Good Design Practice for Medical Devices and Equipment

A Framework

Cambridge Consultants

UNIVERSITY OF CAMBRIDGE

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GOOD DESIGN PRACTICE FOR MEDICAL DEVICES AND EQUIPMENT – A FRAMEWORK

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The research benefited from a very close working relationship with Cambridge Consultants Ltd (CCL). In particular, Duncan Bishop and Stewart Fox contributed a significant amount of their time and gave much valuable advice as work progressed. CCL now make active use of the methodology developed.

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).

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FORWARD

Validation is important in the design, development and production of medical devices, since effective and appropriate validation plays a vital role in defining the success of a product in both technical and economic terms.

Regulations and quality standards lay out the requirements for product validation, but it is left to each individual manufacturer to establish and maintain its own validation procedures. More recently, there has also been a change of emphasis in the regulations and standards encouraging the integration of validation into the development process. However, this poses particular challenges to the manufacturer since there is a distinct lack of guidance to assist this integration.

This workbook provides the first real guidance on good design practices for medical device development. It has been developed through extensive consultation with device manufacturers and analysis of regulatory requirements. The approach is intended to assist manufacturers in meeting the new regulations.

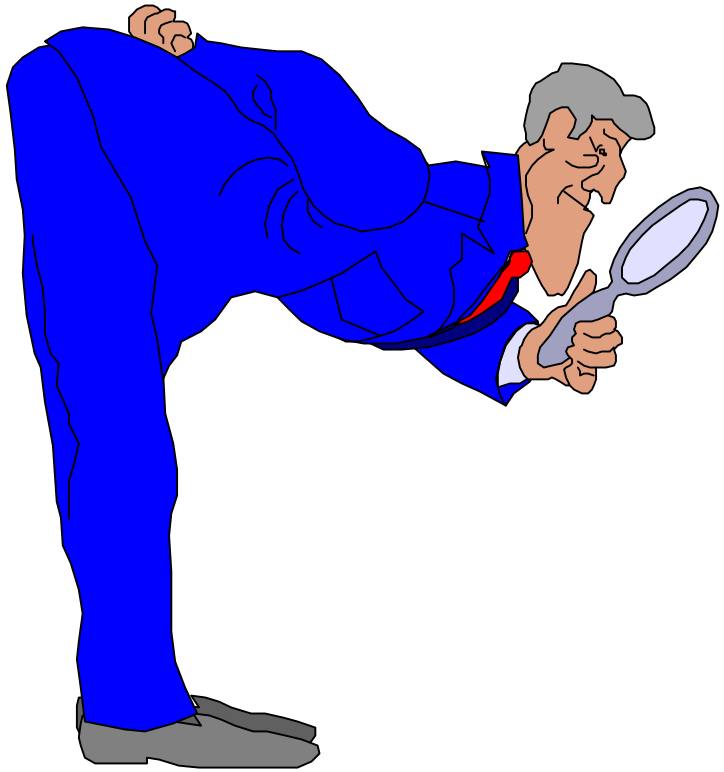
IR Cutler
Vice Chairman, Technical Policy Group
Association of British Healthcare Industries (ABHI)

WORKBOOK OBJECTIVE

The objective of this workbook is to help people design medical devices and equipment that are easier and more economic to validate. The workbook has been developed to satisfy an industry need for guidance to support concurrent design, development and validation.

Regulation in the European Union (EU) and the United States (US) has developed significantly during the last 20 years, moving from a manufacturing process focus to a device design and manufacturing process focus. This is driving the medical device industry to take a more concurrent and integrated approach to design, development and validation. In particular, elements such as design control, which is referred to globally in standards and regulations, require that more attention be focused on the design and validation programme in order to ensure that the device and its associated manufacturing and test equipment are reliable and fit for purpose. Regulations and standards usually specify *what* evidence is necessary to meet the new medical device requirements, but rarely provide useful guidance on *how* to produce the evidence.

The methods and guidance industry needs to address concurrent design, development and validation requirements should be covered by good design practice. Although current good design practice includes concepts such as Design for Manufacture, enabling designers to take a concurrent approach to design and production, and process validation guidance which helps manufacturers integrate production and validation, it falls short of the real target. Current good design practice needs to be extended to include Design for Validation to prompt designers to consider validation during the design of both the device and its related process equipment.



Design for Validation

WHO IS THIS WORKBOOK FOR?

This workbook provides guidance for medical device and process equipment designers, engineers, project managers and procurement personnel. Previous validation experience is not necessary, but experience in medical device design is likely to be helpful.

WHAT DOES IT CONTAIN?

This workbook describes a practical approach to design for validation that can be used to enhance existing medical device design processes in any organisation. The approach extends current ISO and Current Good Manufacturing Practice (CGMP) guidance, helps designers achieve good design practice and is adaptable to both device and process design. The approach has two parts:

- Model of design for validation – this explains the basic design, development and validation activities which occur during a medical device project in the form of a Design for Validation V-Model,

- Design tactics – these relate to specific areas where designers can take a proactive approach to validation during design.

The model and design tactics are used together to provide guidance to enable designers to adopt an integrated approach to design, development and validation.

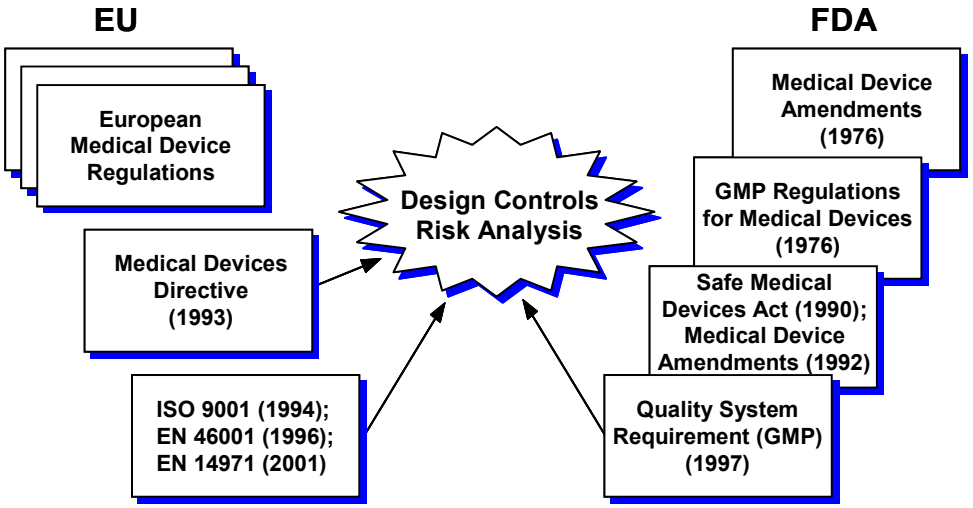
HOW TO USE THIS WORKBOOK

The guidance in this workbook should be used in conjunction with the relevant regulatory requirements for the design and manufacture of medical devices and equipment.

INTRODUCTION TO DESIGN FOR VALIDATION

" 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



The History of EU and US Medical Device Regulation

WHAT IS A MEDICAL DEVICE?

For the purposes of this workbook, the definition of a medical device is taken from the European Union (EU) regulations 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.'
>
> [European Council Directive 93/42/EEC]

Medical devices in the EU are regulated under a series of three directives: Active Implanatable Medical Devices Directive 90/385/EEC, Medical Devices Directive 93/42/EEC and In Vitro Diagnostic Medical Devices Directive 98/79/EC.

Medical devices in the US are regulated by the Food and Drug Administration (FDA) who use the Code of Federal Regulations to enforce the Federal Food, Drug and Cosmetic Act.

VALIDATION AND VERIFICATION

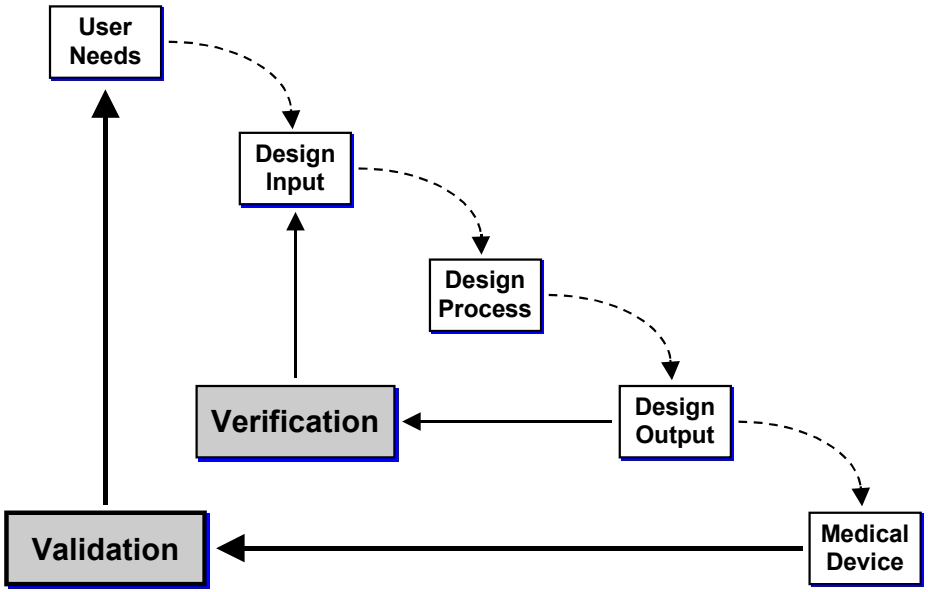
The objectives of the EU and US regulations are somewhat different. The objective of EU regulation is to ensure that devices are safe and perform as the manufacturer intended, while the objective of FDA regulation is to ensure finished devices will be safe, effective and thus present a benefit to the user. However, both the EU and US believe that safety and effectiveness cannot be proven by final inspection or testing and that product development is inherently an evolutionary process. It is validation that ensures a device is fit for purpose throughout that evolutionary process.

Standards such as EN ISO 9001 can be used by manufacturers to meet the quality management system requirements of the EU regulations. US requirements are outlined in the Quality System Regulation (QSR), which is part of the Code of Federal Regulations. In the context of the QSR and EN ISO 9001, validation ensures fitness for purpose by providing documentary evidence that the device, premises, plant, equipment, process and test methods are capable of functioning and continuing to function to their design and specification.

Validation is concerned with demonstrating the consistency and completeness of a design with respect to the initial ideas of what the system should do. This is often confused with verification, which is concerned with ensuring that, as the design and implementation develop, the output from each phase fulfils the requirements specified in the output of the previous phase. Part of the reason for the confusion between validation and verification is the unclear official definitions put forth by the regulatory bodies.

To a medical designer, who may not have the same level of understanding and exposure to the regulations as someone involved in managing the quality aspects of a development programme, the EU and FDA definitions

Official EU Definitions	*Official FDA Definitions*
"Validation is the exercise of carrying out a programme to demonstrate that a process operating within specified limits, will consistently produce product or services complying with predetermined requirements." [EN 724, 1994]	"Validation means confirmation by examination and provision of objective evidence that the particular requirements for a specific intended use can be consistently fulfilled." [US FDA, 1996a]
"Verification is confirmation by examination and provision of objective evidence that specified requirements have been fulfilled." [EN 46001, 1996]	"Verification means confirmation by examination and provision of objective evidence that specified requirements have been fulfilled." [US FDA, 1996a]



Simplified Waterfall Model [US FDA, 1997a]

could easily been seen as confusing and almost contradictory. For this reason, many healthcare organisations have developed their own definitions for validation and verification that are different to the official terms.

In order to clarify some of the concepts, the FDA has included the Waterfall Model in its document entitled *Design Control Guidance for Medical Device Manufacturers.* This model provides a more useful picture of validation and verification than that currently found in the official definitions.

The waterfall model indicates that verification establishes that the design output conforms to the requirements encapsulated in the design input. Verification is a detailed examination of aspects of a design at various stages in the development. A more detailed discussion of the Waterfall Model is included in Part 1 of this workbook.

Validation is a much more involved process than verification. According to the FDA in its design control guidance, design validation is a cumulative summation of all efforts, including design verification, and extends to the assessment to address whether devices produced in accordance with the design actually satisfy user needs and intended uses.

Taking into account the more practical definitions, verification and validation will be viewed in this workbook as a means of answering the following questions:

Verification - "Are we building the thing right?"

Validation - "Have we built the right thing?"

CURRENT DESIGN PRACTICE

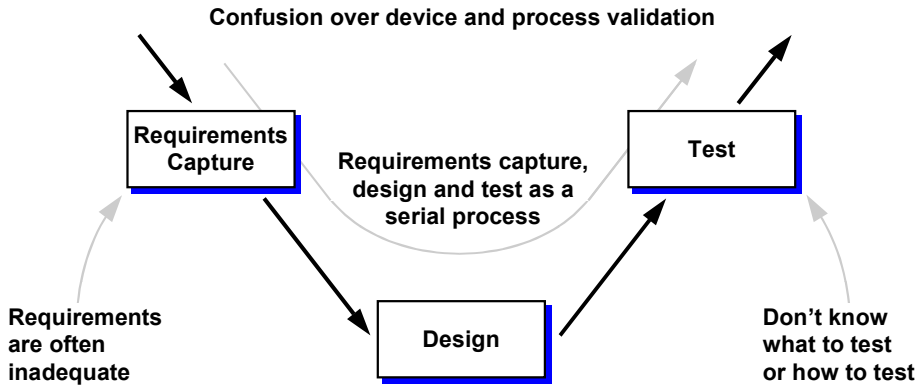
Latest figures issued by FDA in its *FDA/CDRH Annual Report, Fiscal Year 1998* suggest that current design practice is good and a low percentage of new devices fail approval at the first attempt. The figures give no indication of the commercial effectiveness of device development.

Discussions with device developers suggest that current practice is far from good. Most believe that device development times, and hence cost, could be dramatically reduced.

A common observation was that current device development has a tendency to be performed in the serial manner of requirements capture, design and then test. Within this serial approach, the captured requirements were often inadequate, there were frequent difficulties over deciding what to test or how to test and there was confusion over device and process validation.

Serious design errors can arise when requirements capture, design and test are carried out serially. In an example quoted by the FDA in its document entitled *Do it by Design,* a smooth continuous control knob rotation was used to adjust the oxygen flow to a patient. Physicians could select a flow of 2.5 (between 2 and 3) expecting 25% of full flow. What the patient actually received was no oxygen! A requirement for *discrete* flow rates had been incorporated into the design so that only integer flow values, selected via a *continuous* dial, resulted in oxygen being supplied. However, the real requirement of supporting the patient and how the device might be used in the real world had been forgotten when the device was tested and subsequently approved for sale.

Further examples can be found in the FDA's *Enforcement Reports,* which describe notices of product recalls. In just one week at the end of 1998, there were 15 product recalls including: 32 Automatic Implantable



Difficulties Encountered with Current Design Practice

Common Observations of Current Design Practice

New device and manufacturing process requirements are often incomplete, incorrect and lack clarity.

Designers often do not know what to test or how to test the emerging product, particularly novel products.

There is considerable confusion relating to the differences and similarities between device and process validation.

Requirements capture, design and test are frequently regarded as a serial process, often with different departments undertaking each activity.

Cardiovascular Defibrillators with the warning that "the pacemakers may cease functioning without warning due to a compromised hermetic seal on a chip carrier component part" and 74,000 Disposable Pressure Monitoring Kits where "there may be pin holes in the film of the blister package, thereby compromising the sterility of the devices". In both cases, inadequate specification, design or testing of the product or its associated manufacturing processes was to blame for the recall.

Regarding current practice, it was found that, although the majority of medical device designers understood the activities within their device development programmes, albeit a serial approach, most were confused over how validation fitted into the overall development. The confusion exists because it has been commonplace for design and validation to be considered as two separate identities within a project life cycle. Most device designers rely on the 'validation department' to perform independent validation after the product has been designed. This is not an optimal situation because early design decisions can have major implications on validation.

An additional source of difficulty arises because design and validation personnel frequently have opposing views on medical device design. For instance, designers want total freedom to design and develop their device while validation personnel want complete documentation of every design step made throughout the project. Although the parties involved are now aware of a need to align design and validation, progress is extremely slow due to the different goals and languages used by the disciplines involved.

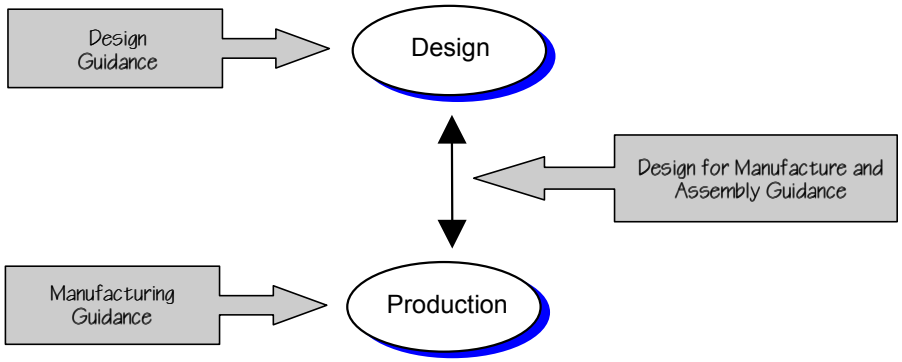
CURRENT DESIGN GUIDANCE

Does following the current regulations for medical devices in both the US and EU guarantee a good product?

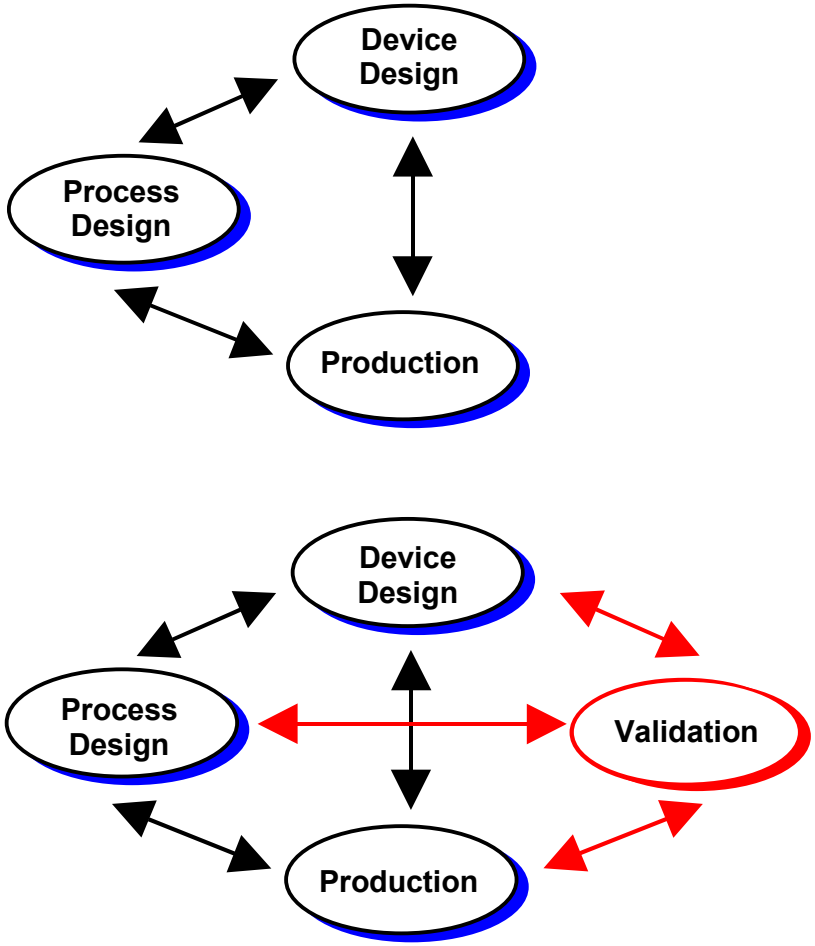
Looking at the figures for reported adverse incidents after products have been approved, this would not appear to be the case. Following the principles of current standards and regulations such as EN ISO 9001, EN 46001 and the QSR does not necessarily guarantee that a product will be successful. Quality systems are a necessary but insufficient condition for good medical device design. Although EN ISO 9001 promotes quality, in practice companies have tended to concentrate on the systems and documentation at the expense of design. Frequently, vast amounts of documentation are produced which have little effect on design. Based on these observations, current practice is by no means good practice.

In addition to the regulations, various guidance documents have been produced in both the EU and US to aid medical device developers. However, much of the guidance still describes *what* must be done rather than *how* it can be done and is therefore of limited value. Also, this guidance has concentrated on design and production - how to design and how to manufacture - with some amount of advice available on linking the two by means of Design for Manufacture and Assembly methods.

Medical devices require a much more integrated approach.



Focus of Current Guidance



Concurrent Design, Production and Validation

GOOD DESIGN PRACTICE

For the purpose of this workbook, at its simplest:

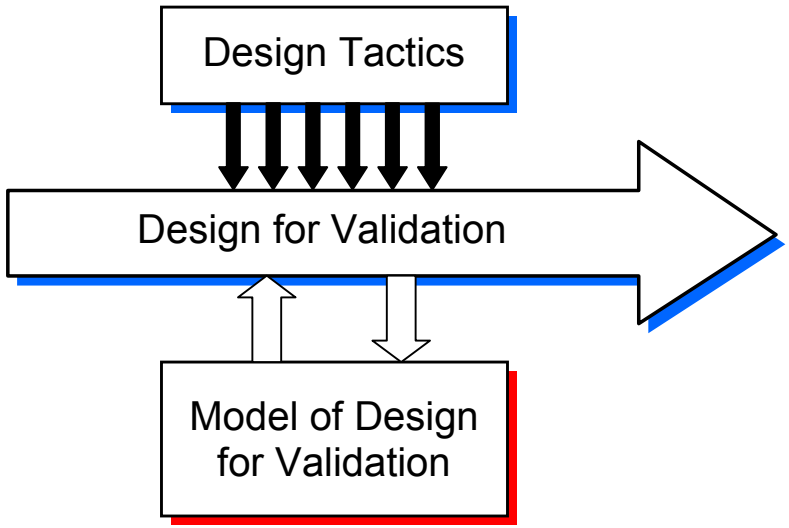
"Good design practice ensures 'fitness for purpose' within commercial reality."

In the QSR regulation, the FDA reports that, in a review of medical device recalls between 1988 and 1991, approximately 30% were due to inadequate design controls. With its latest design control regulations, the FDA is trying to encourage medical device developers to take a much more integrated approach to device design, process design and production. This integrated approach will reportedly benefit public health through fewer deaths and serious injuries, economically benefit the industry through cost savings from fewer recalls and bring productivity gains from improved designs. According to the FDA, most industry experts believe that this change will lead to better quality products, more efficient engineering, lower manufacturing costs and reduced product development time.

Validation throughout the evolutionary product development process ensures that a device is fit for purpose. Validation is a factor that strongly influences product quality, engineering efficiency and product development time and cost. An integrated approach to device design, process design and production must also include validation.

Good practice enables the proposed integrated approach. Not only should a device be designed to be fit for purpose, it should also be demonstrated to be fit for purpose at a reasonable cost. Although documents have been published providing guidance on process validation, there is little information available for validation as it applies to design. This workbook is intended, therefore, to redress this situation by providing good practice guidance focused specifically on the integration of validation with design and production.

PART 1: MODEL OF DESIGN FOR VALIDATION



INTRODUCTION

Validation philosophies for process equipment have been in place for some time, but current methods for device validation are relatively new and not well understood.

Current models of validation as they apply to the activities of design and production development are discussed in the following pages. It can be seen that these models fail to provide an adequate picture of the validation activities required for medical devices and equipment.

A model of design for validation has been developed in an attempt to clearly represent the stages of validation, including verification and qualification, as they apply to the design and development activities of a typical medical device project. The model includes the basic philosophies of design control and process development validation, but shows the activities in the context of the entire project. In doing so, this provides a clear picture to members of the project team, such as a device or process designer, of how the activities involved in his or her particular area of the project will impact other areas and ultimately form part of the overall validation of the device.

BACKGROUND

Validation has been represented in previous literature in the form of the Waterfall Model and the Production Development Validation V-Model. Each of these models presents a clear picture of validation, but only in relationship to specific aspects of a medical device project.

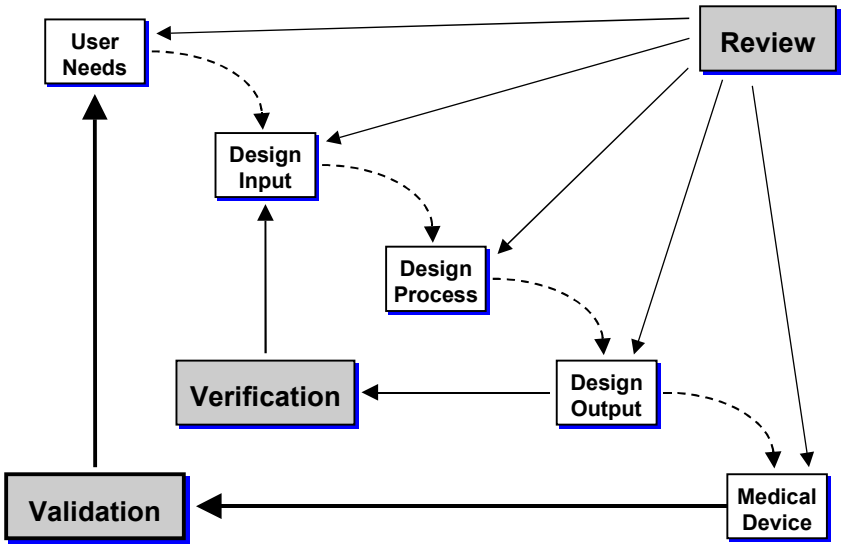
The Waterfall Model shows validation as proving that a medical device meets its user needs and intended uses. Although validation and verification are shown as they relate to the major steps of design, the Waterfall Model does not show validation as it applies to process equipment development.

The Production Development Validation V-Model shows validation as it applies to the development of the production equipment in the form of Installation Qualification, Operational Qualification and Performance Qualification. The UK Pharmaceutical Industry Computer Systems Validation Forum defines the qualifications as follows:

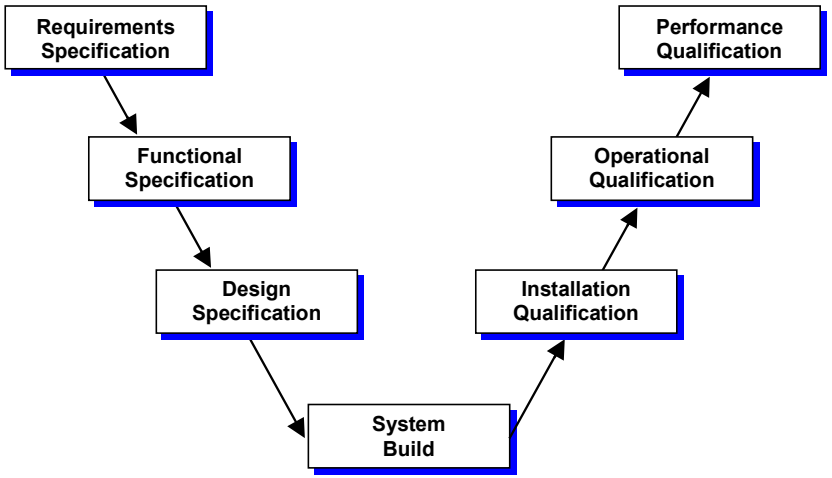
Installation Qualification (IQ) is documentation demonstrating that the equipment design and configuration is as intended, that instrumentation has adequate accuracy, precision and range for intended use and that services (such as power supplies) are of adequate quality.

Operational Qualification (OQ) is documentation demonstrating that the equipment or system operates as intended throughout representative or anticipated operating ranges.

Performance Qualification (PQ) is documentation demonstrating that when operated within set parameters the process will consistently produce product meeting its predetermined specifications.



Waterfall Model [US FDA, 1997a]



Production Development Validation V-Model

IQ, OQ and PQ relate to three levels of specifications that can be described as follows:

Requirements Specification describes what the equipment or system is supposed to do and, as such, is normally written by the pharmaceutical manufacturer. This links to Performance Qualification that tests these Requirements.

Functional Specification is documentation, normally written by the supplier describing the detailed functions of the equipment or system (i.e. what the system will do). This links to Operational Qualification that tests all the functions specified.

Design Specification is a complete definition of the equipment or system in sufficient detail to enable it to be built. This links to Installation Qualification, which checks that the correct equipment or system is supplied, that it meets the required standards and that it is installed correctly.

Although it provides a picture of the stages missing in the Waterfall Diagram, the Production Development Validation V-Model does not represent validation or verification as it applies to design. The specifications of the V-Model are outputs of the design process, thus the qualification activities are shown to occur after the device and process equipment have been designed and built.

The Waterfall model and Production Development Validation V-Model represent specific aspects of validation, but both lacking the overall picture of validation as it applies to device design, process design and production development. Based on these representations, it is no surprise that designers consider device validation to be completely different from process development validation.

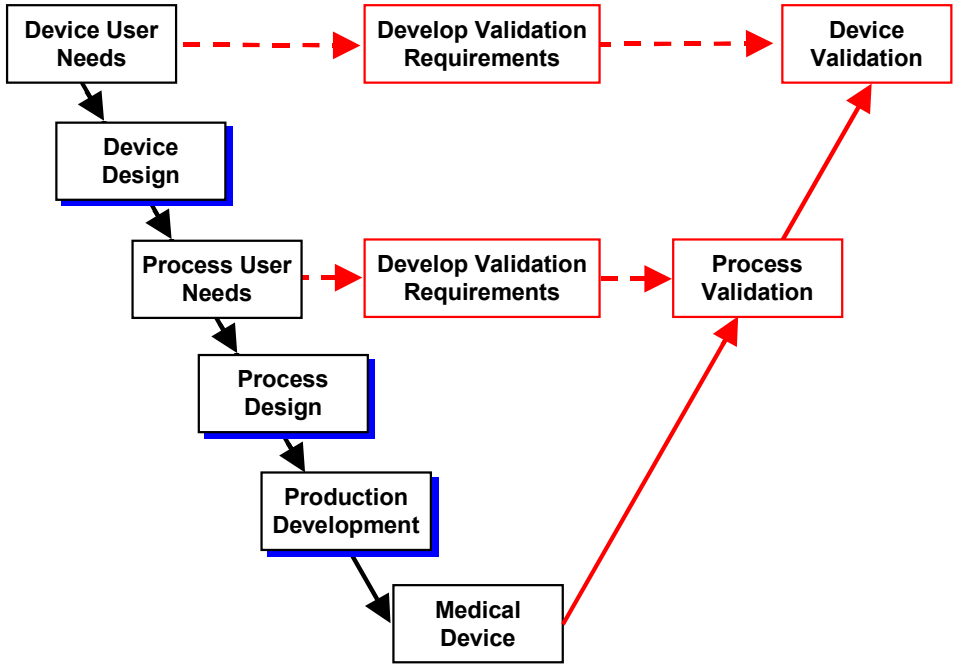
DESIGN FOR VALIDATION MODEL DERIVATION

Good practice proposes that the overall philosophy of validation is the same whether it is for a device or its associated manufacturing process equipment. Validation answers the question: Have we built the right thing? For a device, this is ultimately achieved by showing that the final device meets the original user needs and intended uses. Process validation represents the same concept and shows that the process equipment meets the original user needs and intended uses.

Validation can be shown as it applies to the design and development of a medical device. The major steps in transforming user needs to the final medical device are shown as shadowed boxes on the left hand side of the diagram in terms of device design, process design and production development. Although these steps are often concurrent, for simplicity, they are shown serially. It can be see in this diagram that the development of validation requirements should commence as soon as the user needs are known.

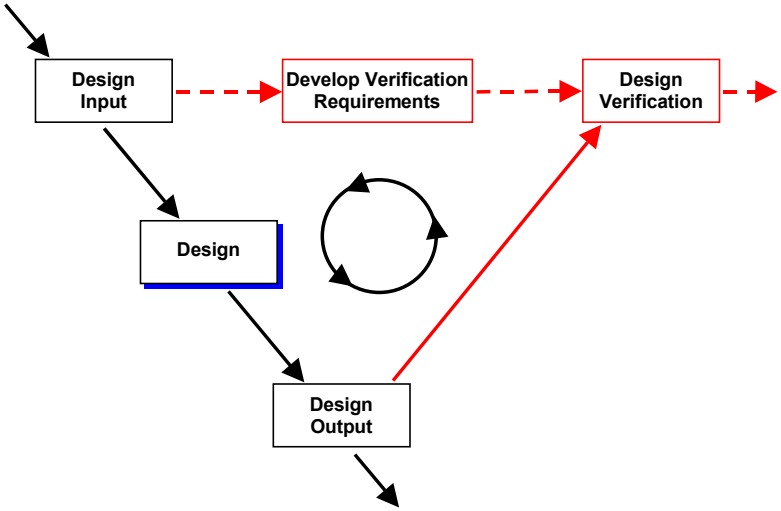
While device validation encompasses all activities within the large "Device Validation V" on the diagram, process validation involves all of the activities within the "Process Validation V" including process design and production development. Although process design and production development are shown serially to simplify the diagram, production development usually occurs within the activity of process design. For instance, the prototype manufacturing equipment used for verification during process design ultimately becomes the final manufacturing equipment at the end of production development.

Before the medical device regulations focused on design control, process validation was often viewed by designers as only being applicable to production development and not process design.

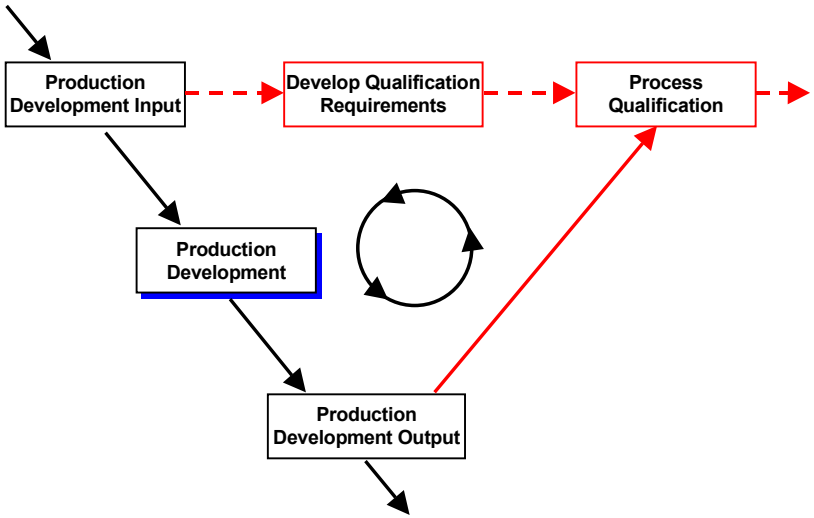


Validation as it Applies to the Design and Development Process

'The development of validation requirements should commence as soon as the user needs are known.'



Activities Associated with Design Verification



Activities Associated with Process Qualification

The final step of validation, whether for the device or process equipment, is performed against user needs. Essentially, process user needs consist of the device design specification and the process equipment requirements that are often derived during the device design process. Device user needs are not so clearly defined. Device user needs must be derived from a multitude of different sources and their derivation is by no means a straightforward process. Thus, device validation can be much more complicated than process validation.

Validation, or proving fitness for purpose, involves an evidence building process through all of the activities of the design and development process. The last stage of validation, performed after production and verification of the final device, usually involves clinical trials or evaluations to ensure that the final product meets the original user needs and intended uses. Verification is a process that occurs within each of the device design, process design and production development activities and provides a means for answering the question: Are we building the thing right? Verification can be illustrated using a more detailed representation of the design and development activities.

Design verification is the process of proving that design outputs meet design inputs. Since the verification steps occur sequentially during the iterations of the design and development activities, a spiral is shown in the centre of the diagram. In the same way as validation requirements, verification requirements can be developed as the design inputs are developed. The verification requirements and the results of design verification are used later for 'final device design verification'. Once the design has been verified, the design output is used to confirm 'process user needs'.

Process qualification, similar to design verification, is a means of proving that process development output meets process development input during the development of all the manufacturing and test equipment. The sequence of steps associated with this activity, mainly IQ, OQ and PQ are

related to the Production Development Validation V-Model shown previously on page 15. The process qualification requirements and the results of process qualification are used later in 'final process design verification'. The production processes, once qualified, are used to manufacture the final device.

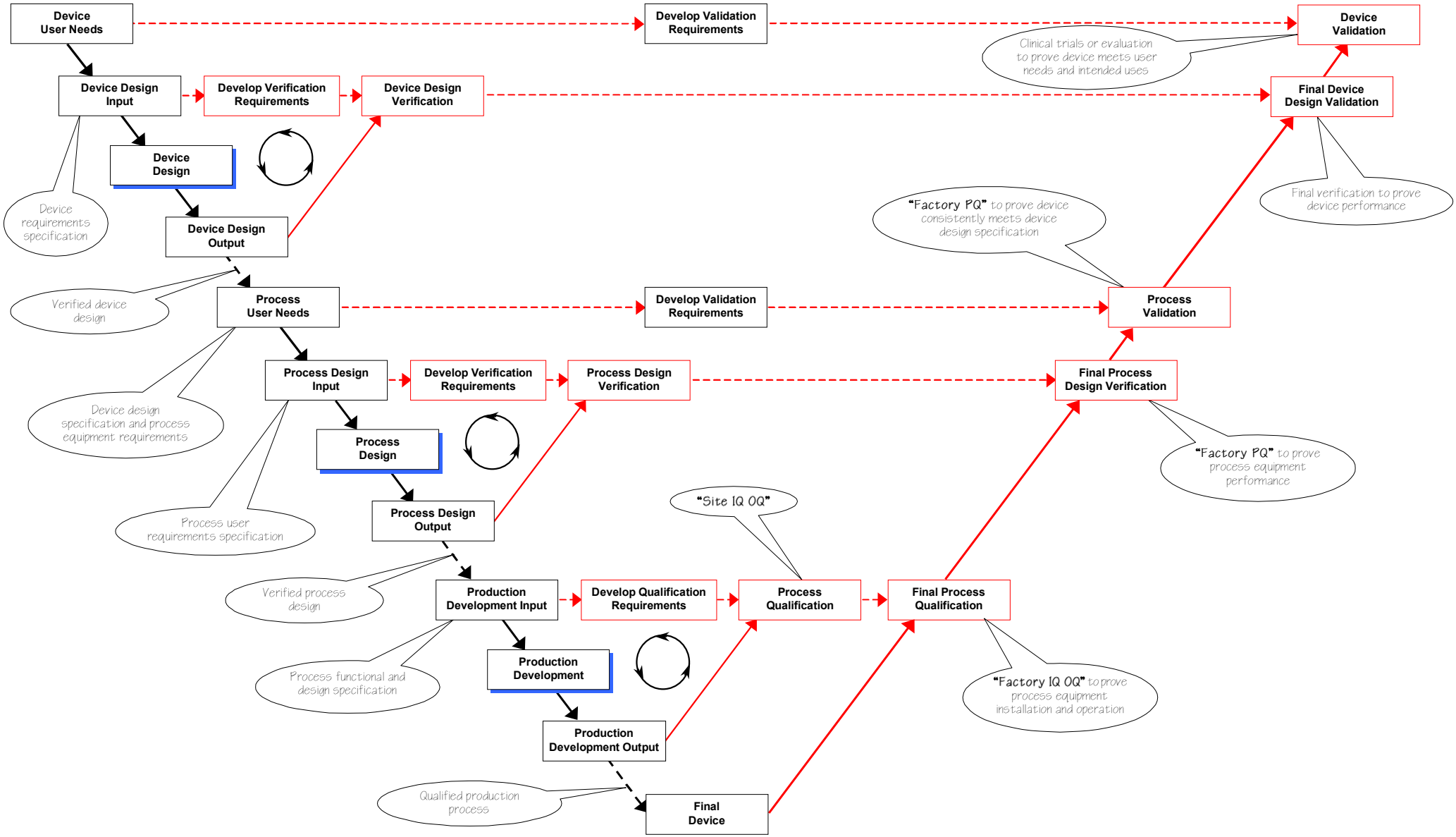
The diagrams representing design verification and process qualification are contained within the design and production development activities of the diagram on page 16. The result is the Design for Validation (DFV) V-Model on page 19, which shows the validation of a medical device as an evidence gathering process, from user needs to the final product, demonstrating that the device is fit for purpose. The large "Device Validation V", representing the overall process of validation, contains smaller verification and qualification V's which ensure that output meets input during the design and production development activities.

Of note in the DFV V-Model is that iterations should take place within the design and development activities, preferably before the production of the final devices. Iterations required after the production of the final devices, such as when design or validation problems are discovered during user or clinical trials, can be extremely costly and time consuming.

The annotations on the DFV V-Model explain the final verification steps. Process qualification occurring within the production development loop would involve IQ and OQ activities on site to prove the process equipment meets the functional and design specifications. *Final process qualification*, commonly known as factory IQ and OQ, involves proving the final production equipment meets the functional and design specification when the equipment is installed and operated in the factory. Process equipment performance qualification (PQ) is represented by two different activities in the DFV V-Model. *Final process design verification* proves that the process equipment performs to the process user requirements specification. The final step of process validation, also considered part of PQ, proves that the produced device consistently meets the device design specification. This step cannot take place without the proof of all the other verification and qualification activities associated with process design and production development.

Final device design verification proves the performance of the device by showing that it meets the device requirements specification. The final step of *device validation*, which requires the proof of all the activities along the left and right hand side of the DFV V-Model, involves clinical trials or evaluations to prove the final device meets the initial user needs and intended uses.

The DFV V-Model promotes thinking ahead to validation and verification requirements while at the input stages of the design and development activities, as illustrated by the dashed red lines in the model. For instance, during the initial stages of the project, the team needs to think ahead to the type of clinical trials or evaluations that will be required for the final stage of device validation. While at the design input stages, designers need to think ahead to the design verification and process qualification that will be required. Good design practice techniques, such as Design for Usability, should be considered when planning the appropriate verification and validation activities.



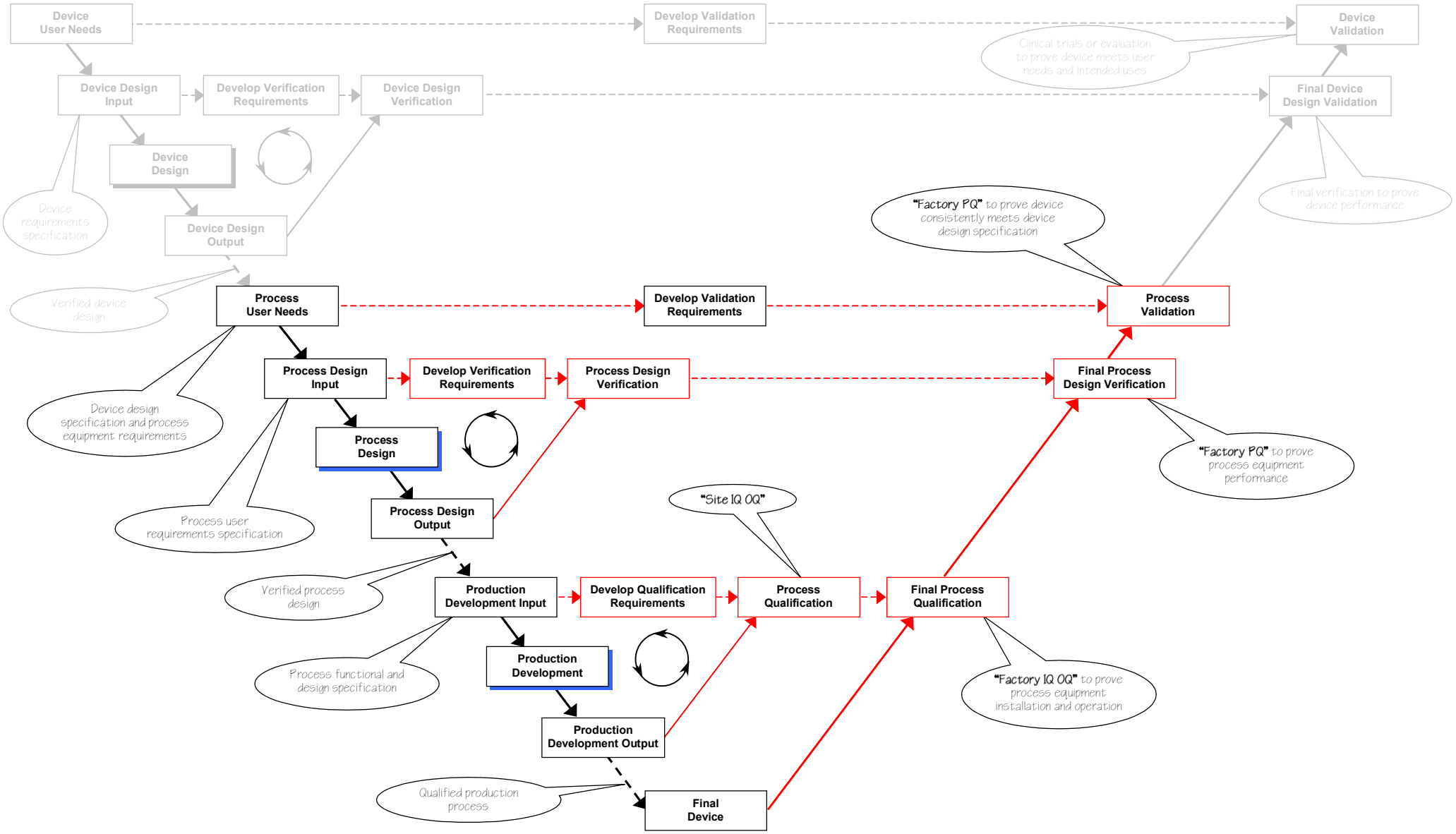
Design for Validation (DFV) V-Model

PROCESS VALIDATION

A misconception amongst medical device designers is that qualification of the production equipment, in the form of IQ, OQ and PQ, equates to process validation. In some cases, the qualifications are even confused with device validation. The DFV V-Model clearly shows that qualification of the process equipment is a subset of both process validation and device validation.

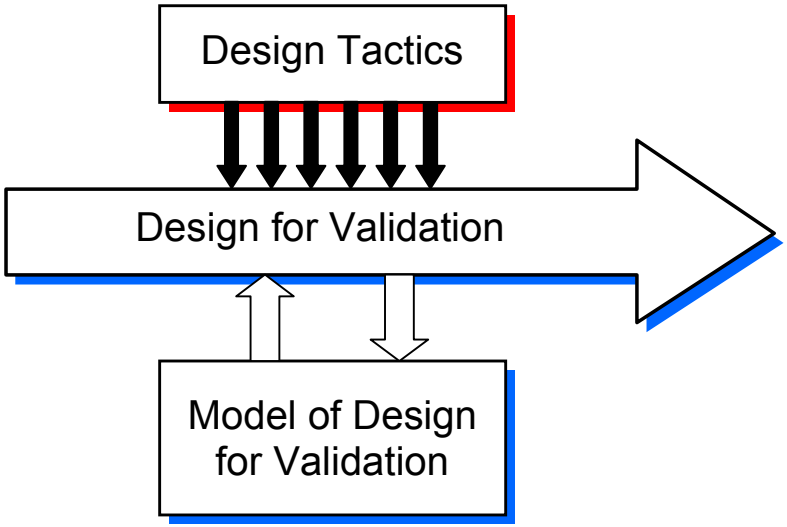
Design controls should apply equally to device design and to process design. Therefore, what is commonly known as “process validation” should encompass the activities associated with both process design and production development. This is shown in the DFV V-Model overleaf.

Process design and production development are often concurrent activities. However, they are shown as separate identities in the Design for Validation V-Model to illustrate the need for both process design verification and process qualification to occur within process validation and device validation.



Activities Associated with Process Validation

PART 2: DESIGN TACTICS



INTRODUCTION

By encouraging designers to think ahead to validation and verification, the DFV V-Model provides a framework for designers to take a proactive role towards validation. However, additional guidance is necessary in order to help designers focus their proactive efforts on specific activities during design. Design tactics are used for this purpose because they are:

- applicable to a wide range of devices,
- enhance existing design methods,
- extend the current medical device regulation guidance,
- provide practical guidance to help designers achieve good practice,
- adaptable to device and process design.

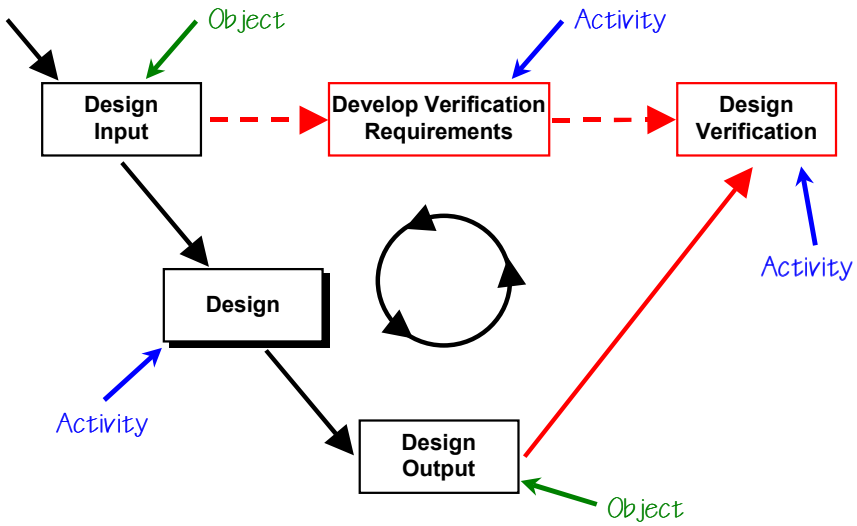
At the heart of the design tactics lies a generic verification model, which is a simple derivative of the DFV V-Model and will now be derived. Once formulated, it is used to present each of the six design tactics.

DERIVATION OF A GENERIC VERIFICATION MODEL

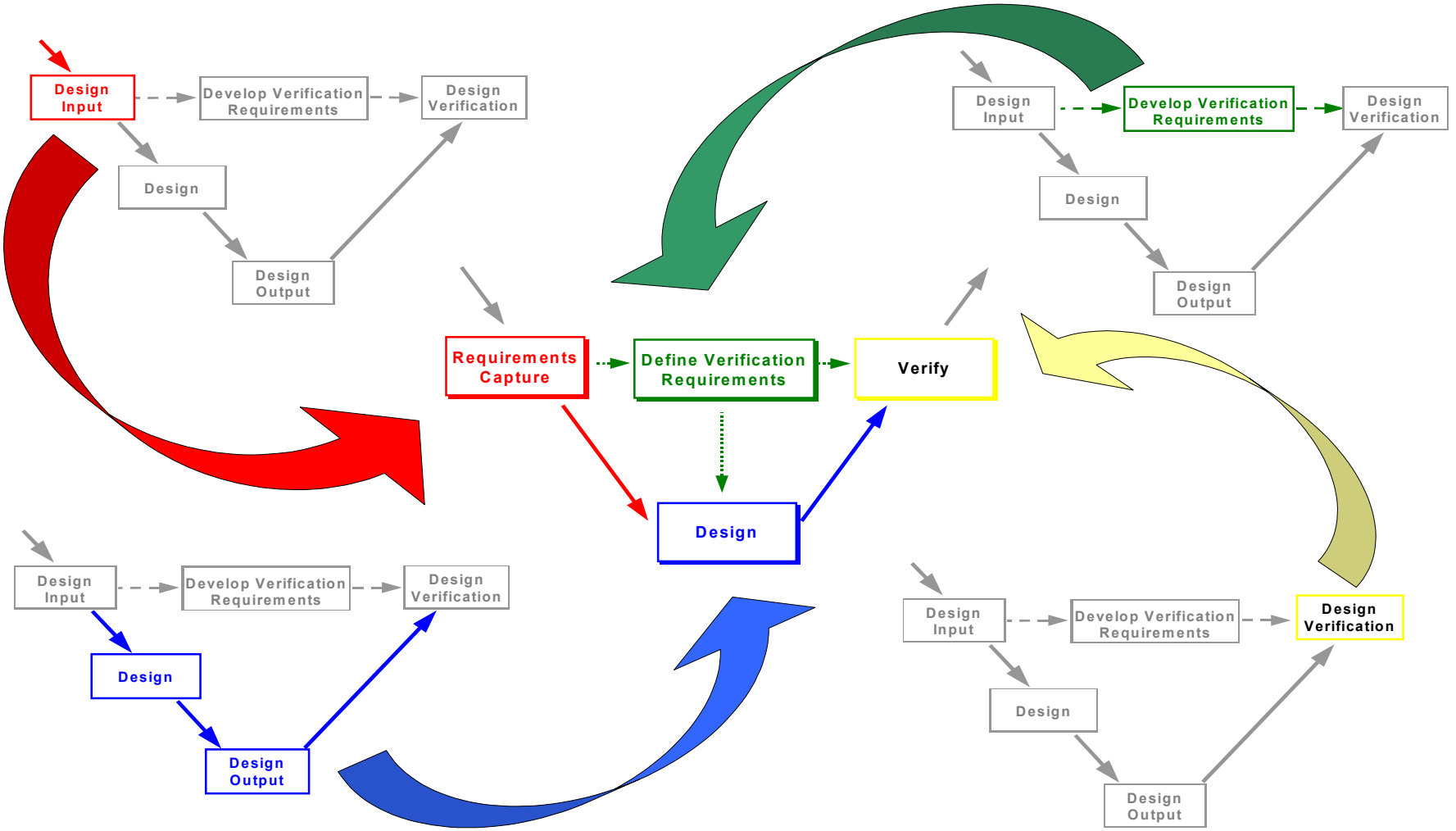
The sequence of verification activities presented in the DFV V-Model contains a mixture of objects and activities. To clarify presentation of the design tactics, a generic verification model can be derived which represents all activities as boxes and all objects as arrows.

The diagram on the opposite page shows that the design verification model can be reorganised into a generic verification model consisting of the following activities: Requirements Capture, Define Verification Requirements, Design and Verify.

- "Design Input" and its associated arrow can be combined to form the activity of "Requirements Capture"
- "Design", "Design Output" and the associated arrows can be combined into one activity called "Design"
- "Develop Verification Requirements" with its input and output arrows can be combined into the activity of "Define Verification Requirements"
- "Design Verification" can be renamed as "Verify".



Classification of Activities in Design Verification



Creation of a Generic Verification Model from Design Verification

The reorganisation results in the well-known requirements capture, design and verify sequence found in most product development models and is a simplified version of the larger model found in software engineering texts. The ideal execution of the sequence for the generic verification model is:

i) Capture requirements

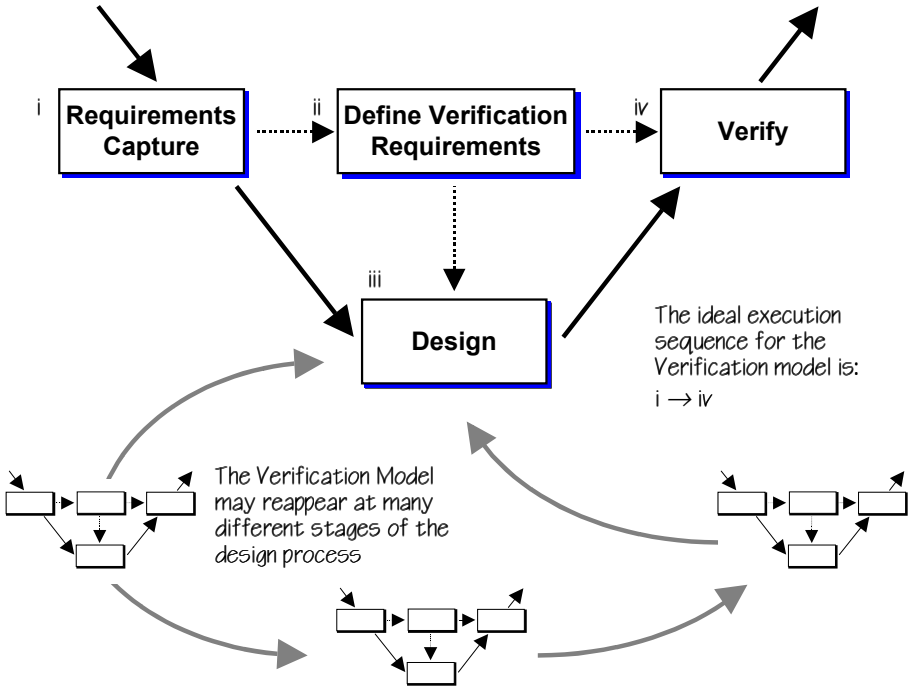
ii) Define verification requirements

iii) Design

iv) Verify

The sequence of activities contained in the generic verification model occurs repeatedly as the device and process design is refined and progresses from initial requirements through to detailed design.

One key element in the generic model, which is not formally represented in product development models, is the activity of defining verification requirements. Verification requirements should be derived, as far as it is possible, from the product requirements before starting the design. In practice, the verification requirements, which are part of the verification and validation process, will be refined as the design progresses.



Generic Verification Model

DESIGN TACTICS

A series of six design tactics are presented on the following pages using the common framework of the generic verification model:

Tactic 1 Capture implicit and explicit requirements

Tactic 2 Check that requirements are verifiable

Tactic 3 Use a risk-based approach to design and verification

Tactic 4 Consider the effects of re-design on requirements

Tactic 5 Consider the effects of device requirements, design, and verification of process requirements and validation

Tactic 6 Consider the effects of process re-design on device requirements

The tactics are based on the principles of good practice and aimed at specific areas of the design and development process where design for validation can be particularly effective.

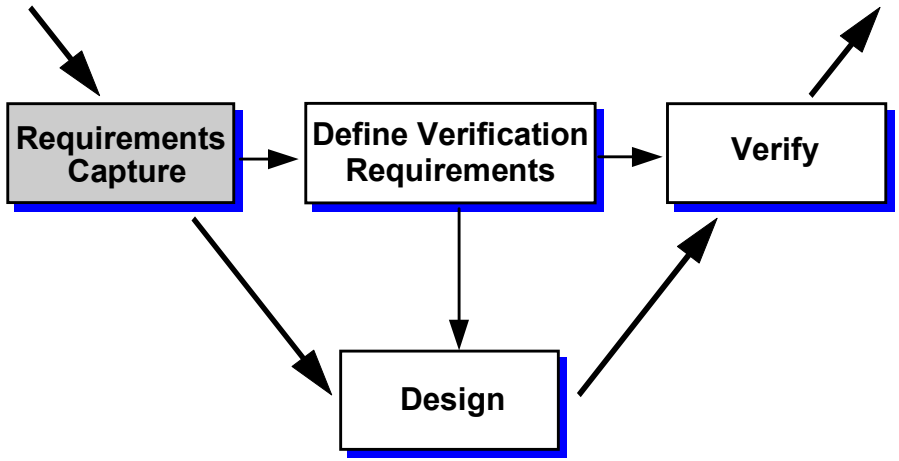
1 CAPTURE IMPLICIT AND EXPLICIT REQUIREMENTS

Validation involves proving that a product meets its user needs and intended uses. Requirements for a product can be in either explicit or implicit form. Explicit requirements are those that are clearly expressed while implicit requirements are those that are indirectly expressed. Unidentified or incorrect requirements can lead to excessive development costs or, in the worst case, the development of a product that is not fit for purpose. Thus, a systematic approach should be used to ensure the explicit and implicit requirements for a device and its process equipment are captured. In essence, the real need for a product must be identified.

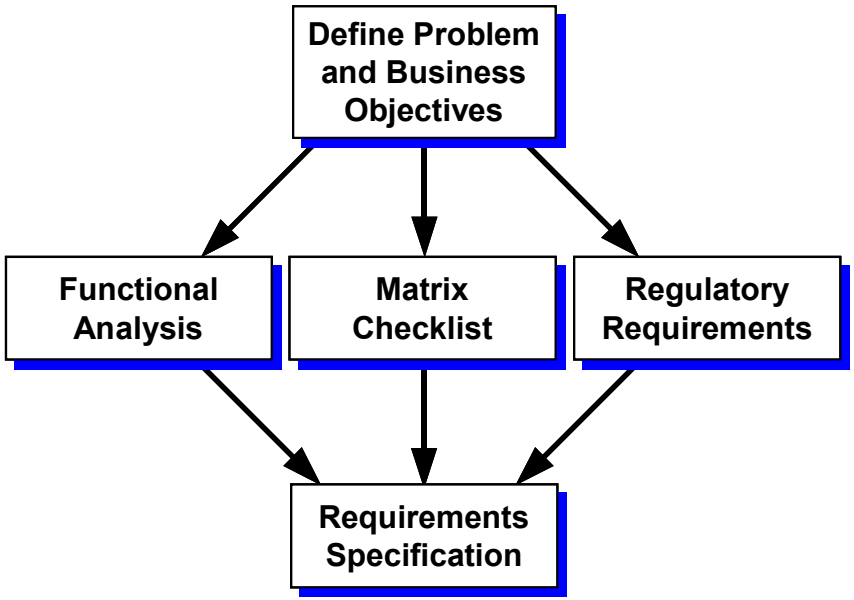
> Requirements capture is the identification and documentation of the requirements that the design must satisfy. The requirements lay the foundation for the rest of the design. Therefore, it is essential that they are correct. A good requirements specification may increase quality of the product and reduce design time and costs. A bad requirements specification may result in delays, additional costs, or at worst, the wrong product.
>
> [Shefelbine, 1998]

The above statement can be underscored using the case of NASA's desire to develop a *pen* for use in space. Using the requirement for a pen to use in space, NASA spent several million US dollars to develop a device capable of writing under zero gravity conditions. When the Russians were faced with the same task, their requirement was for a means to *write* in space. As a result, they took a pencil!

Requirements should be correct, complete, clear and represent the needs of all users of the product throughout its entire lifecycle. For a medical



Mapping of Tactic 1 onto the Generic Verification Model



Requirements Capture Method [Shefelbine et al, 2001]

device, as well as the patient, users could include doctors, nurses, installation and service personnel, production and validation experts, marketing and business mangers and many others. The requirements, which can be written in the form of demands or wishes, should be kept in solution neutral terms that specify *what* the design must achieve, but not *how* it will be achieved. Demands are the requirements that the product must satisfy. Wishes are requirements that are desirable for the design to satisfy, but are not essential.

A method for capturing implicit and explicit requirements for medical devices has been proposed in a workbook entitled *Good Design Practice for Medical Devices and Equipment - Requirements Capture*.

The method involves three phases:

i) defining the problem and the business requirements,

ii) determining and detailing the functions required to satisfy the problem by applying three tools - functional analysis, a matrix checklist and regulatory requirements guidelines,

iii) documenting the results in a requirements specification by following a basic template with standard headings.

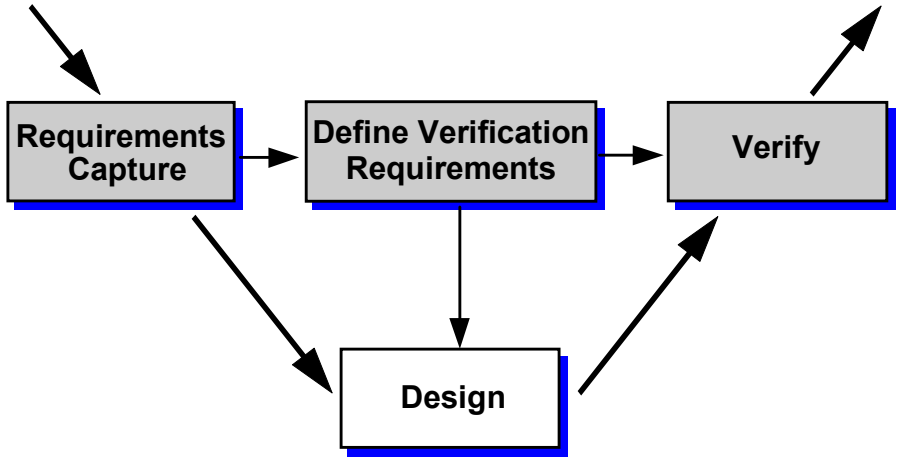
A structured method, such as the one proposed by Shefelbine et al, can be used in conjunction with Design for Usability techniques to help the designer take a lifecycle approach to requirements generation in order to produce a requirements specification, which is broad-based as well as being concise and clear.

2 CHECK THAT ALL REQUIREMENTS ARE VERIFIABLE

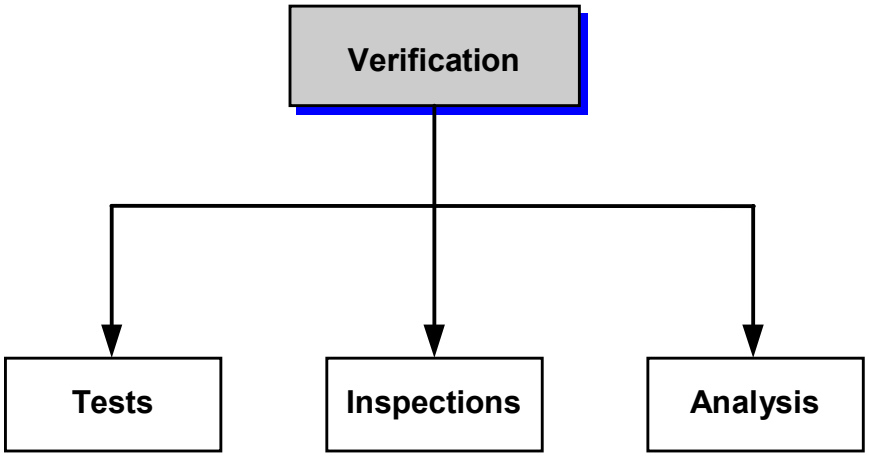
All requirements are defined in order to be fulfilled. This is part of the process of showing that the device is fit for purpose. Thus, each requirement should have an associated performance target that can be measured in order to verify that the requirement has been met. Such targets should, where possible, be quantitative with numerical limits. Where requirements cannot be defined quantitatively, evaluation against qualitative criteria should be considered. For example, Design for Usability provides guidance on assessing aesthetic and usability requirements via user trials.

Consider the case of an infusion pump. Initially, a requirement stated that "the device should maintain the patient's body temperature during infusion". However, is it practical to expect an infusion pump to measure and control body temperature or would it be better for the requirement to read "fluid should be transfused at normal body temperature"? Thinking ahead to verification during the development of the initial requirements would have highlighted the difficulty in proving the device maintained body temperature during infusion.

Requirements contained in all specifications throughout the design and development process need to be verifiable. Specifications serve as a design input during the spiralling nature of design. Design control regulations specify that design output must be verified against design input. Thus, every design input must be verified to show that it has been fulfilled.



Mapping of Tactic 2 onto the Generic Verification Model



Three-Pronged Approach to Verification [US FDA, 1997a]

Although verification is often thought to be synonymous with testing, the FDA state in its document *Design Control Guidance for Medical Device Manufacturers* that design verification can include tests, inspections and analysis. Examples of various analysis techniques include comparing the design to an established and successfully used product, worst-case analysis, thermal analysis, Fault Tree Analysis (FTA) or Failure Mode and Effect Analysis (FMEA). Using the three-pronged approach suggested by the FDA, a designer must also decide on the appropriate method of verification for each design requirement.

One of the keys to good design and validation is the production of straightforward and verifiable specifications before the work is commenced at each stage of the design and development process. Defining verification requirements in parallel with all design requirements allows non-testable requirements to be identified and at a very early stage. Thus, for every design requirement contained in a design specification, there should be a corresponding verification requirement with acceptance criteria contained in a verification specification. As a result, qualitative requirements can be addressed up front before further design is carried out and alternative verification methods or even a change in requirement can be implemented.

In summary, designers must think ahead and plan the verification of each design requirement. It is good practice to develop verification specifications in parallel with the formulation of requirements specifications. This helps designers to identify requirements needing special qualitative verification procedures that could be costly and time consuming if not identified early in the design process.

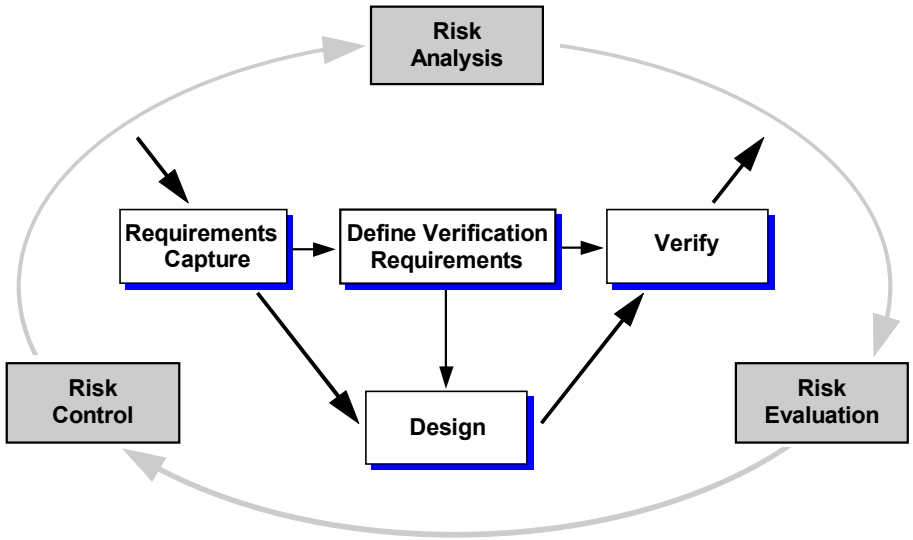
3 USE A RISK-BASED APPROACH TO DESIGN AND VERIFICATION

Risk analysis and risk management should play an important role in the design and verification of medical devices. Both the EU and the US require risk analysis as part of design control. The cycle of risk analysis, risk evaluation and risk control forms part of risk management.

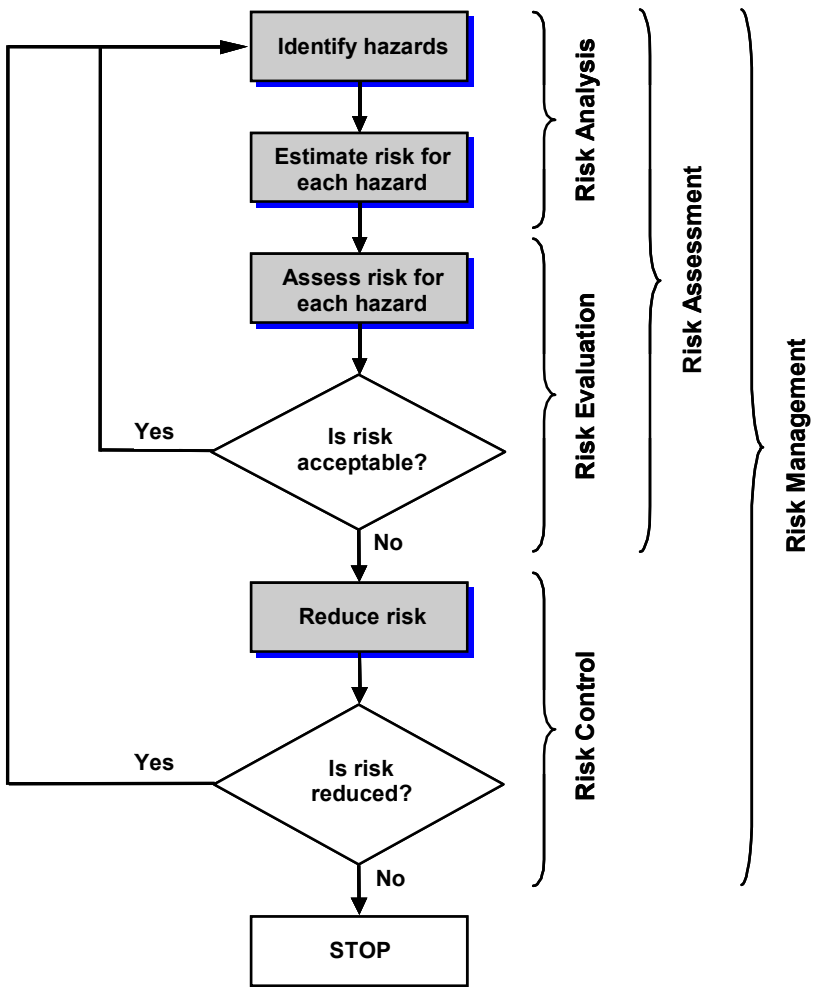
A risk management programme should start with a preliminary hazard analysis performed on the user needs and continue through the lifecycle of the device until it is removed from service. An integrated approach to risk management, including device design, process design and production development, will drive the verification of the design, the qualification of the production equipment and contribute to validation of the final device.

Risk analysis can be achieved through the use of tools such as Fault Tree Analysis (FTA), Failure Mode and Effect Analysis (FMEA), Failure Mode Effect and Criticality Analysis (FMECA), Hazard Analysis Critical Control Points (HACCP) and Hazard and Operability Study (HAZOP). These tools can also be used to identify the failure modes and risks as well as critical device/user interactions. For instance, drug delivery devices such as pen injectors often require as many as twenty separate actions to ensure proper use. Of these actions, possibly five are critical for safe operation. Such critical actions demand special care during design either to ensure foolproof operation through sound ergonomic design or to reduce their criticality.

Although risk control is critical because it influences verification requirements and design, studies show that this is currently not well implemented. Risk control, addressed in standards such as EN ISO 14971 and EN 60601-1-4, should focus on reducing a risk's severity and/or likelihood until the risk is deemed acceptable. If it is not possible to reduce the risk to



Mapping of Tactic 3 onto the Generic Verification Model



Typical Procedure for Risk Analysis, Evaluation and Control

acceptable levels by design measures, then risks should be brought to an acceptable level through mitigation efforts such as process qualification.

The adjacent diagram shows a typical procedure for risk analysis, risk evaluation and risk control that occurs throughout the design and development process. This procedure can be used for both the device and its associated manufacturing, assembly and test equipment. The procedure starts with the identification of hazards. Risks for each hazard are then estimated and assessed. Risk control is necessary for risks that are not deemed to be acceptable. If a risk is not reduced to an acceptable level following risk reduction procedures, the project may have to be terminated.

In the early stages of a project, risk management is used to identify weaknesses in the design. In the later stages of a project as the design becomes more detailed, risk management is used to show robustness and safety of the product or process. Addressing risks at a design level is much more cost effective than addressing risks at the validation stage where the product and processes have been finalised. Risk management is particularly useful for innovative products and processes as it provides designers with an excellent basis for making their design and verification decisions.

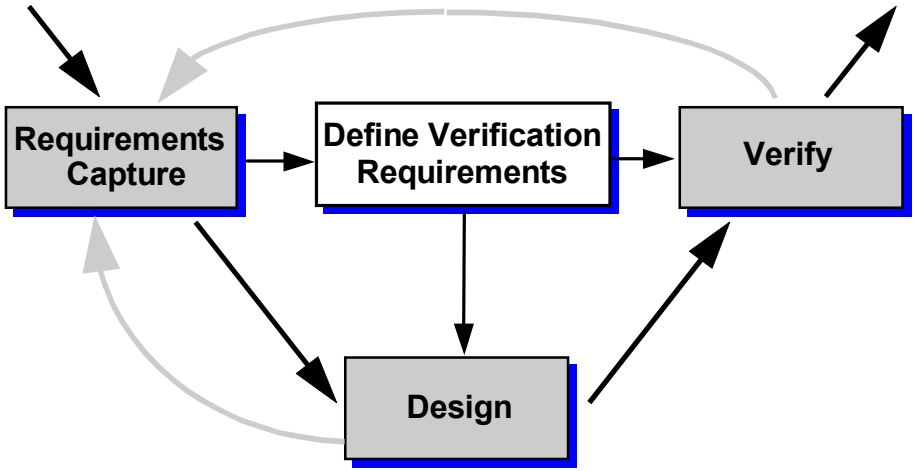
In summary, it is good practice to use risk management throughout a medical device project. Systematic methods such as FTA and FMEA can be used to analyse and assess potential risks from the requirements capture stage through to detailed design. Although it is preferable to reduce unacceptable risks through design measures, it may also be possible to use verification as a form of mitigation. Thus, a risk-based approach can be used to drive both the design and verification of a device and its related process equipment.

4 CONSIDER THE EFFECTS OF RE-DESIGN ON REQUIREMENTS

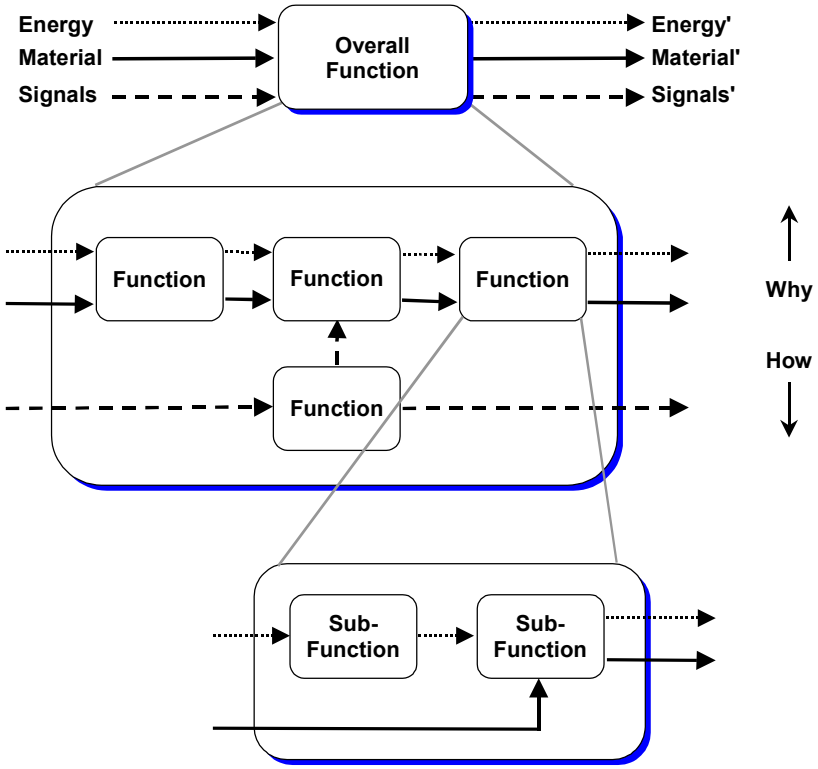
When re-design is required as a result of verification or the identification of errors in design, the effects of the re-design on the ability of the device or process to meet the requirements should be considered. In some cases, this may lead to requirements being clarified or changed and in all cases, the revised design will require re-verification. This latter point is particularly true in software design. It is all too easy to 'fix' software faults with the minimum of re-verification. However, in most cases this inevitably leads to the introduction of further faults. It is a sobering thought that in the software design industry, it is widely accepted that as many faults as are discovered during verification are left undetected in the final code.

Design is a process consisting of different phases. Thus, there are requirements for each phase of the design such as user requirements, functional requirements, embodiment requirements or detailed design requirements. The effects of a re-design will have to be explored, verified and possibly validated with the appropriate requirements.

For instance, a detailed design change might only require verification against the detailed design requirements. However, a detailed design change could also bring about the generation of an entirely new requirement. The effort required to implement a new requirement might be substantial as the designer must track back to the beginning of the design process to implement the change along with the appropriate verification and validation measures to ensure that the new requirement has been properly addressed.



Mapping of Tactic 4 onto the Generic Verification Model



Example of a Functional Model

The key to re-design is to understand the implications of the change on other areas of design and validation. This requires an accurate set of design requirements and a well-documented and understood design. Functional models are particularly useful for helping visualise the implications of a re-design. The impacts of a design change can be tracked up through the hierarchical layers of the model.

According to Pahl and Beitz, a function can be described as the relationship between inputs and outputs of a plant, machine or assembly. A functional model, such as the one shown in the adjacent diagram, is a block diagram consisting of functions connected by the flow of energy, material and signals. The overall function consists of one function block, described with a verb/noun pair, with inputs and outputs. This overall function can be broken down into functions and sub-functions that are also connected by the flow of energy, material and signals. The result is a hierarchical functional model with each level becoming more detailed, but always remaining independent of any solution. Function blocks at a higher level of the model describe why a function is performed while function blocks at a lower level of the model describe how a function is to be performed.

Activities such as design reviews and revisiting the hazard and fault analysis also aid the designer in understanding the full implications of the required change. Overall, a plan should be put together at the beginning of a project, which outlines the structured activities to be implemented if a re-design is required. All too often, planning does not take place until after the need for a re-design has been discovered. This can lead to the situation where project teams scramble to implement a quick-fix solution without proper verification or validation.

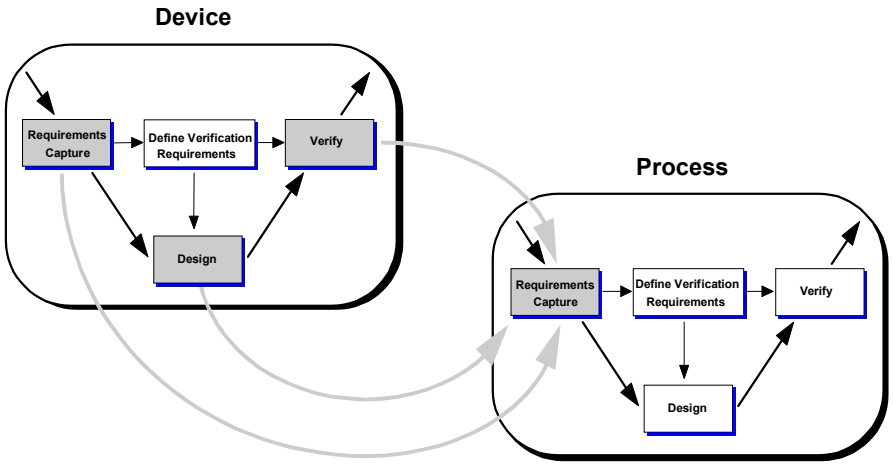
In summary, it is imperative that designers explore and assess the impact of re-design on the whole of the design process.

5 CONSIDER THE EFFECTS OF DEVICE REQUIREMENTS, DESIGN AND VERIFICATION ON PROCESS REQUIREMENTS AND VALIDATION

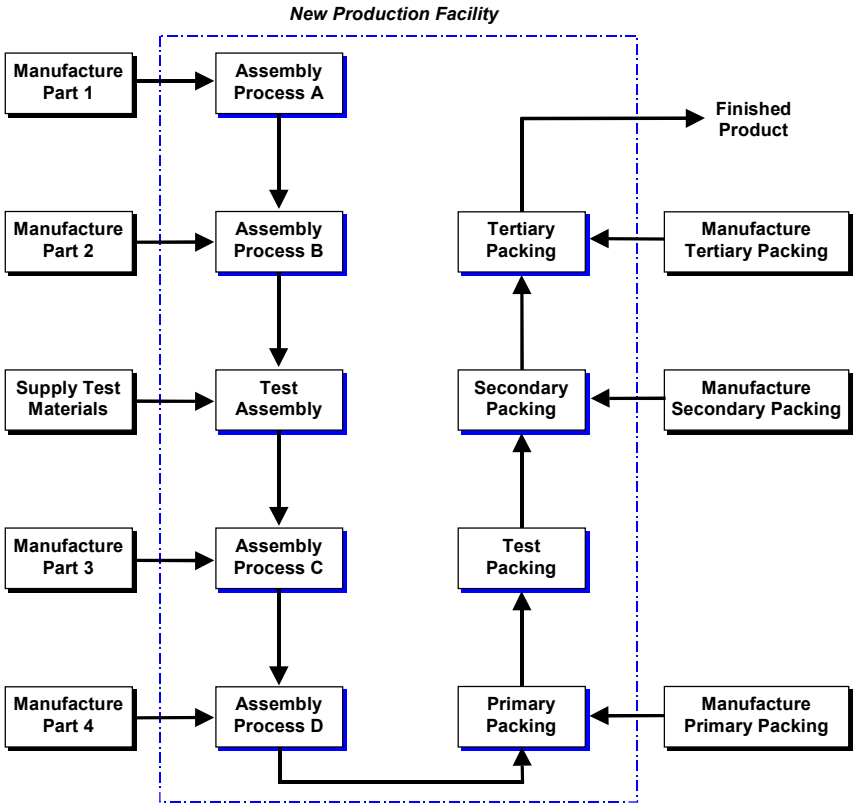
Decisions made during the device requirements capture, design and verification activities must be explored to understand their impact on the requirements for the related process equipment. This review must also consider the validation requirements of such equipment. This is particularly true for novel devices where little is known initially about the robustness of the device design.

The product and manufacturing process can be defined in parallel. During the early stages of device design, whether it is at the user requirements specification or at the initial device concept stage, designers must think ahead to what processes will be required to manufacture the product. As a step further, the designer must also explore the required process verification and qualification.

Processes and materials have limitations and a designer must be aware of those limitations during the design of the device. Processes such as sterilisation can place constraints on the design and potentially cause device quality problems. Risk analysis can play a key role in highlighting process design, verification and validation requirements during device design.



Mapping of Tactic 5 onto the Generic Verification Model



Example of a Process Flow Diagram

This tactic may appear to be a statement of the obvious. However, numerous FDA warning notices relate the failure to verify critical device functions during manufacture or to validate the associated manufacturing processes. Consider, for example, the following FDA warning notice: "There is insufficient evidence to support that the sterilisation dose is capable of achieving the specified sterility assurance level." Consideration of manufacturing process validation during device design would have made this particular product recall unlikely.

One method that can be used to explore the manufacturing process is to construct a process flow diagram based on the device concept. A simple process flow diagram, similar to the one shown in the adjacent figure, should include the required manufacturing, assembly and test operations. The inputs and outputs to each operation form the basic requirements for each process step.

Initially, the requirements for each operation will be very general. However, the requirements become more specific as the device design and process design become more detailed. By the end of the device design process, there should be a detailed process flow diagram with the required states of all of the operations. Thus, a detailed requirement specification can be written for each machine or operation.

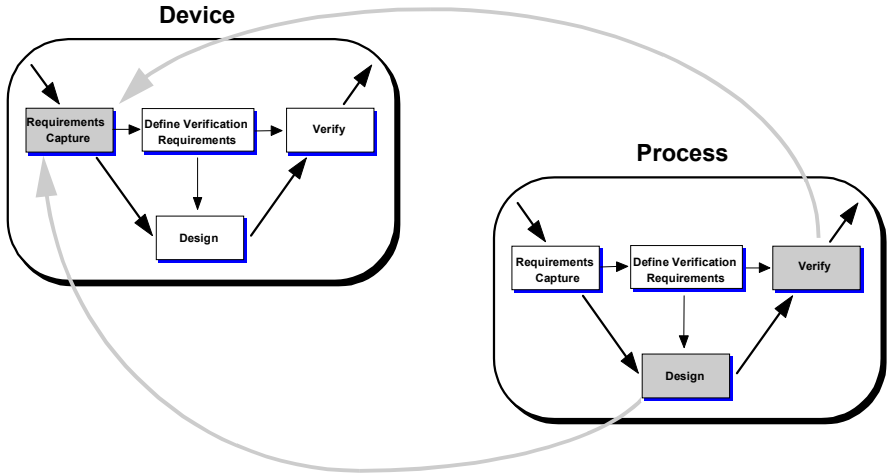
In summary, designers must understand the relationships between the design, verification and validation of a device and its associated process equipment.

6 CONSIDER THE EFFECTS OF PROCESS RE-DESIGN ON DEVICE REQUIREMENTS

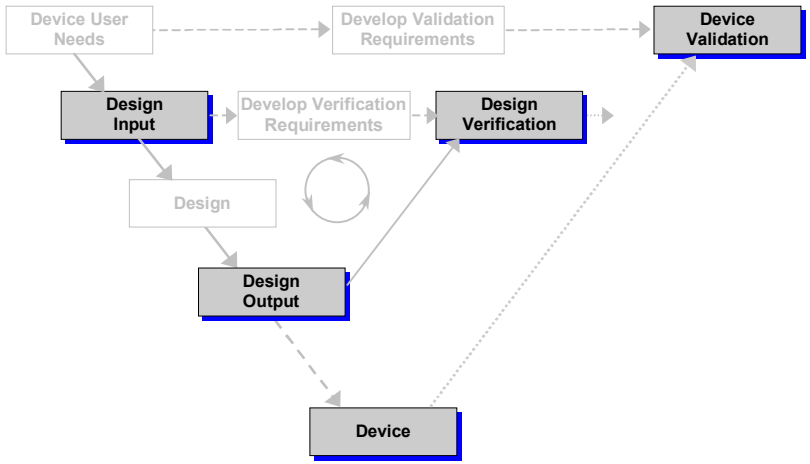
The effects of re-design performed during the manufacturing process design and development must be understood and, if necessary, reflected in the device requirements. Innovative devices often demand innovative manu-facturing processes and where these processes fail to perform adequately, the performance of the resulting device may also be compromised.

Process design and development might bring to light problems that had not been addressed during device design. In the past, there has been a tendency to make design changes during the process development stage without considering the full implications of the changes on other areas of design and validation.

For example, during the manufacturing process of a particular device, the thread of the device handle was cut at an incorrect pitch. The error was judged not to be critical and the process specification was subsequently amended to reflect the change. However, it was later discovered during clinical evaluations that the product was not functioning properly. An in depth analysis of the problem showed that the original thread pitch was critical to the proper functioning of the device. Therefore, the change in pitch contributed to the entire device being unfit for its intended purpose. A more thorough review following the initial error could have avoided further costly re-design that was discovered late in the development process.



Mapping of Tactic 6 onto the Generic Verification Model



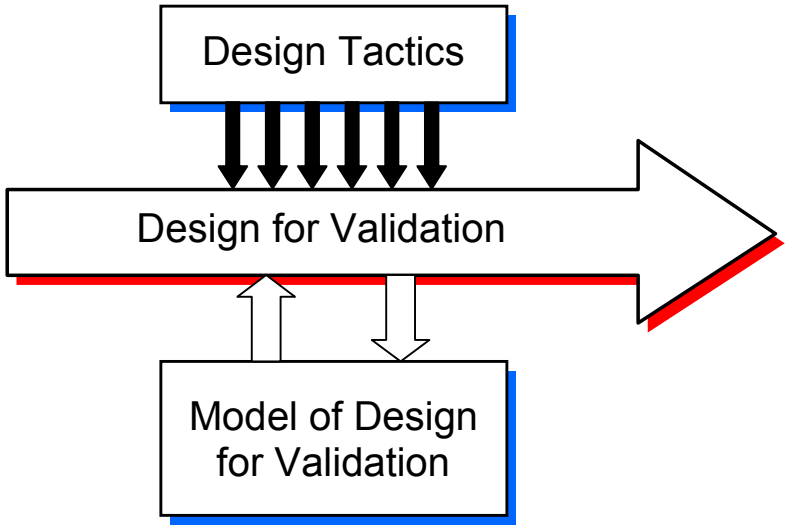
Exploring the Effects of Process Re-design Using the DFV V-Model

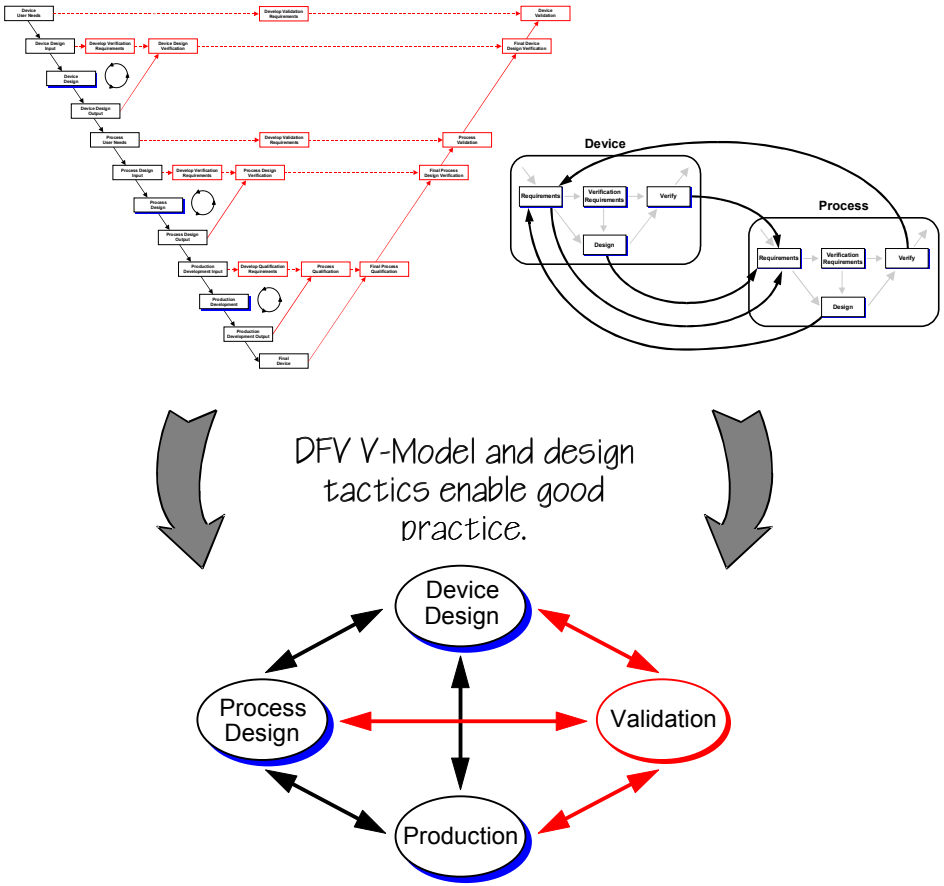
In order to understand the influences of process re-design on the device, the designer must explore the impacts on device design input, design output, design verification and the entire device validation. This is shown in terms of the Design for Validation V-Model on the adjacent diagram.

For instance, making slight changes to the product in order for process equipment to operate more effectively is a temptation that project teams face on a regular basis, especially when trying to meet product delivery deadlines. However, this type of action could have major implications on the overall 'fitness for purpose' of the product because the re-design could result in a change to the device design. Previous efforts to show that a proper device design process had been followed with design outputs meeting design inputs and user needs might not be valid. The worst case might be that there is a need to repeat all validation including clinical trials. This is true for device design changes as well as the use of new processes, materials or packaging on an existing design.

In summary, designers must explore the impacts of changes made to the design of the manufacturing equipment. This includes investigating the impacts of any process equipment re-design on the design, verification and overall validation of the medical device.

PART 3: IMPLEMENTATION OF DESIGN FOR VALIDATION





INTRODUCTION

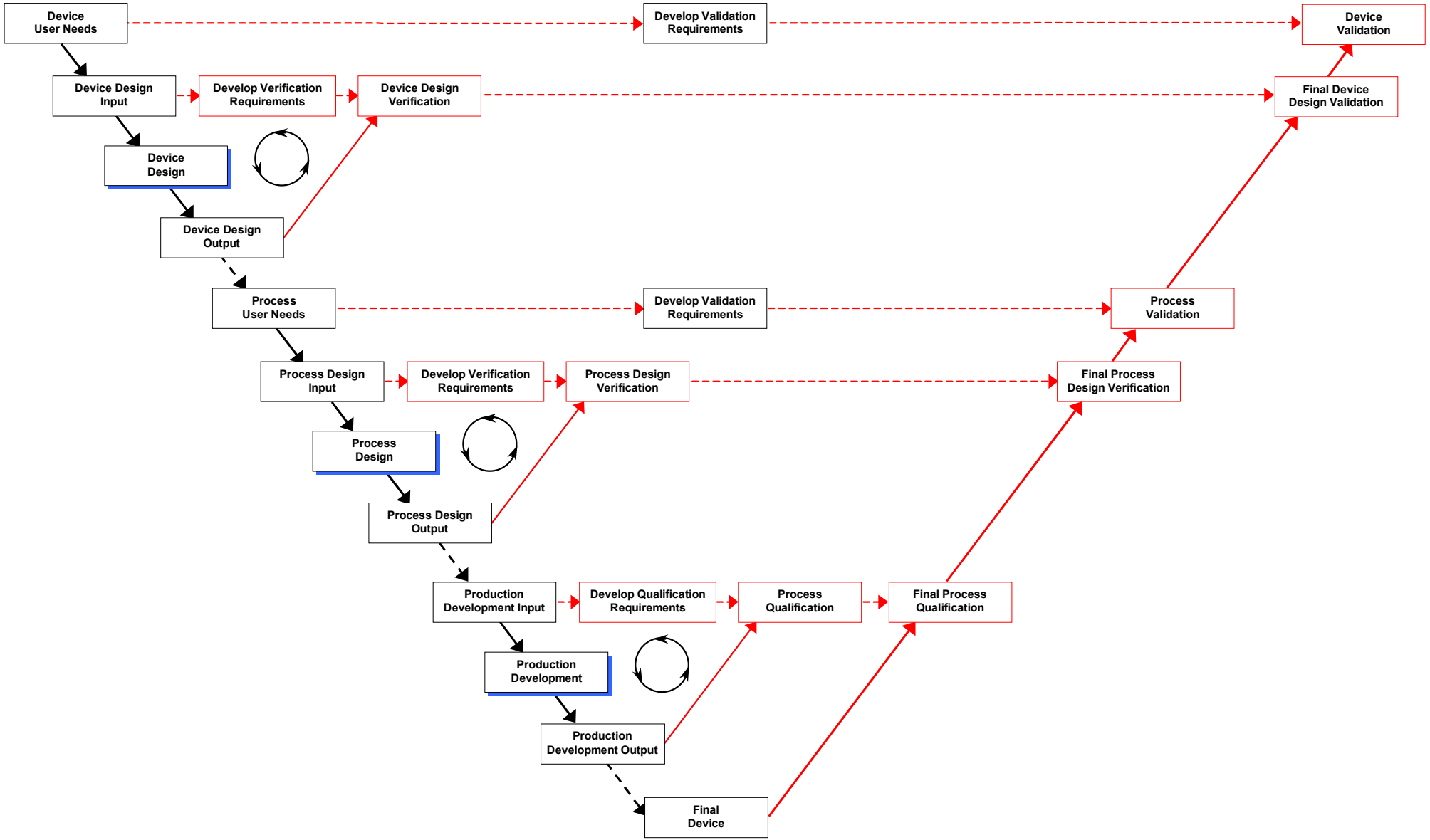
The prescriptive approach to design for validation proposed in this workbook provides good practice guidance for designers to enable integrated design, development and validation. The Design for Validation V-Model and six design tactics form a practical approach which is applicable to a wide range of devices, enhances existing design methods, extends the current medical device regulation guidance and is adaptable to device and process design.

This part of the workbook presents a practical guide to the implementation of design for validation through the use of simple audit checklists that are relevant to the DFV V-Model and design tactics.

USE OF THE DESIGN FOR VALIDATION MODEL

The DFV V-Model outlines the major stages of verification and validation that should occur during a medical device project. The model can be used as tool to help manufacturers audit their existing system of design and development.

- ❑ Does your system have the activities shown in the DFV V-Model?
- ❑ Does your design team understand the difference between verification and validation?
- ❑ Do you attempt to capture all of the user needs and all of the intended uses of the device before commencing with the design and development?
- ❑ Have you set up a validation strategy?
- ❑ Have you set up verification requirements for each design input?
- ❑ Have you verified each design output against a design input?
- ❑ Have you set up a process validation strategy?
- ❑ Have you set up process qualification requirements?
- ❑ Have you qualified the final process equipment?
- ❑ Have you proven that the final device meets its initial device requirements (is verification complete)?
- ❑ Have you proven that the final device meets all of the user needs and all of the intended uses (is validation complete)?



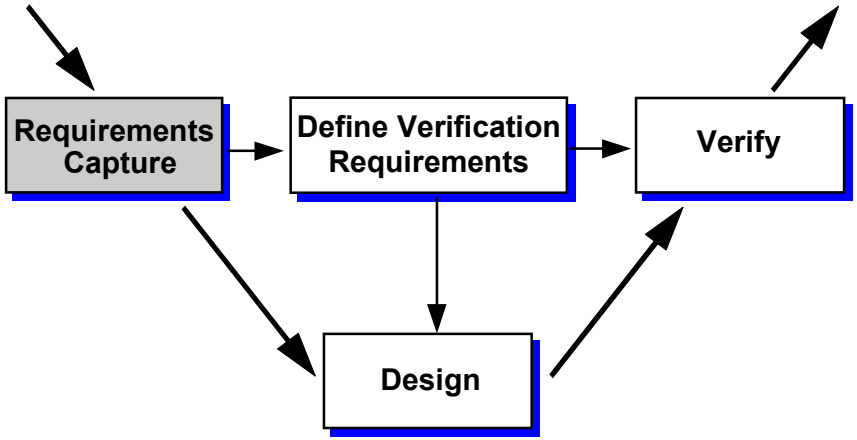
Design for Validation (DFV) V-Model

USE OF THE DESIGN TACTICS

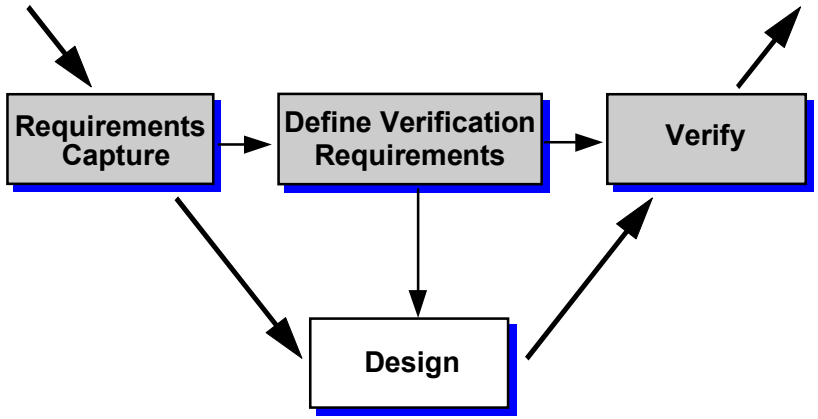
The six design tactics are used to help designers take a proactive role towards validation during the design and development phases of a medical device project. Although the tactics are simple, their effective implementation can have a major effect on a medical device project. A simple audit can be used to check if the tactics are currently in use within an organisation.

Tactic 1: Capture implicit and explicit requirements

- ❑ Do you use a systematic method to capture requirements?
- ❑ Do you have a method in place to ensure that both implicit and explicit requirements are captured?
- ❑ Have you considered all users and stakeholders of the device?
- ❑ Have you considered the device throughout its lifecycle?
- ❑ Have you considered the requirements for regulatory approval?
- ❑ Have you considered the requirements for validation?
- ❑ Have you defined a procedure for reviewing and changing requirements?
- ❑ Do you perform the above for both device and process?



Focus of Tactic 1



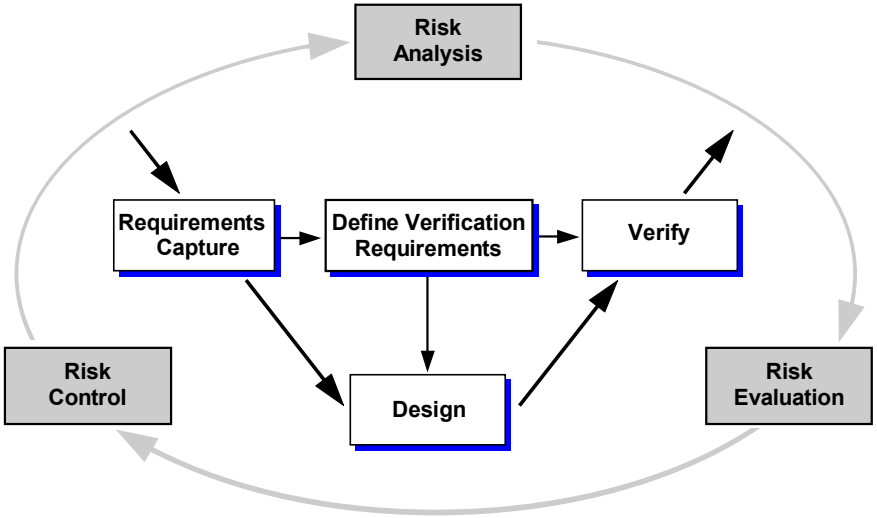
Focus of Tactic 2

Tactic 2: Check that all requirements are verifiable

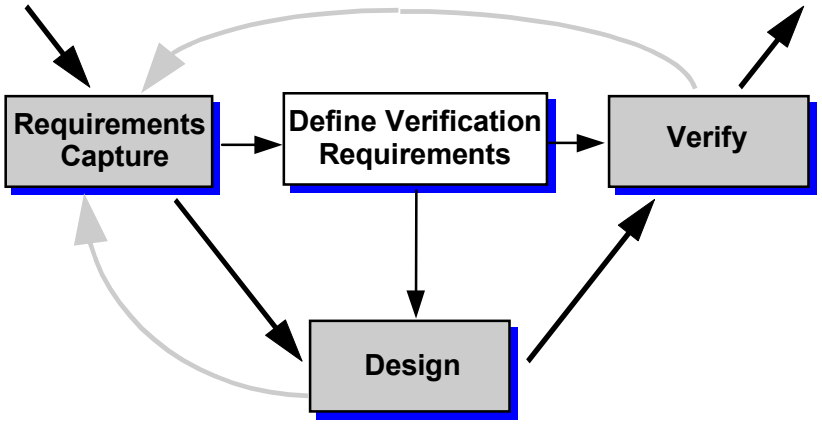
- ❑ Do you have a systematic procedure for ensuring that requirements are verifiable?
- ❑ Does every requirement have quantitative performance targets?
- ❑ If it is not possible to set quantitative targets, have you identified alternative methods of verification?
- ❑ Are specifications and verification requirements formulated, where possible, before design and verification are carried out?
- ❑ Are the verification requirements communicated to the design team?
- ❑ Do you perform the above for both device and process?

Tactic 3: Use a risk-based approach to design and verification

- ❑ Do you have a systematic risk management programme in place?
- ❑ Do you have representatives from the users and stakeholders involved in the risk management process?
- ❑ Do you use the cycle of risk analysis, risk evaluation and risk control throughout the design and development project?
- ❑ Do you use risk management to drive design and verification of the device and process equipment?
- ❑ Do you perform a preliminary hazard analysis on the user requirements?
- ❑ Do you consider the lifecycle of the product in your risk management?
- ❑ Do you use systematic tools such as FTA, FMEA, FMECA, HAZOP or HACCP to analyse and assess risks?
- ❑ Do you identify critical device/user interfaces?
- ❑ Do you communicate the results of the risk management process to the product development teams?
- ❑ Do you perform the above for both device and process?



Focus of Tactic 3



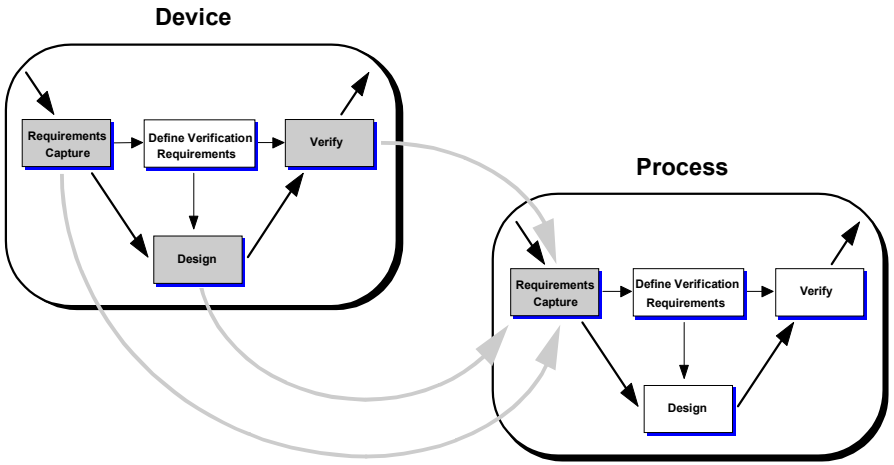
Focus of Tactic 4

Tactic 4: Consider the effects of re-design on requirements

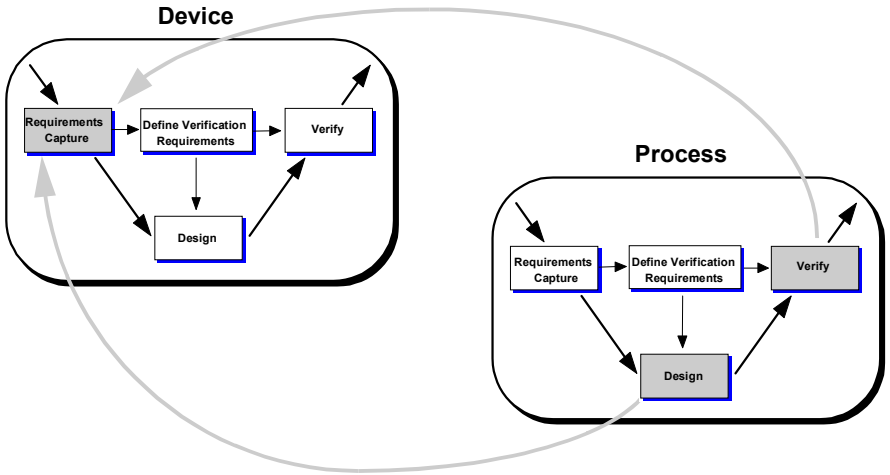
- ❑ Do you have a re-design strategy or procedure in place at the beginning of a project (change management system)?
- ❑ Do you have a systematic procedure for considering the effects of re-design on all requirements?
- ❑ Do you revisit the hazard, fault and risk analysis when conducting re-design?
- ❑ Do you conduct design reviews to investigate the effects of re-design?
- ❑ Do you re-verify changes in requirements?
- ❑ Do you perform the above for both device and process?

Tactic 5: Consider the effects of device requirements, design and verification on process requirements and validation

- ❑ Do you have a systematic procedure to encourage communication between device design, process design and production development personnel?
- ❑ Do you design the device and process equipment in parallel?
- ❑ Do device designers think ahead to process design issues?
- ❑ Do device designers think ahead to process verification and qualification issues?
- ❑ Do device designers think ahead to process validation issues?
- ❑ Are device designers aware of the limits of the process equipment?
- ❑ Are device designers aware of the limits of the materials?
- ❑ Does the device risk management process activity influence the process?
- ❑ Are process flow diagrams used early in the device design and developed as the design of the product becomes more detailed?
- ❑ Are process flow diagrams used as a basis to develop process specifications?



Focus of Tactic 5



Focus of Tactic 6

Tactic 6: Consider the effects of process re-design on device requirements

- ❑ Is there a systematic procedure to explore the effects of process re-design on device requirements (change control)?
- ❑ Do you conduct design reviews to investigate the effects of process re-design of device design?
- ❑ Do you revisit the hazard, fault and risk analysis on the process and/or device as appropriate?
- ❑ Do you re-verify changes in process and/or device requirements as appropriate?

GLOSSARY

CGMP
: Current Good Manufacturing Practice (now called the QSR): Used by the FDA to regulate medical devices.

Design Process
: A series of steps taken by a designer to develop a product or process from initial requirements to final design specifications.

Design Input
: The physical and performance requirements of a device that are used as a basis for design [US FDA, 1996a].

Design Output
: The results of a design effort at each design phase and at the end of the total design effort [US FDA, 1996a].

Design Review
: A documented, comprehensive, systematic examination of a design to evaluate the adequacy of the design requirements, to evaluate the capability of the design to meet these requirements and to identify problems [US FDA, 1996a].

Design Specification
: A complete definition of the device, equipment or system in sufficient detail to enable it to be built [UK Pharmaceutical, 1995].

Design Validation
: Provides confirmation through objective evidence that device specifications conform with user needs and intended uses [FDA, 1996a].

Design Verification
: Provides confirmation through objective evidence that design outputs meet design inputs.

DFA
: Design for Assembly: A structured methodology for analysing product concepts or existing products for simplification of the design and its assembly process. The main goal of DFA techniques is to reduce parts and assembly operations and to change part geometry to ease assembly [Fries, 1997].

DFM
: Design for Manufacture: A technique to analyse the detailed design of a product to eliminate non-functional parts and reduce the number of functional parts [Fries, 1997].

DFMA
: Design for Manufacture and Assembly: A systematic procedure utilising both DFM and DFA techniques to make the fullest use of the manufacturing process that exists and keep the number of parts in an assembly to a minimum [Boothroyd, 1996].

DFV
: Design for Validation: An approach aimed at designing medical devices to make them easier and more economic to validate.

FDA
: Food and Drug Administration: The regulatory body in the United States, which oversees medical devices, food, medicines and radiation, emitting products.

FMEA

Failure Mode and Effect Analysis: A qualitative technique by which the consequences of an individual component fault mode are systematically identified and evaluated. Components are analysed one at a time, thus generally looking at a single fault condition. This is done in a 'bottom-up' mode, i.e. following the process to the next higher functional system level [EN ISO 14971, 2000].

FMECA

Failure Mode and Criticality Analysis: A variation of FMEA, which also assesses the criticality of fault modes.

FTA

Fault Tree Analysis: A means of analysing hazards identified by other techniques. Starts from a postulated undesired consequence also called a 'top event'. In a deductive manner, starting with the top event, the possible causes of fault modes of the next lower functional system level causing the undesired consequence are identified [EN ISO 14971, 2000].

Functional Specification

Documentation describing the detailed functions of a device, equipment or system (i.e. what the product or system will do) [UK Pharmaceutical, 1995].

Good Design Practice

Activities undertaken during design to ensure that a product is fit for purpose within commercial reality. Includes techniques such as DFMA, DFR, Design for Usability and DFV.

HACCP

Hazard Analysis Critical Control Points: A method of exercising control throughout a manufacturing process by detecting and correcting defects at 'critical control points' before the product is completely processed and packaged. This technique is usually associated with food safety programs.

Harm

Physical injury and/or damage to health or property [EN ISO 14971, 2000].

Hazard

A potential source of harm [EN ISO 14971, 2000].

HAZOP

Hazard and Operability Study: Considered to be a form of FMEA. It is a systematic technique for identifying hazards and operability problems, originally developed for use in the chemical process industry [EN ISO 14971, 2000].

IQ

Installation Qualification: Documentation demonstrating that the equipment design and configuration is as intended, that instrumentation has adequate accuracy, precision and range for intended use and that services (such as power supplies) are of adequate quality [UK Pharmaceutical, 1995].

Manufacturer

Any person or organisation who designs, manufactures, fabricates, assembles or processes a finished device [US FDA, 1996a].

Medical Device

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 [European Council Directive 93/42/EEC, 1993].

OQ

Operational Qualification: Documentation demonstrating that the equipment of a system operates as intended throughout representative or anticipated operating ranges [UK Pharmaceutical, 1995].

Process

Any equipment or procedure used to manufacture, assemble or test a medical device.

Process Qualification

The activities involved in proving that production development outputs meet production development inputs.

Process Validation

Provides confirmation through objective evidence that a process consistently produces a result or product meeting its predetermined specifications.

Product

Components, manufacturing materials, in-process devices, finished devices and returned devices [FDA, 1996a].

Production Development

The development of the process equipment or procedures used to manufacture, assemble or test a medical device.

Production Development Input

The physical and performance specifications of a process that are used as a basis for production development.

Production Development Output

The results of a development effort at each production development phase and at the end of the total development effort.

PQ

Performance Qualification: Documentation demonstrating that when operated within set parameters the process will consistently produce product meeting its predetermined specifications [UK Pharmaceutical, 1995].

QSR

Quality System Regulation: New name for the CGMP used by the FDA to regulate medical devices.

Re-design
: Action taken to change the design of a product so that it will fulfil specified requirements.

Re-work
: Action taken on a nonconforming product so that it will fulfil specified requirements [US FDA, 1996a].

Risk
: The probable rate of occurrence of a hazard causing harm and the degree of severity of the harm [EN ISO 14971, 2000].

Risk Analysis
: The investigation of available information to identify hazards and to estimate risks [EN ISO 14971, 2000].

Risk Management
: The systematic application of management policies, procedures and practices to the tasks of identifying, analysing, controlling and monitoring risk [US FDA, 1997a].

Safety
: Freedom from unacceptable risk of harm [EN ISO 14971, 2000].

Specification
: A document that describes the requirements with which a product, process, service or other activity must conform [Fries, 1997; US FDA, 1996a].

URS
: User Requirements Specification: Describes what the equipment or system is supposed to do [UK Pharmaceutical, 1995]. Usually associated with process equipment.

Validation
: Provides a means of answering the question: Have we built the right thing? Validation is concerned with demonstrating the consistency and completeness of a design with respect to the initial ideas of what the system should do.

Verification
: Provides a means of answering the question: Are we building the thing right? Verification is concerned with ensuring that, as the design and implementation develop, the output from each phase fulfils the requirements specified in the output from the previous phase. Verification can comprise tests, inspections and analysis [FDA, 1997a].

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* GHTF Guidance Documents can be obtained at http://www.ghtf.org/default.htm

** US FDA Documents can be obtained at http://www.fda.gov

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 – requirements capture

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

edical 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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