the measure of your business

A structured workbook showing how to achieve:

- the right mix of financial and non-financial measures
- measures that help predict what is about to happen
- measures which encourage staff to do the right things
- a systematic process for reviewing the effectiveness of measures

Make-or-Buy - a practical guide to industrial sourcing decisions

A step-by-step guide to addressing make-or-buy decisions in a consistent and structured manner. The workbook:

- shows how to review all the factors relevant to make-or-buy decisions - not just cost
- reveals the 'hidden' costs of buying in from a supplier
- provides examples, illustrative case studies and tips to help you
- includes software to automatically analyse the data

Designing for low-volume production

A practical workbook for companies involved in low-volume production. It offers cost analysis techniques and design tactics to boost sales margins of products manufactured in small batches. Illustrated with numerous examples, the book shows how to make design trade-offs to maximize margins and get the best leverage from ready-made technology.

Good design practice for medical devices and equipment – a framework

This workbook provides designers with a method for capturing requirements, arguably the most important aspect of the design process because it lays the foundation for the rest of the design. Three tools are provided to facilitate the process: functional analysis, a comprehensive matrix checklist and regulatory guidelines.

Good design practice for medical devices and equipment – design verification

Medical devices must be proven to be fit for purpose before they are placed on the market. Part of this proof is given by documenting evidence of design verification activities, which show that device design requirements have been met. This workbook presents an approach for identifying and selecting verification methods, determining when verification should occur in the design process and ensuring that it is carried out within a commercially viable framework.

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