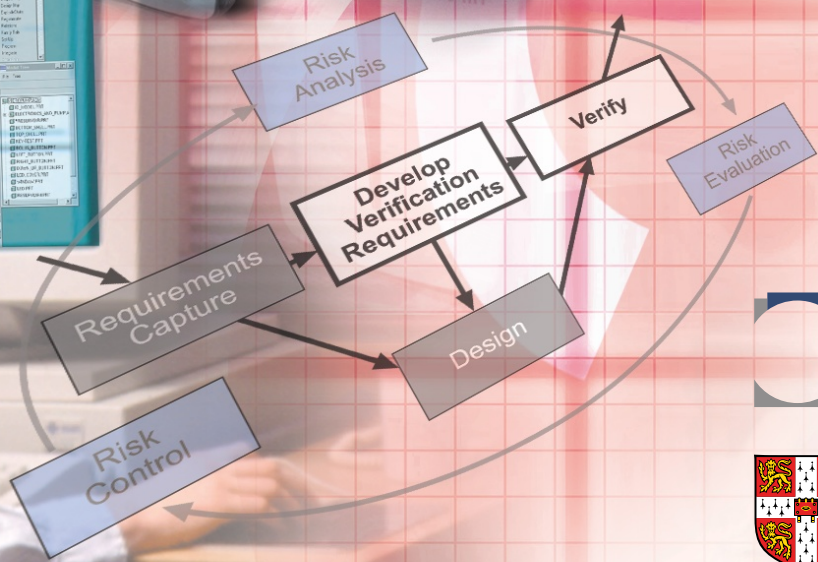


# Good Design Practice for Medical Devices and Equipment Design Verification

| Process         | Component of Process | Fault-Causing Concern           | Immediate effect          | End Effect                | Use (User) | Use (Operator) |
|-----------------|----------------------|---------------------------------|---------------------------|---------------------------|------------|----------------|
| System build up | BIDS checks          | detect-able with hardware       | BIDS checks               | system doesn't work       | operator   | operator       |
|                 | Windows NT starts    | NT Administrator (or processes) | Application doesn't start | Application doesn't start | operator   | operator       |
|                 | Initialisation       | Application doesn't load        | Application doesn't load  | Application doesn't start | operator   | operator       |



 Cambridge Consultants

 UNIVERSITY OF CAMBRIDGE

## THE AUTHORS



James Ward is a Research Associate at the Cambridge Engineering Design Centre and this work-book is based on his PhD thesis, 'Design Verification in the Medical Device Industry'. He is now focusing on the role of usability and clinical trials in medical device design.



Duncan Bishop leads the Process Definition Group at Cambridge Consultants Limited (CCL®). He has considerable experience in design and the requirements for design verification for both medical devices and military aerospace equipment.



Dr John Clarkson is a University Reader in Engineering Design and Director of the Cambridge Engineering Design Centre. He supervised the research work and has been closely involved with the development of the workbook.



Stewart Fox is a former leader of the Mechanical Product Design Group in CCL®. He worked closely with James during the research work, providing information and advice from his experience of medical device development.



**CAMBRIDGE  
ENGINEERING DESIGN  
CENTRE**

Since its inception in 1991, the EDC has earned an international reputation for research in Engineering Design through its publications, software tools and presentations at international conferences, through collaborations with industry and through networking with other design research groups. Details of the Centre, its programmes and research staff may be seen at:

[www-edc.eng.cam.ac.uk](http://www-edc.eng.cam.ac.uk)



Cambridge Consultants Limited designs and develops innovative new products, processes and systems. With a team of over 250 engineers and scientists, it offers solutions across a diverse range of industries including healthcare, telecoms, industrial and consumer products, automotive and aerospace. For more details of products and services see:

[www.CambridgeConsultants.com](http://www.CambridgeConsultants.com)

# **GOOD DESIGN PRACTICE FOR MEDICAL DEVICES AND EQUIPMENT – DESIGN VERIFICATION**

By:  
James Ward  
John Clarkson  
Engineering Design Centre, University of Cambridge  
and  
Duncan Bishop  
Stewart Fox  
Cambridge Consultants Limited

## **ACKNOWLEDGEMENTS**

This workbook is based upon the PhD thesis of James Ward and research led by Dr John Clarkson carried out at the University of Cambridge Engineering Design Centre.

The research benefited from working closely with Cambridge Consultants Limited (CCL). In particular, Duncan Bishop and Stewart Fox contributed a significant amount of their time and gave much valuable advice as work progressed. Also, much thanks is due to a number of designers, project managers, quality assurance managers, regulatory affairs managers and consultants who have assisted greatly in providing input to this workbook, from both within CCL and from other companies. Many of the quotations in this workbook were collected during interviews with these people as they discussed the successes and failures that they had experienced in the design and evaluation of medical devices.

Thanks are also due to Professor Roy Farmer for his guidance and many helpful suggestions as the workbook neared completion.

## **GOOD DESIGN PRACTICE FOR MEDICAL DEVICES – DESIGN VERIFICATION**

Copyright © University of Cambridge Engineering Design Centre. All rights reserved.

First published in Great Britain 2002, jointly by the University of Cambridge Engineering Design Centre, Trumpington Street, Cambridge, CB2 1PZ, and the University of Cambridge Institute for Manufacturing\*, Mill Lane Cambridge CB2 1RX.

**ISBN 1-902546-12-1**

No part of this publication may be reproduced, stored in a retrieval system or transmitted in any form or by any means without the prior permission in writing of the publishers, nor be otherwise circulated in any form of binding or cover other than that in which it is published and without a similar condition including this condition being imposed on the subsequent publisher.

\*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).

# TABLE OF CONTENTS

|   |          |   |           |
|---|----------|---|-----------|
| Acknowledgements  | ii       | <b>PART 2 – Implementation of Good Verification Practice</b>    | <b>27</b> |
| Table of contents   | iii      | Setting out the verification approach                           | 28        |
| Introduction  | iv       | <i>Using the method</i>   | 29        |
| What does this workbook contain?                              | v        | <b>Stage I – Outline verification plan</b>                      | <b>31</b> |
| Workbook objectives   | v        | <i>Review requirements and outline protocols</i>                | 33        |
| Who is this workbook for?                                     | vi       | <i>Assess risks</i>   | 34        |
| How to use this workbook                                      | vii      | <i>Draft verification plan</i>                                  | 39        |
| <b>PART 1 – An Introduction to Good Verification Practice</b> | <b>1</b> | <b>Stage II – Refine verification plan</b>                      | <b>40</b> |
| <b>The verification process</b>                               | <b>2</b> | <i>Determine verification demand</i>                            | 42        |
| <i>The role of verification</i>                               | 2        | <i>Review candidate verification methods</i>                    | 46        |
| <i>When is Verification Guidance needed?</i>                  | 4        | <i>Assess benefits/limitations of each method</i>               | 47        |
| <i>Why is verification important?</i>                         | 6        | <i>Select preferred approach</i>                                | 52        |
| <i>Verification basics</i>                                    | 9        | <i>Validate selected methods</i>                                | 54        |
| <i>Design scenarios and verification action</i>               | 12       | <b>Stage III – Execute protocols</b>                            | <b>56</b> |
| <i>Verification – a risk based process</i>                    | 14       | <i>Complete protocols</i>                                       | 56        |
| <i>Types of risk</i>  | 16       | <i>Carry out protocols</i>                                      | 56        |
| <i>Using risk to influence verification practice</i>          | 20       | <b>PART 3 – Supplementary guidance</b>                          | <b>57</b> |
| <i>Model of risk-based design and verification</i>            | 26       | <b>Developing verification methods</b>                          | <b>58</b> |
|   |          | <i>Draft the verification method</i>                            | 61        |
|   |          | <i>Check the verification method</i>                            | 68        |
|   |          | <b>Documenting plans and protocols</b>                          | <b>72</b> |
|   |          | <b>Managing changes in the design process</b>                   | <b>76</b> |
|   |          | <b>APPENDIX –Web-based Standards and Regulatory Information</b> | <b>79</b> |

## INTRODUCTION

The UK Medical Devices Agency defines medical devices as any products – excluding medicines – that are intended to diagnose, prevent, monitor or treat illnesses or handicaps. Medical device technology combines the fields of engineering and medicine to provide technical solutions to medical problems.

For many medical device manufacturers, the design of a medical device presents a number of engineering and project management-related challenges during the design process. Although these challenges often surface during the design of standard products, the complexity and safety-critical nature of many medical devices tend to exacerbate the difficulties. Case histories show that the effects of releasing a device that is unfit for purpose to market can be catastrophic – for those who use the device and the manufacturer.

Despite such problems, little guidance exists on how to tackle them, hence the rationale for developing a new series of workbooks to encourage ‘good practice’ in the design, development and evaluation of medical devices.

*Good Design Practice for Medical Devices and Equipment – Requirements Capture* is the first workbook in this series. This covers one of the key activities in the design process, the systematic collection of design requirements. These lay the foundation for the rest of the design.

The second workbook in this series – *Good Design Practice for Medical Devices and Equipment – A Framework* – contains guidance on how to manage the design process so that validation, and hence rework, problems are minimised. Several ‘design tactics’ are provided to help designers achieve this objective.



Examples of the enormous range of medical devices:

1. urea monitors for haemodialysis (Gambro)
2. wound dressings (Smith and Nephew)
3. the robotic da Vinci™ Surgical System (Intuitive Surgical Inc.)

## WHAT DOES THIS WORKBOOK CONTAIN?

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 – the third in the series – 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.

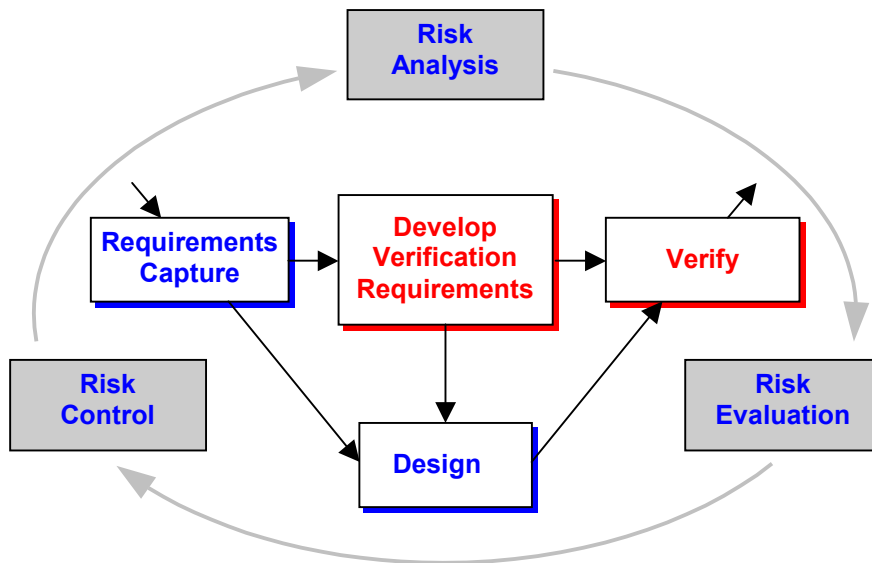
The workbook is divided into three parts plus a short appendix:

*Part 1* introduces the basic theory behind verification and shows how risk assessments may be used to influence its timing and quality.

*Part 2* presents a method for determining the verification approach, when it should occur and what methods should be used.

*Part 3* includes additional guidance to help apply *Part 2*.

The *Appendix* lists web sites from which standards and regulatory affairs information may be obtained.



Model of risk-based design and verification

## WORKBOOK OBJECTIVES

The purposes of this workbook are to:

1. explain why medical device verification is important,
2. set out good practice principles and provide guidance for verification,
3. help designers develop devices that are fit for purpose and on time to market within the bounds of commercial reality.

## WHO IS THIS WORKBOOK FOR?

This workbook is primarily intended for designers, test engineers and project managers involved in the development of medical devices for markets in Europe and the USA. However, other technical staff, such as those engaged in device research and development, quality management, regulatory affairs and manufacturing, might also find it useful.

It is hoped that all manufacturers involved in device design will benefit by adopting some or all of the verification guidance to improve existing working practices. The workbook may be particularly useful for companies developing more innovative devices, where little guidance exists on verification strategies or managing the process of verification.





## HOW TO USE THIS WORKBOOK

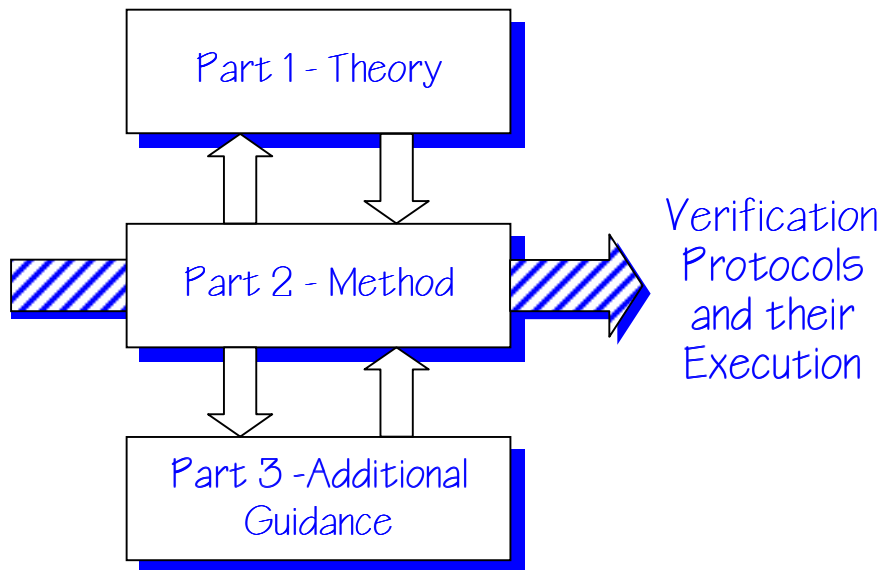
Companies, projects and individuals vary considerably – what may be good practice for one may be unreasonable for another. Ideally, the workbook should be used in conjunction with pre-existing working practices and, perhaps even more importantly, in addition to the array of regulations for medical device design. ***Thus, the degree with which and the manner in which the guidance is adopted is very much at the user’s discretion.***

The basic theory of verification and why verification is necessary is explained in *Part 1*. This should be of general interest as well as useful for clarifying various aspects of the method.

The method given in *Part 2* will help to assure that the timing and quality of the verification are appropriate from a regulatory and commercial point of view. *Part 2* may be used to augment existing verification procedures or used to set up new verification procedures, particularly when the device is novel. On very large projects, the full rigour of *Part 2* may only be justified for the high priority or the most critically important requirements. Nevertheless, the principles of how and when to verify that are at the core of this workbook should be borne in mind throughout the design process.

*Part 3* contains additional guidance on developing verification methods, documenting plans and protocols and managing changes in the design process.

In the adjacent diagram, it can be seen that the verification methods and details of when they should be performed in the design process are derived by adapting the *Part 2* method to project needs, referring where necessary to the *Part 1* theory and the further guidance in *Part 3*. The protocols are updated and executed as development proceeds.



Using the workbook to perform verification



## **PART 1 – AN INTRODUCTION TO GOOD VERIFICATION PRACTICE**

*“They must first be tested; and then if there is  
nothing against them, let them serve...”*

Paul, in a letter to Timothy, ~AD70

# THE VERIFICATION PROCESS

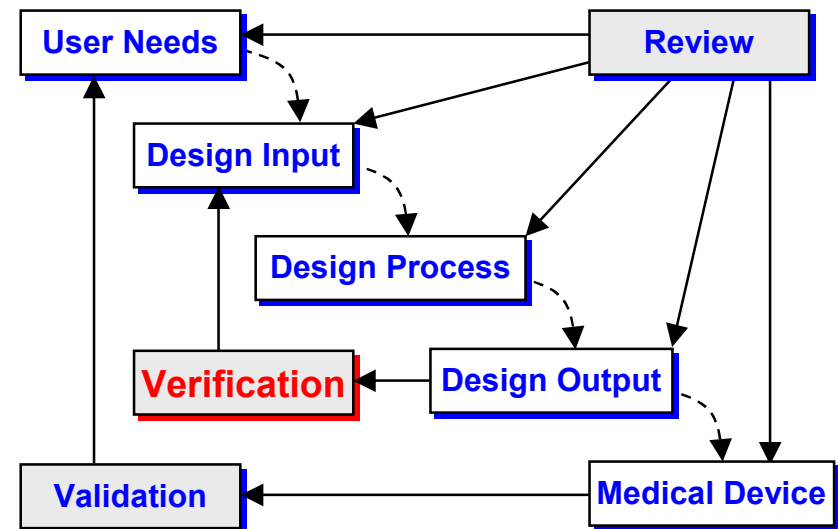
## THE ROLE OF VERIFICATION

Verification is an evaluative activity to check that a device design meets its requirements. Contrary to popular belief, verification does not just involve testing but includes any activity that provides proof that requirements are being fulfilled. In the USA, medical devices are regulated by the Food and Drug Administration (FDA), which describes verification as a ‘three-pronged approach’ of tests, analyses and inspections. ‘Simulations’ and ‘measurements’ can also be added to this list.

The Waterfall Model<sup>1</sup>, shown opposite, is a simplified interpretation of the device design process, from the conversion of user needs into requirements to the translation of these into a finished device. The various evaluative activities that accompany this process are highlighted in grey. It can be seen that verification is one of several evaluative activities that occur.

Specifically, verification involves checking that what has been designed (design outputs) meets its requirements (design inputs). Design inputs are simply the requirements for the device design. Design outputs are any product that either describes the design directly, such as engineering drawings and prototypes, or an attribute of the design, such as risk analysis results. Essentially, verification helps to check that the device design is on track. It helps answer the question, “Are we building the thing right?”

The Waterfall Model also shows how iterative and interactive design activities are. Verification goes hand in hand with design and should never be regarded as an isolated activity.



The ‘Waterfall’ Model of Design

<sup>1</sup> The FDA has included the Waterfall Model in its document entitled *Design Control Guidance for Medical Device Manufacturers*. Should further information be required on the elements of the model, this document is an excellent reference source.

## **Reviews**

Design reviews have a more general focus than design verification. Rather than just evaluating design outputs against inputs, design reviews may be used to: evaluate the overall progress of the project, highlight problems with design inputs or investigate the design itself.

## **Validation**

Design validation involves any evaluative activity that compares the device design against user needs. In this context, users are any persons who come into direct contact with the device, such as patients, clinicians and care providers.

Validation may also include the evaluation of a device prototype in a usability trial. It is broader than design verification, because it aims to bypass design inputs and go straight back to the user needs. Ultimately, it involves evaluating the finished device against user needs. Validation helps answer the question, “Have we built the right thing?”

## WHEN IS VERIFICATION GUIDANCE NEEDED?

### Minor design changes

Most 'new' devices that are placed on the market do not represent major advances in device technology. When design changes are largely cosmetic or comprise minor technical improvements, much widely available and specific guidance usually exists for device design and evaluation. In these circumstances, manufacturers often have a good understanding of how to design and evaluate devices successfully and have their "set arsenal of tests".

### Simple designs and low-risk devices

In other instances, manufacturers design relatively novel but simple devices, or devices which are judged to present a low safety risk. Thus, the pitfalls and challenges in designing these, and the risks to users once the devices have been marketed, may be well understood and carefully controlled. Experienced designers may face few problems.

### Innovative design and applications

Nevertheless, many notably innovative devices do enter the market each year. Furthermore, changes such as the marked increase in home-use devices, the take-up of new technologies and rising user expectations present new challenges for device manufacturers and these need to be met through appropriate device design and evaluation.

Designing and evaluating innovative or complex devices, particularly those that are safety-critical as well, may be far from straightforward, and the questions of how to perform verification in an economical and timely manner may not be easy to answer.



Why use this guidance? –

*“It’s not a problem. We have our set arsenal of tests.”*

*(Medical device QA Manager)*

*“Verification... should be performed as appropriate during the development process.”*

*(BS EN ISO 9000-3:1997 §4.4.7)*

*Often, regulatory guidance sheds little light on good verification practice!*

### **Managing verification activities**

Experienced designers and project managers recognise the importance of trying to optimise the timing of verification activities during the design process. They also appreciate the need to select verification methods that are cost effective, that is, those that give a suitable degree of assurance of device fitness-for-purpose without being too costly.

Evaluation-related guidance in the software and electronics industries indicates how this balance might be achieved for these design disciplines. Alas, neither presents an integrated approach to verification planning, which is needed to facilitate the management of verification activities and the selection of suitable verification methods for the entire device.

In contrast, regulatory and quality system requirements exist regarding the requirements for and the management of verification activities during medical device design. However, these either relate to the evaluation of particular devices, or are so general as to provide little practical assistance in the management of the process; essentially they say, “do verification”, and provide little assistance on how to carry this out on a day to day basis.

## WHY IS VERIFICATION IMPORTANT?

Good verification practice minimises commercial risks, risk to users and the cost of satisfying regulatory requirements.

Poor verification practice can increase project costs, reduce sales revenues and expose the company to negligence claims if, as a result, some or all of the following occur:

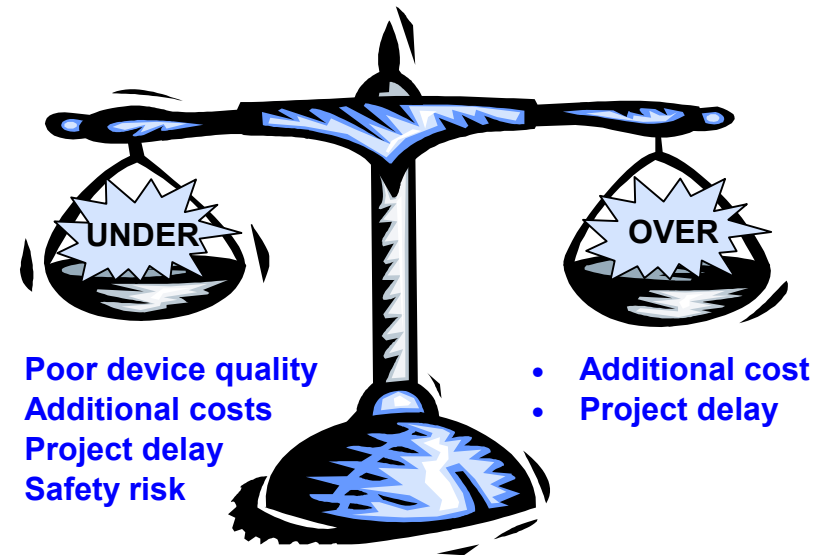
- *project inefficiencies*
- *failure to gain regulatory approval*
- *reduction in device fitness for purpose*
- *failure to protect those involved in clinical evaluations*
- *in-market device modifications*
- *loss of company image*
- *recalls*
- *liability and litigation*
- *user injuries and deaths*

### Project inefficiencies

If device design problems are not discovered in a timely manner, significant rework may be required, the project will be delayed and costs will escalate. Similarly, if the quality of the verification is poor, such problems may not be identified until later in the design process, if at all. In contrast to such 'under-verification', 'over-verification' can also result in additional costs and delay if an overly expensive verification approach (quality and regularity of verification) is chosen. Thus, a balance needs to be struck.

### Failure to gain regulatory approval

If it cannot be shown that the verification process has met regulatory requirements, a variety of problems may result, including the need to



A balance needs to be struck between 'under-verification' and 'over-verification'.



gather further verification-related evidence before the device can be released to market.

### **Reduction in device fitness for purpose**

If a problem is uncovered late in the design process, there may be little choice but to implement a 'quick fix' to the device design. Worse still, a manufacturer knowingly may risk placing an inadequate device on the market in an attempt to recover investment costs. Thus, device quality is compromised.

### **Failure to protect those involved in clinical evaluations**

Verification can complement clinical evaluations because it should provide assurance that the device is safe before evaluations start.

### **In-market device modifications**

Once the device has been placed on the market, design modifications may be required if it is found that it is not suitable for use. These can be extremely costly.

### **Loss of company image**

In-market device problems can result in a loss of company image and reduce future sales.

### **Recalls**

In cases where device performance is unsatisfactory, the device may be recalled from the market. The effects of such a recall can be disastrous for a company, as illustrated opposite.

### **Liability and litigation**

In-market device problems can result in legal action being taken against the manufacturer, also as illustrated opposite.

*“As a result of poor clinical performance of their hip implant, a large multinational manufacturer faced over 800 lawsuits in mid 2001. They received preliminary approval for an out-of-court settlement offer of US\$780m, although it is possible that the actual payout could be even higher.”*

## User injuries and deaths

The effects of device-related errors in human terms can be catastrophic. During 2001 the MDA received 7896 reports of adverse incidents involving medical devices in the UK. 141 reports were connected with a fatality and 650 with a serious injury.

## Good practice

It can be seen that good verification practice should de-risk the design in a timely and economical manner. Bad verification practice can result in project over-runs, over-spends and, at worst, recalls, patient harm and legal action.

So, it is crucial that verification is performed appropriately in order to ensure an economical and efficient device development process, and to provide suitable proof of the fitness for purpose of the device before it is released to market.

**News - CLINIPAD CORPORATION CEASES OPERATIONS**

Setting Standards for Quality, Innovation and Value

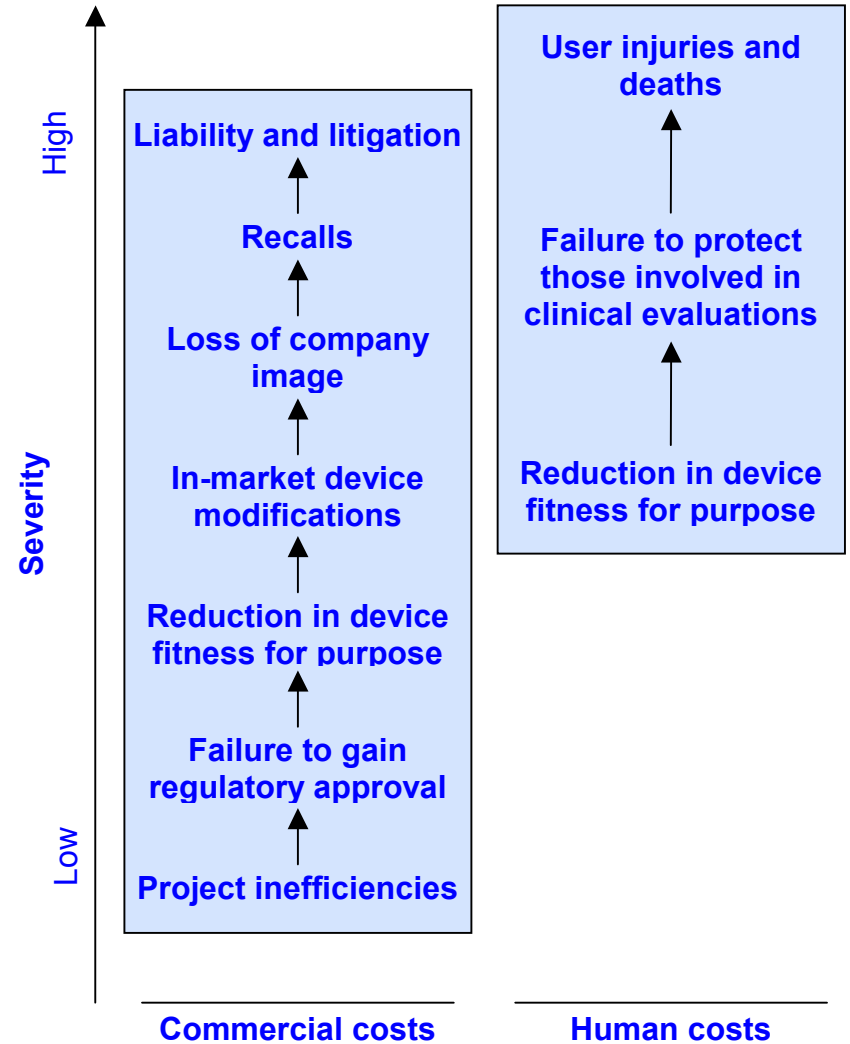
**Contact:** Vice President, Administration  
**Phone:**                      **Ext:**

**CLINIPAD CORPORATION CEASES OPERATIONS**  
 March 28, 2000

**ROCKY HILL, CT,** The Clinipad Corporation announced today that it has permanently ceased all production and operations effective March 28, 2000, which will affect approximately 220 employees.

The company recently initiated a significant recall of previously marketed product which has had a serious, adverse effect on the company finances and operations. Accordingly, the company has decided to cease operations and to close its facilities.

In early 2000, the discovery of a quality problem sadly led to the liquidation of a company, employing approximately 220 employees.



The results of poor verification practice in terms of commercial and human costs

(the severity of the outcome may vary greatly from scenario to scenario)

## VERIFICATION BASICS

### The three verification elements

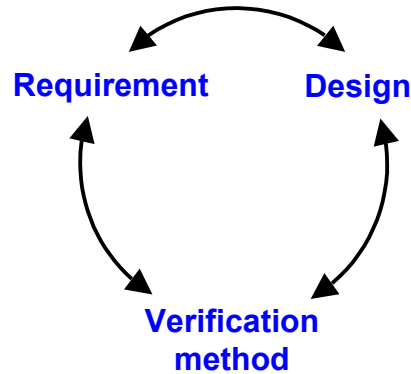
Prior to carrying out verification it is necessary to have three elements:

- 1) a *requirement*, specifying what the design has to achieve – for example, the device must pass the corrosion resistance test in BS 6196:1989,
- 2) a *model (the device design)*, representing the part of the design to be evaluated – for example a prototype, and
- 3) a *method*, normally defined in a document called a ‘verification protocol’, which defines how the verification is to be carried out – for example, the test method as specified in BS 6196:1989.

Problems with any of the above can cause verification-related difficulties.

All three elements are linked together – a change to one element may bring about the need to implement further changes to one or two others.

For example, incorrectly specified requirements may necessitate the associated verification activities to be repeated or modified, adding costs and delay to the project. This is a very common problem, particularly when the full range of in-use conditions has not been assessed. Other problems arise with models that do not represent the true properties of the design, and inaccurate methods, which can bring about misleading verification results and lead to incorrect decision making.



The three verification ‘elements’  
necessary to carry out verification

## Verification timing

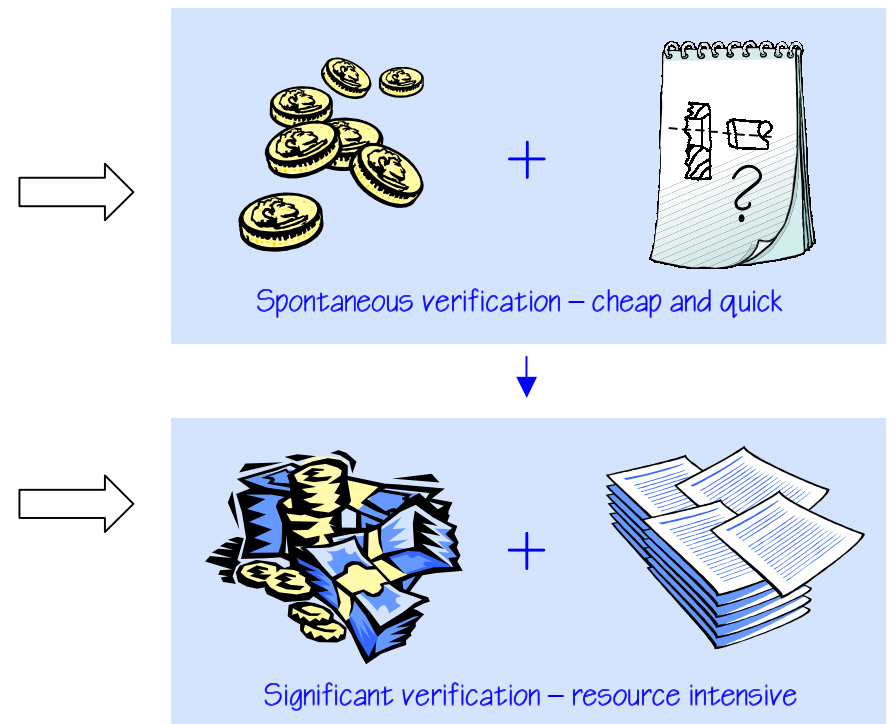
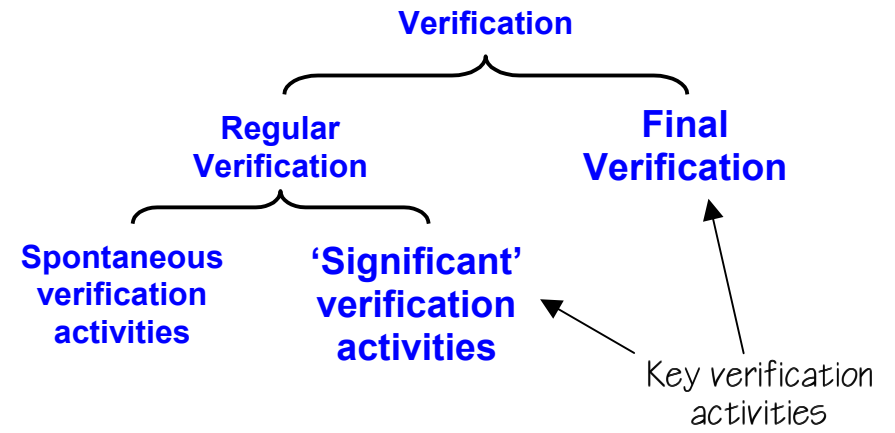
Verification is rarely a once-only final effort at the end of the design process. Usually, it is carried out many times and in many different ways throughout the development of the device. It is helpful to separate such activities during the design process into two distinct types – ‘regular’ and ‘final’ – as each has different objectives:

- **regular verification** occurs as design progresses – it minimises risks by providing adequate assurance, in a timely and economical manner, that the developing design meets its requirements,
- **final verification** provides the ultimate proof of meeting device design requirement towards the end of the design process.

## Regular verification

Regular verification may be further separated into spontaneous activities and significant activities:

- **Spontaneous verification activities** tend to occur on an ad-hoc basis – for example, by means of a quick ‘back of the envelope’ calculation or by simply casting an eye over the design and basing decisions on experience or gut feeling in the form of “that looks about right” decisions. Such activities may occur very frequently during design. Generally, they are motivated by their ease of execution, the minimal cost they incur and the designer’s confidence in what is being designed.
- **Significant verification activities**, in contrast, incur a notable drain on project resources and/or are required to provide a greater degree of assurance in the quality of their results. When compared with spontaneous verification activities, they often involve the production of more costly models of the design, for instance a finite element mesh or a physical prototype, and the use of more rigorous and costly verification methods – for example, finite element analysis or tensile strength testing.



### **Final verification**

A more costly but more accurate verification method may be employed at this stage. It should be commensurate with the degree of proof required and the potential effects of a failure once the device is in service.

The key issue is to provide sufficient proof that the device will meet its acceptable quality limit (AQL). In this instance, the quality of verification is of paramount importance, rather than any cost-saving considerations.

### **Key verification activities**

Both the 'significant' regular verification activities and the final verification activities tend to incur the greatest costs in terms of time and effort. In this workbook these are considered to be the '*key*' **verification activities**.

In general, details of all key verification activities, particularly the methods used and the results obtained, must be formally documented.

## DESIGN SCENARIOS AND VERIFICATION ACTION

Once performance-related device requirements have been established and a concept design has been produced, it is possible to assess how well the device is likely to meet these requirements.

As design progresses, both device design and device evaluation occur in parallel, but the priority attached to each may vary. The following scenarios, which illustrate this concept, introduce the need for and the purpose of verification.

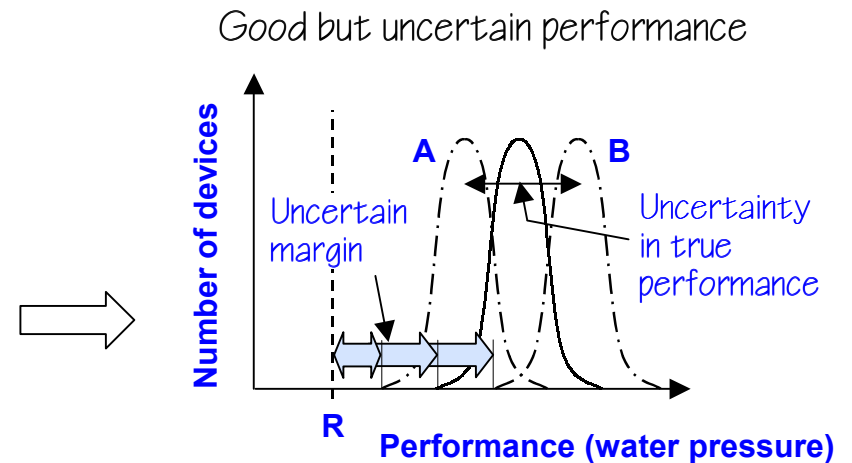
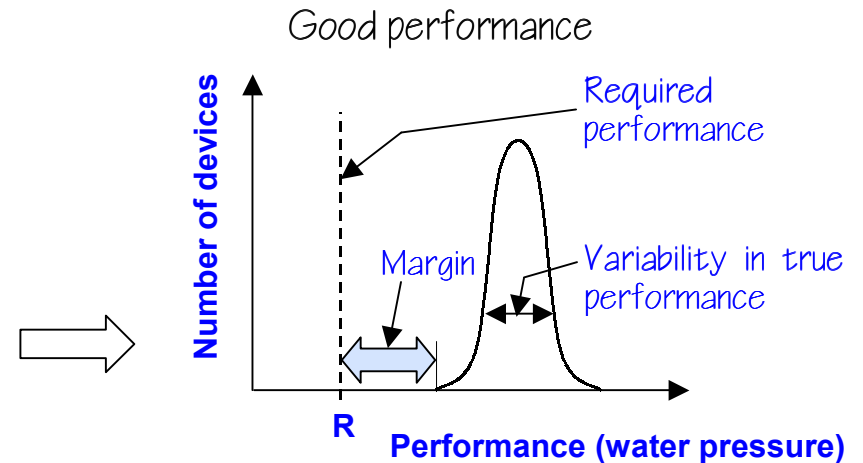
### Potentially good performance

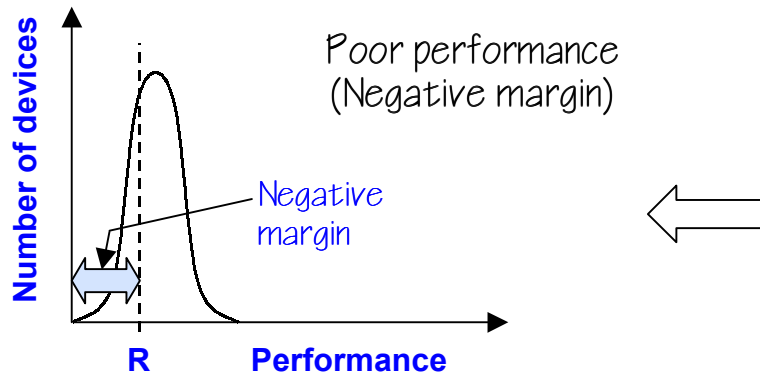
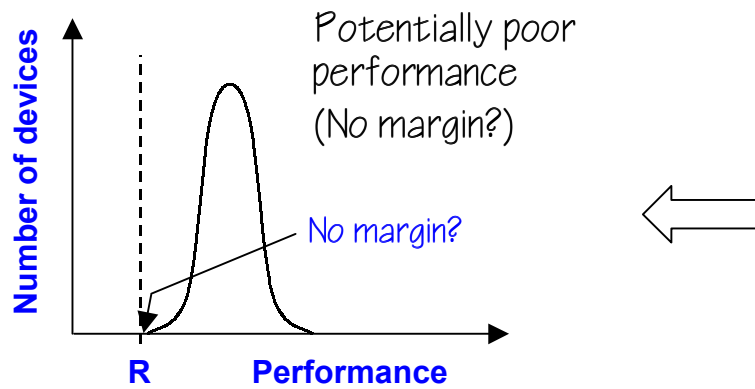
Take the case of a device that must resist water ingress. Several components may work in combination to meet this performance requirement – for example, an enclosure, a lid and an o-ring seal. Their collective performance will exhibit a certain degree of variability – as illustrated by the normal distribution curve in the adjacent figure. The fundamental properties of the design dictate the position of the curve and the expected variabilities in manufacturing dictate its shape. R is the required performance, which all devices must satisfy.

It can be seen that the concept device design appears to perform well. There is a considerable margin – or safety factor – between worst-case and target performance. Therefore, the device has a high chance of exceeding its performance requirement.

### Potentially good but uncertain performance

Early in the design process, it is generally not possible to know the exact behaviour of the device. So, there may be some degree of uncertainty in the location of the curve, as shown in the ‘worst-case’ (A) and ‘best-case’ (B) estimations of performance. Much of the ability to estimate true device performance will depend upon the designer’s experience of similar designs, but verification can help to clarify the situation. In this example, even if the





worst-case scenario (A) is true, the device will easily meet its requirement and, thus, there may be little point in carrying out further verification.

### Potentially poor performance

Conversely, a different design may have an estimated performance that is much closer to the required performance, as shown opposite. In these circumstances, there is a significantly greater chance that the design could fail, especially if there is some uncertainty in the performance estimate, which would tend to shift the curve to the left. In this case, verification would be undertaken to quantify the performance of the device more precisely.

Clearly, it is prudent to re-design the device to improve performance and increase the performance margin. The re-design target may be to reduce the spread of device performance – for example, by tightening dimensional tolerances or including labelling to restrict abuse, or to simply improve the average performance by adding a more effective seal.

In the worst scenario shown in the lower diagram, there is little chance that the device will perform as required. Unless the estimated performance is extremely inaccurate, there may be little point in verifying the device. Either it needs to be redesigned, or the requirement needs to be modified.

### Recommended action

Once a concept design is available, an initial estimate of device performance should be made. This will indicate whether the required performance is likely to be met, and whether verification or redesign (or both) is necessary. Uncertainty in the performance measured may be resolved through future verification.

## VERIFICATION – A RISK-BASED PROCESS

Determining future action by assessing how likely it is that a design will meet its requirements is only part of the story. The importance of meeting each requirement must also be considered.

*If maintaining a seal were a safety-critical requisite (perhaps to prevent microbiological contamination) the device manufacturer would feel more confident if the performance in this respect exceeded requirements by a considerable margin. Thus, the device should be designed so that the chance of seal failure is remote. Furthermore, although a device design may be suitable in theory, a greater safety factor may be required in practice, even if this is more costly to implement.*

### Good practice

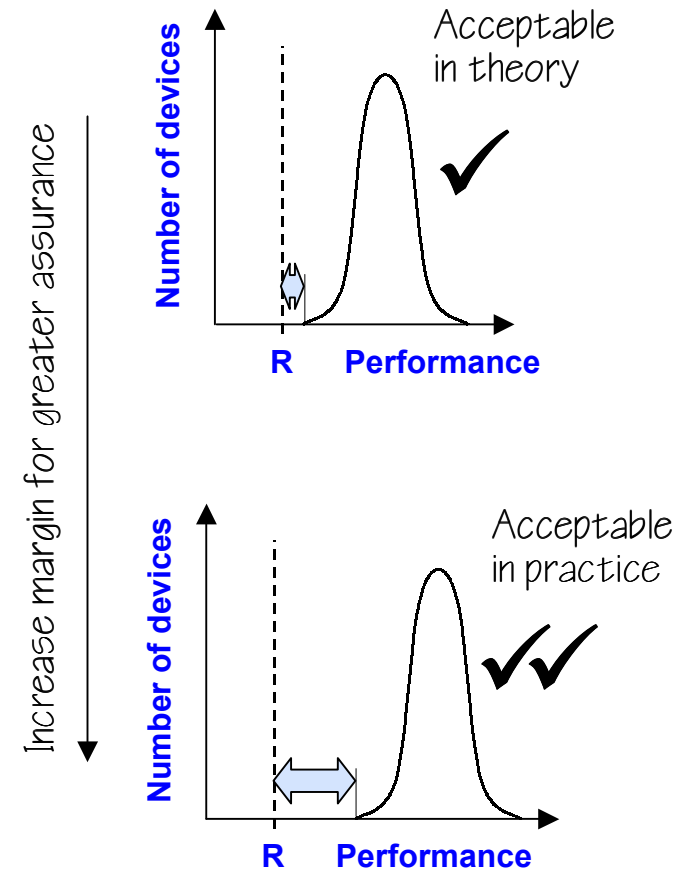
**Risk** is normally defined as a combination of the probability of an event occurring and the resulting impact. It is well established that design should be a risk-based process. However, verification is also influenced by the likelihood of a failure (and the associated uncertainty in this estimate) and the effects of that failure. Therefore, a good practice approach to verification should also be risk-based.

Underlining this, the FDA states that:

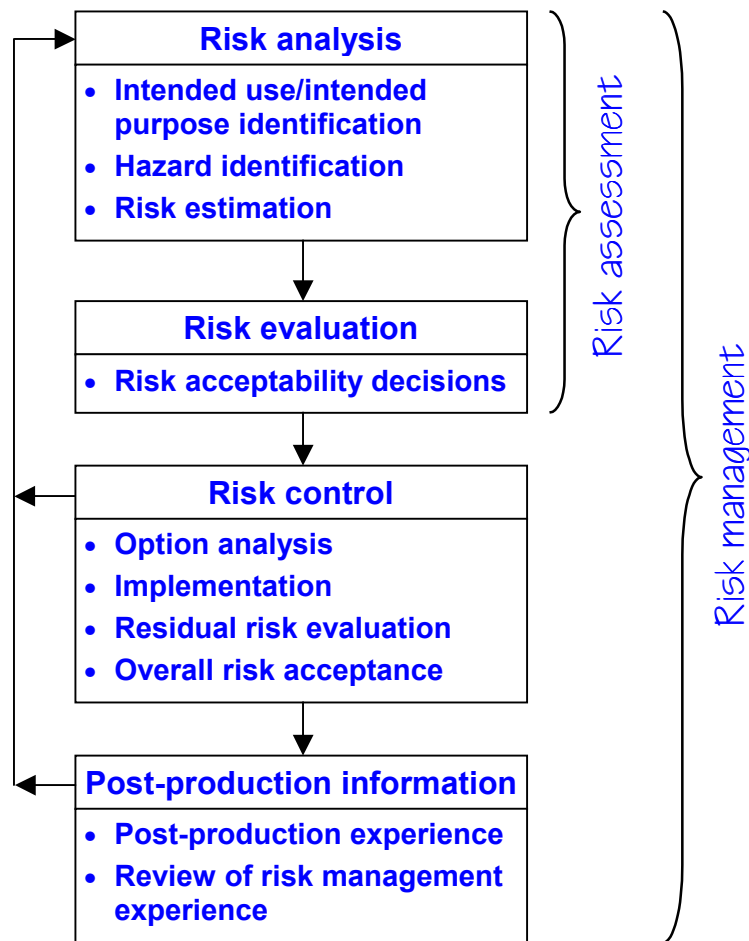
*“the extent of testing should be governed by the risk(s) the device will present if it fails.”*

(FDA (1996), 21 Code of Federal Regulations, Parts 808, 812, and 820, *Medical Devices...*, p52620).

Ultimately, it is essential to be confident and to show objectively that risks have been reduced to an acceptable level. This process is accomplished through a combination of device re-design, which can ameliorate the risks, and verification, which can reduce the uncertainty in these estimates.







The risk management process  
(from EN ISO 14971:2000)

## Risk analysis and risk management

**Risk analysis** involves the systematic identification of hazards (potential sources of harm) and their risks, how likely they are to cause a problem and how severe it would be if they did. It plays a key part in successful device development as it can be used to provide a sound basis for further action, such as the allocation of a greater proportion of project resources to areas of the project that are at potentially higher risk. The entire process of identifying hazards, analysing risks and controlling them is referred to as **risk management** and can be outlined as follows:

- 1) **hazard identification** – identify what can go wrong,
- 2) **risk estimation** – assess the combination of the likelihood of an outcome and the severity of each hazard,
- 3) **risk evaluation** – decide whether risks are acceptable,
- 4) **risk control** – reduce any unacceptable risks to acceptable levels, and
- 5) **risk monitoring**.

Risks influence the overall design, manufacture and use of the device. Thus, the principle of risk management must be considered throughout the device lifecycle and must be borne in mind from as early as investigating project feasibility, to device disposal.

Much guidance exists on the general process of risk management. Part 3 of BS 8444 focuses on the risk management of technological systems, such as medical devices, and EN ISO 14971:2000 focuses on the application of risk management to the design of medical devices specifically (both are referenced in *Developing verification methods, Step 1.4 in Part 3*). It is assumed that good risk management practice in accordance with such standards will be employed.

However, although it has already been suggested that risk analysis can be used as a basis for making verification-related decisions, the standards do not indicate how this can be achieved in practice.

## TYPES OF RISK

In order to achieve commercial success, it is vitally important to identify and mitigate risks in a timely manner throughout the product life cycle, that is, from concept design to device disposal.

From the diagram on the right, it can be seen that the principal sources of risk are *performance risks*, *management risks* and *external risks*. Each of these can lead to *development risks* or *support risks* and hence to *commercial risks* or each may lead to *commercial risks* directly.

### Performance risks

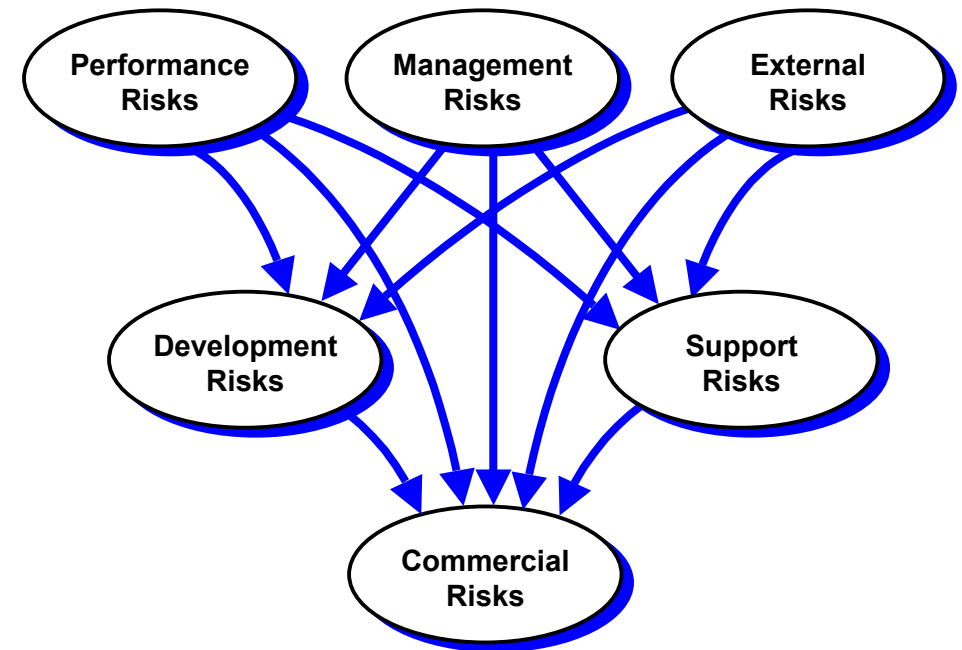
Performance risks – or *technical risks* – ultimately affect device users. They relate to the likelihood of a device failure and the effect that has on the user. Failures might range from mild inconvenience – perhaps through using a bewildering user interface – to more serious outcomes such as injury or death. Performance risks may be specifically safety-related and, in general, relate to any device malfunction. Designers try to identify potential performance risks early in the design process so that appropriate design and verification activities can be planned, but performance risks often lead to development risks, see below.

### Management risks

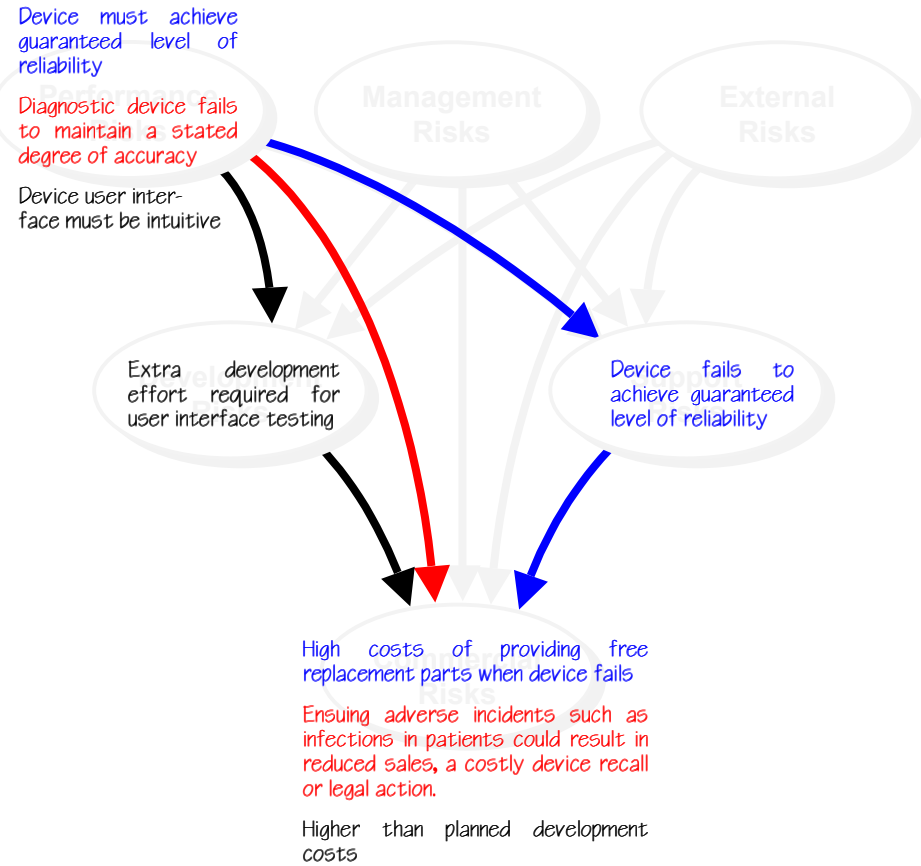
Typically, these are related to the availability and capability of resources and the setting of constraints such as time and budget.

### Development risks

Development risks – or *project risks* – usually affect the project time scale and budget. They combine the perceived likelihood of failing to meet a project-related requirement and the consequential impact this has on project progress.



Types of risk and risk propagation



Examples of risks and risk propagation

### Support risks

Once the device has been marketed, **support risks** are present if the level of product support provided is inadequate and fails to meet customer expectations.

### External risks

Project viability may also be threatened by external factors, such as the impact of competitor activity, the emergence of a new technology or unexpected changes in the trading environment – for example, exchange rate fluctuations. These may occur at any time during the product life cycle.

### Commercial risks

It can be seen that the various types of risk usually have a knock-on effect and create commercial risks for the device manufacturer, the impact of which may be wide ranging.

There are interesting compromises. Designing an easily used device may increase the device development costs and time, as additional effort may be required to design and evaluate the device. However, such a device may incur fewer costs once it has been put into service, by reducing training and other forms of support. Customer satisfaction may also bring further benefits, such as increased sales.

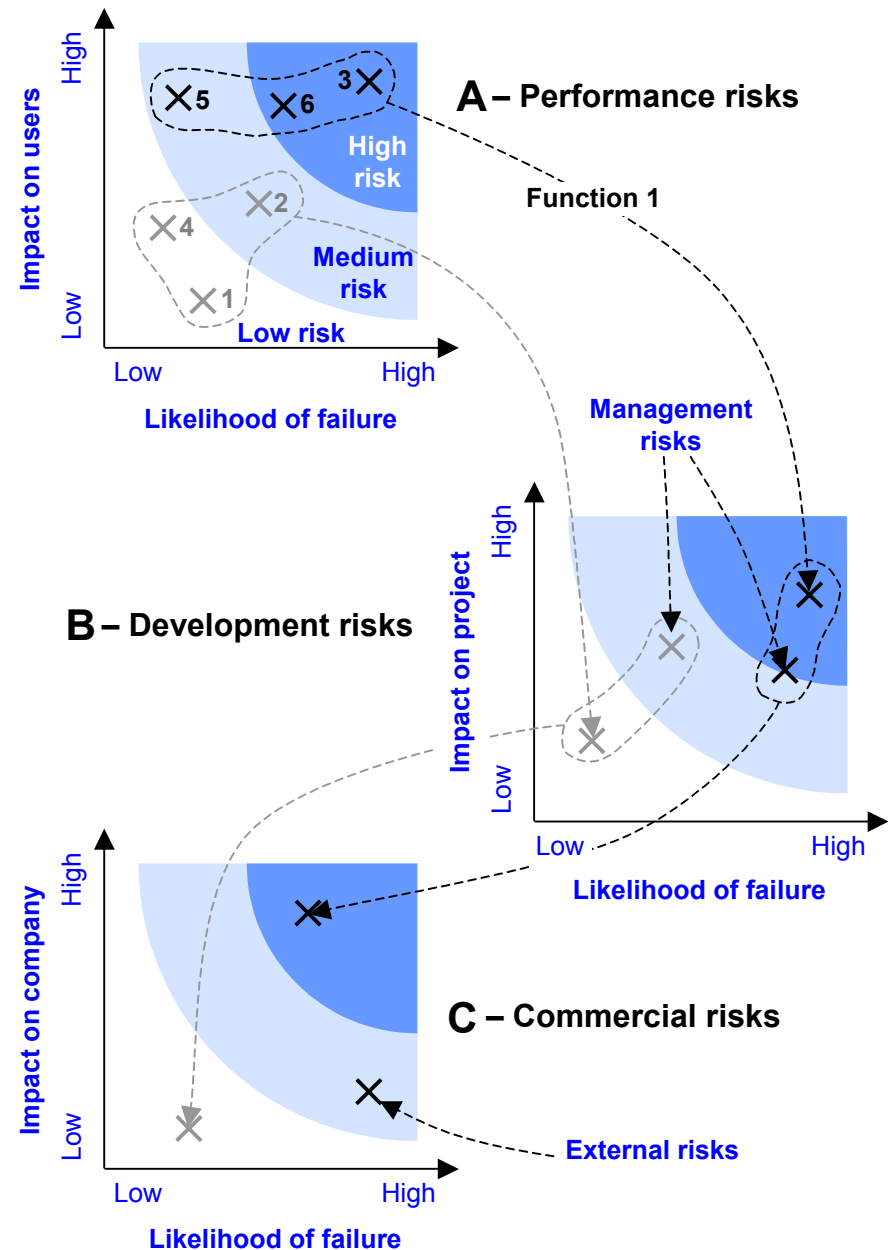
## Plotting the risks

Project-related decisions and risk comparisons may be easier to make if the risks are visualised graphically.

Start off by plotting the performance risks – the likelihood of a failure to meet a requirement versus the estimated impact of such a failure, as shown in plot A. Each cross relates to one requirement and is labelled with a number to aid identification. It can be seen that there is a high risk of failure in meeting requirements 3 and 6 individually.

Similar plots may be used to visualise the other types of risk – the development and commercial risks are shown in plots B and C respectively. In these cases each cross represents the likelihood and impact of any event that potentially affects the product lifecycle, the project or the company. It can be seen that development risks may also be influenced by management risks, and commercial risks by external risks.

The dashed arrows show that risks may propagate from one graph to the other. The risk of a failure to meet one or more requirements may lead to a development risk, which in turn leads to a commercial risk.



### **An example illustrated by the plots opposite**

*In the design of a surgical lamp, performance requirements 3, 5 and 6 all influence a single function (F1), the object of which is to ensure that the intensity of light is sufficient over a designated distance and area. These performance requirements relate to the power of the light source, the ability of any shielding to reflect light and the ability of a lens to focus the light onto a designated area.*

*In terms of development risks, the design effort required to achieve this function may result in time overruns and significantly delay the project.*

Project delays may be compounded by management risks because the need for certain design skills has not been recognised or adequate resources have not been provided.

A commercial risk may then arise in terms of late delivery to market. External risks can also influence the company, such as the introduction of a competitor's device.

It can be seen that many of these risks interact with each other – the occurrence of one event often influences others.

## USING RISK TO INFLUENCE VERIFICATION PRACTICE

A risk-based approach can be used to fine-tune verification-related action and gain the benefits of good verification practice. However, although it has been established that the extent of verification is linked to the risk involved, this does not explain how risk influences the verification approach in practical terms. The following sections present a more detailed outline of how risks may influence verification practice.

### Early or late verification?

The design of some parts of the device, such as those which pose a particular design challenge due to their novelty, may incur higher development and commercial risks than others. During the design process, the design and verification of these selected parts may need to be prioritised in order to investigate and, if necessary, reduce risks.

For example, early in the design process if there is a considerable degree of uncertainty in the performance of part of the device, verification may be required immediately. Alternatively, if risks are high and appear to be difficult to reduce, it may be best to redesign the part, change the requirements or stop the project altogether.

In practice, selecting the most appropriate time to verify may not be straightforward, since a balance should be struck between ‘early’ and ‘late’ verification – the pros and cons are summarised on the right.

As design rework is frequently the greatest source of project cost and schedule crises, there is a strong argument for verification to be carried out early in the design process.

### Early verification:



- Helps learn about the properties of the device and helps influence future action.
- May help identify design problems early in the design process and therefore reduce rework.



- Results may be misleading due to verifying a model that is a poor representation of the final design.
- Verification may have to be repeated, incurring extra costs, as the design is likely to change.

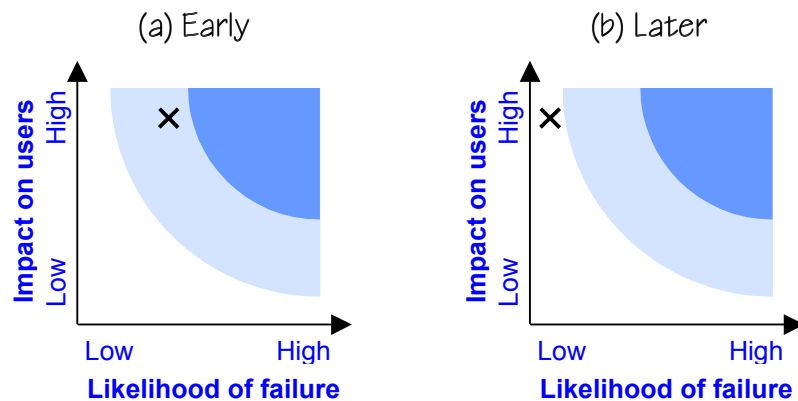
However, each verification method will incur costs, which can mount up rapidly if verification has to be repeated. This is particularly true early in the design process when much iteration may occur between requirements, device design and verification. Furthermore, if verification is performed early in the design process, when the device model may be considerably different from the final device, the results may be misleading.

Final verification activities can also incur significant costs, so there is a counter-argument that verification should be conducted late in the design process.

### Circumstances often drive verification timing

Consider a company producing a device that needs to maintain a microbial seal. If the designers are unfamiliar with the designing of such seals, there is a significant chance that the original design concept will perform poorly.

The following verification scenarios, illustrated opposite, are likely:



Changes in risk and uncertainty - early and later in the design process

- a) **Early in the design process.** Once one or more concepts have been designed there may be a considerable lack of certainty in their ability to meet the requirement. Thus, despite the costs, verification may be prioritised to determine which concept is the most suitable and whether further design modifications may be required. Ultimately, a failure of the seal could result in the death of a patient, and hence the impact is potentially very high.
- b) **Later in the design process, just before a product prototype demonstration.** At this point in the design process there may now be a much higher degree of confidence that the requirement will be achieved. However, it may be crucial that the demonstration is successful, so further verification may be scheduled before the demonstration.

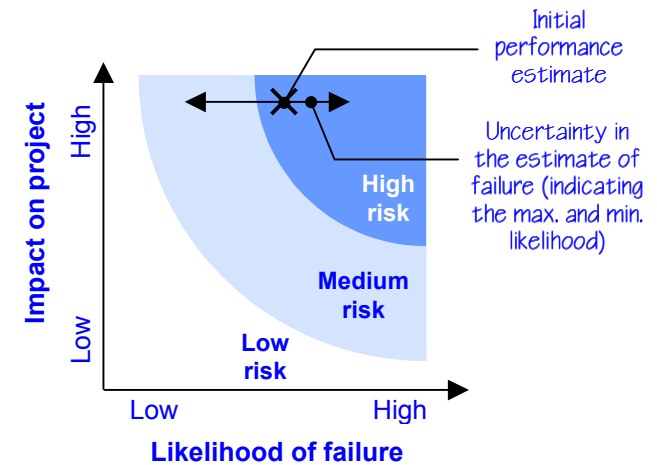
## Determining the optimum timing

Determining the optimum timing for verification involves the consideration of a number of factors and making trade-offs between them.

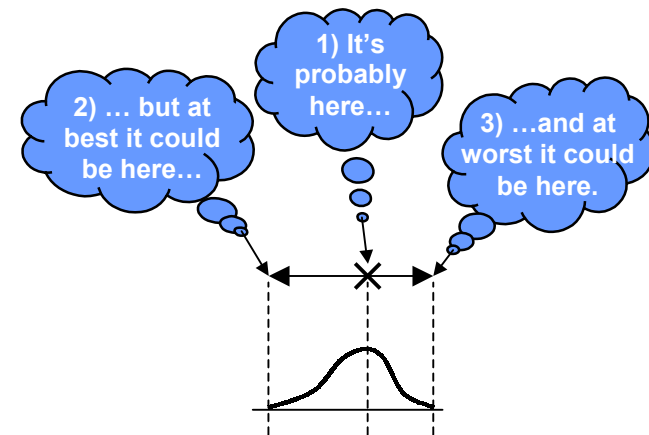
To start with, the performance risks may be assessed for each requirement, but these should then be related to their potential impact on project timescale and budget and plotted as shown opposite. Decisions about the timing of verification may then be made.

The precise location of each cross may be difficult or even impossible to determine, as it depends on what knowledge and experience exists of the specific situation. Although the impact of a failure may be relatively easy to determine, the likelihood of failure is usually more difficult to estimate. For each likelihood estimate, the *uncertainty* may be represented by means of a horizontal double-headed arrow. The left tip of the arrow represents the best performance estimate; the right tip the worst. The combination of the cross and arrows characterises a distribution of the probability of a failure to perform, as indicated in the lower diagram, so the extremities may or may not be equidistant from the initial estimate of performance.

The plot, when completed, is a snapshot of the risks to the project. It can also be the basis for deciding whether the risks are tolerable for the time being, or whether they need to be prioritised for reduction through redesign, or clarification through verification.

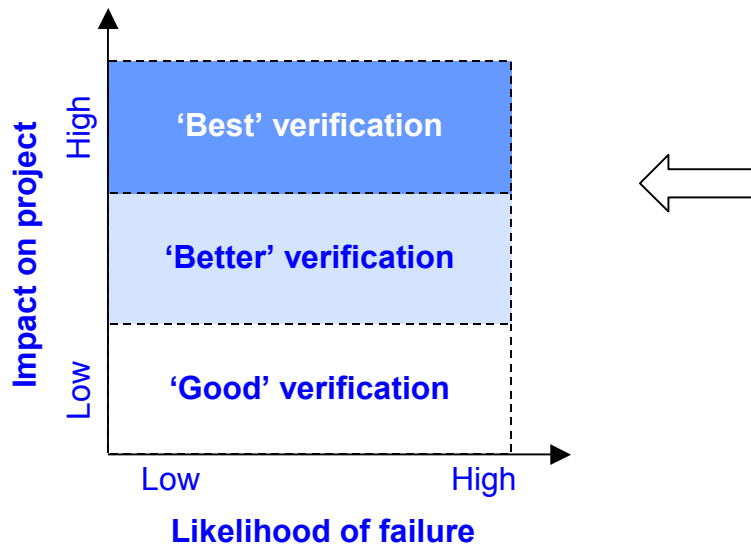


Risks to the project timescale and budget (development risks) dictate the priority of verification activities.



The performance estimate and uncertainty in this create a probability distribution.





Development risks will dictate the quality of the verification approach.

### The quality of verification

The degree of assurance necessary to demonstrate that requirements have been met is also influenced by both development and commercial risks. The accuracy of the results that the method produces – and hence the choice of method – should be commensurate with these, as shown opposite.

A high degree of assurance may be required when verifying requirements relating to device safety. In comparison, an inexpensive verification method may be chosen where a lesser degree of accuracy can be tolerated – for example, when performing a spontaneous verification activity in the form of a ‘quick check’.

### Choice of verification method

When choosing a suitable verification method, it is important to consider what impact a false, and hence misleading, result might have on the project. A development risk and/or a support risk could well be incurred, as illustrated below.

#### *Development risks*

As design progresses, the quality required of regular verification activities will be influenced by the potential impact a false result might have on the project.

*For example, some time into the design process, the ability of a prototype device to maintain a microbial seal may be investigated through using a cheap and easy-to-use dye penetrant test. This may not provide the definitive result, but its practical benefits are likely to outweigh the costs of using a more sophisticated laboratory-based method using live bacteria.*

#### *Support risks*

The post-development impact of a device that does not meet its requirements must also be considered during the design process.

Final verification is normally the last practical opportunity to determine how the device will perform on the market, on a model that is close to the final form of the design. The ultimate proof of having met requirements is required and there should be no compromise on the quality of the verification method for reasons of economy at this stage.

*Referring once more to the previous example, at final verification the ability of the device to maintain a microbial seal may be evaluated by placing the device into a 'soup' of live bacteria and detecting whether the bacteria penetrate the seal. This would be done after exposure by attempting to grow a culture from a sample taken from the inside of the device.*

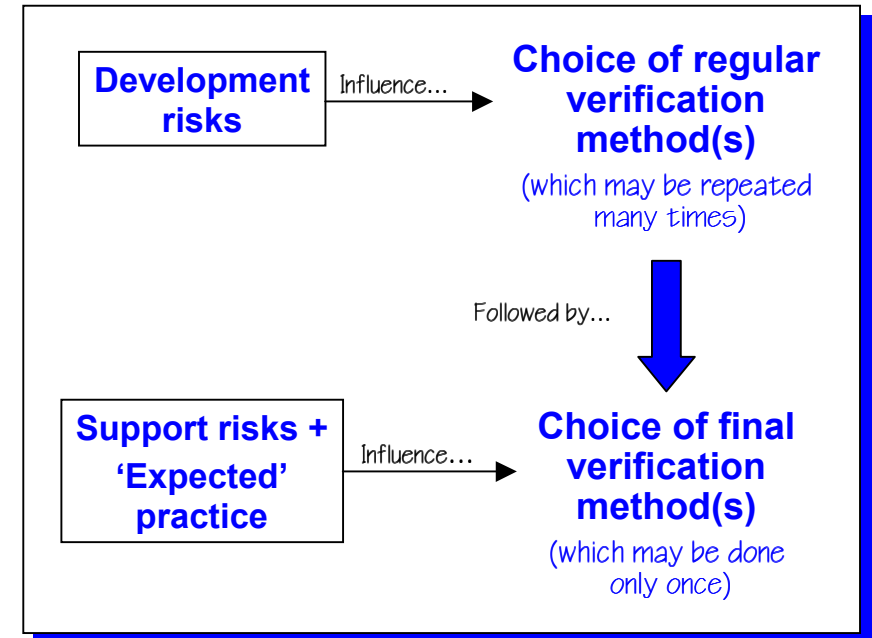
### Other factors

Other factors influence the choice and hence quality of the verification methods; particularly at the final verification stage. These include:

- what is known specifically about the device in question,
- what is generally accepted about other similar devices that have been marketed previously, and
- the degree of novelty and complexity of the device.

In general:

1. For well-understood and lower risk devices, such as syringes, tongue depressors and stethoscopes, the degree of proof required is less than that for devices involving new technologies, novel applications of existing technologies or for safety-critical devices.
2. When questions are raised about the safety and effectiveness of the device, particularly if it exhibits a degree of novelty, the required degree of proof to demonstrate fitness-for-purpose will be correspondingly higher. This will be reflected in the type and rigour of the verification that takes place.



Development risks dictate the quality of the verification approach.



Verification may be relatively straightforward for well-understood and/or lower risk devices.



Verification may be more complex and resource intensive for novel and and/or higher risk devices.

It is also important to note that, for similar reasons, the wisest choice of verification method may also be one that represents generally-accepted practice. This will be discussed later in the workbook.

*For example, a highly novel device for use with patients who are critically ill, and which maintains a life-supporting function, will raise many questions about its safety and effectiveness. Consequently, a considerable amount of supporting data, which has been produced from accurate (and probably costly) verification methods, will be required.*

### **Commercial risks**

Finally, it cannot be overstated that commercial risks must also be considered when determining the timing of the verification and the choice of method. For various reasons, performance and development risks frequently propagate into a commercial risk, which may be considerably different from the other forms of risk, yet may play a crucial role in determining the verification approach.

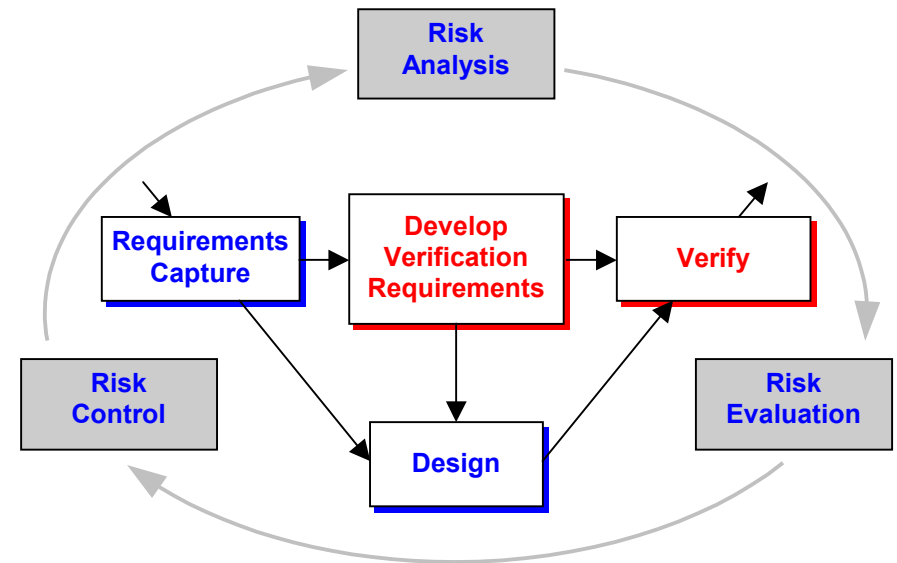
## MODEL OF RISK-BASED DESIGN AND VERIFICATION

In *Part 1*, it has been shown that different types of risk and estimating uncertainties have a key part to play in dictating verification practice in terms of its timing and accuracy.

All risks should be considered if an efficient and effective verification approach is to be followed. At any point in the design process the risks may differ significantly and, taken singly or in combination, they may propagate from one type to another. The risks may also change as design progresses.

The adjacent model<sup>2</sup> shows how risk management integrates with and influences the design process, including verification practice in terms of the development of the requirements for the verification (the plans and protocols) and its execution.

The development of the verification requirements and the verification method itself follows in *Part 2*.



<sup>2</sup> Source: *Good Design Practice for Medical Devices and Equipment – A Framework*

## **PART 2 – IMPLEMENTATION OF GOOD VERIFICATION PRACTICE**

*“See, I will refine and test them, for what else can I do?”*

Jeremiah, 626 – 593BC

## SETTING OUT THE VERIFICATION APPROACH

It is not uncommon for a manufacturer to have an appropriate and effective verification strategy. This is particularly true when experts are involved – those who have the necessary experience to judge the ability of the device design to meet its requirements and the effectiveness of the verification approach.

However, the following problems may still arise:

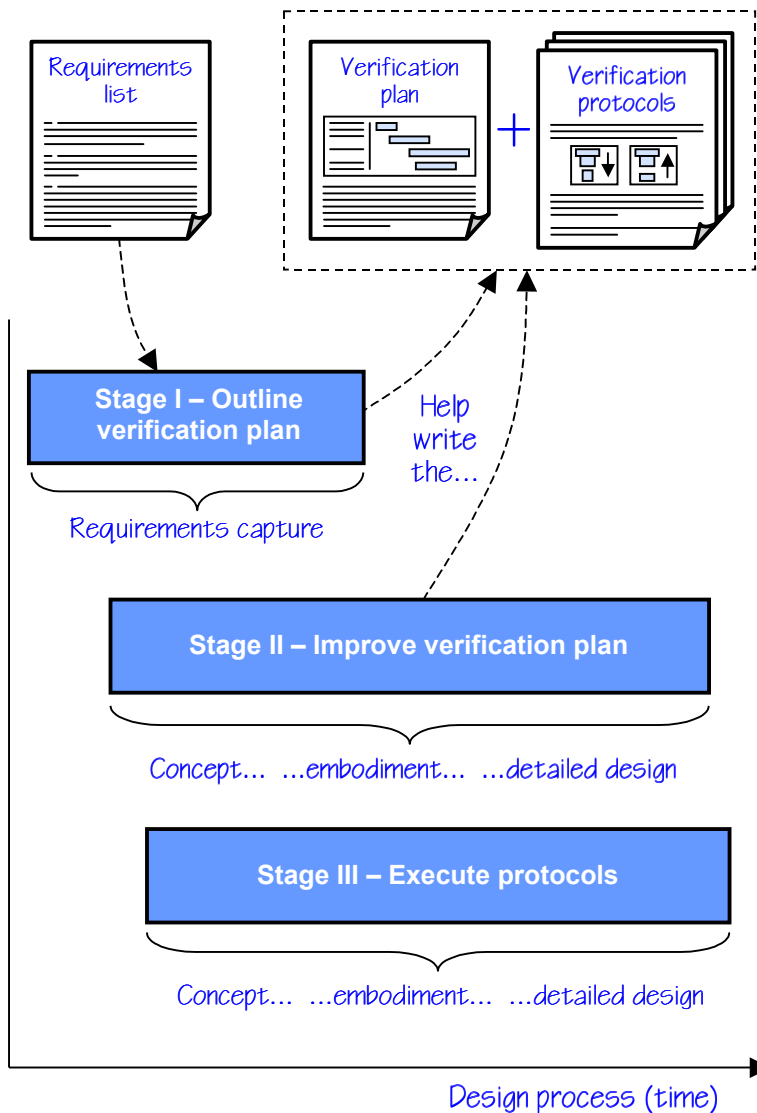
- **verification actions** do not fully account for factors such as development risks, commercial risks and impending changes to the design, requirements or verification method,
- **planning and execution** of key verification activities may be overlooked or disregarded until just before the event,
- **the rationale behind the verification approach is poorly documented** – this may be necessary to prove the fitness for purpose of the device and the design process integrity for regulatory and commercial reasons.

Verification action could therefore be inefficient and/or ineffective, increase costs, introduce delays and even reduce the fitness-for-purpose of the device. Furthermore, no experts may be available, particularly if the device is novel.

A method will now be proposed that helps to overcome these problems by providing a ‘route map’ through the verification process, thereby encouraging good practice and helping ensure that the timing and quality of the verification are appropriate from a regulatory and commercial point of view.

The method may be adapted to meet individual company or project needs.





When to use the method

The method consists of three stages, divided into 10 steps, as follows:

- *Stage I – Outline verification plan (Steps 1-3)*. Assess when verification should occur, and outline what methods should be followed.
- *Stage II – Improve verification plan (Steps 4-8)*. Determine the details of each verification method and fine-tune the timing of regular verification activities.
- *Stage III – Execute protocols (Steps 9 and 10)*. Check the protocols before they are executed and record the verification results.

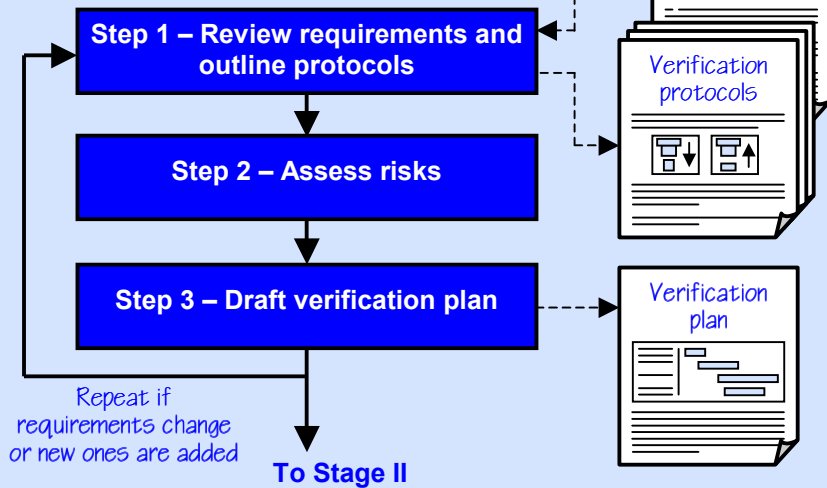
### USING THE METHOD

Rather than being used only once, it is likely that all three stages will need to be repeated regularly during the design process:

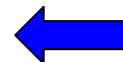
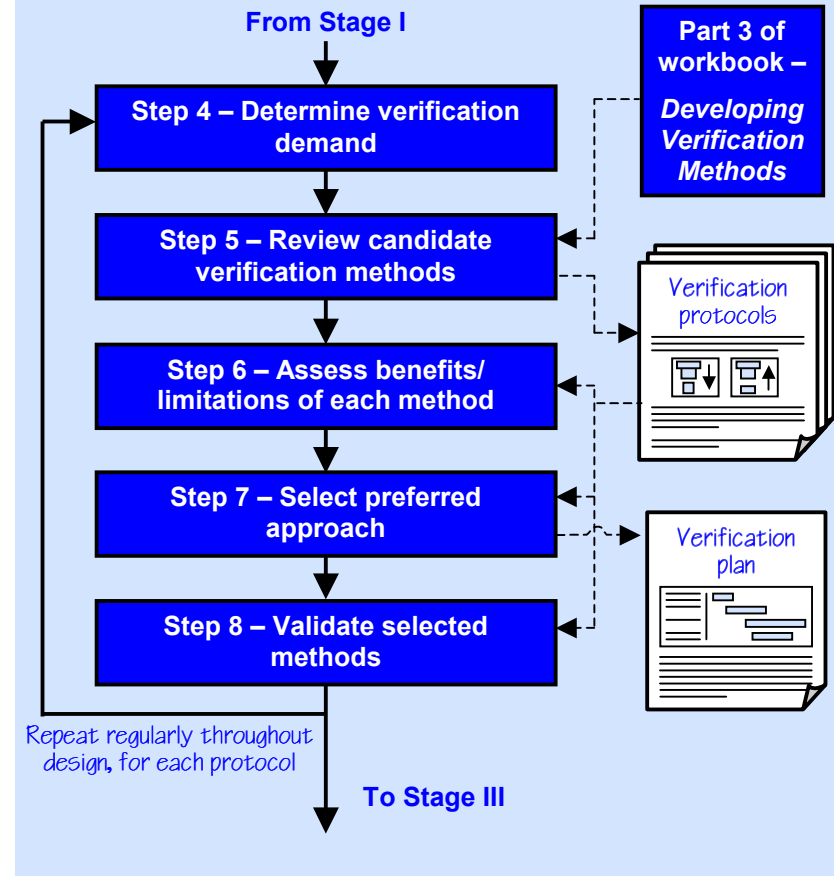
- From the adjacent diagram it can be seen that *Stage I* may be used throughout the requirements capture phase and begins quite early in the design process. It will be repeated well into the device design phase, whenever new requirements are introduced or old ones changed.
- *Stage II* begins once a degree of concept design has been carried out. Use of this stage is likely to continue throughout the remainder of the design process.
- *Stage III* may run in tandem with *Stage II*, but will mostly be used towards the end of the design process.

An outline of the three stages is presented overleaf.

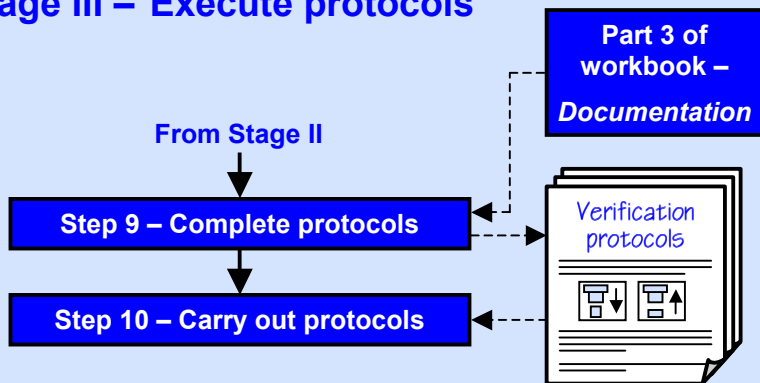
### Stage I – Outline verification plan



### Stage II – Refine verification plan

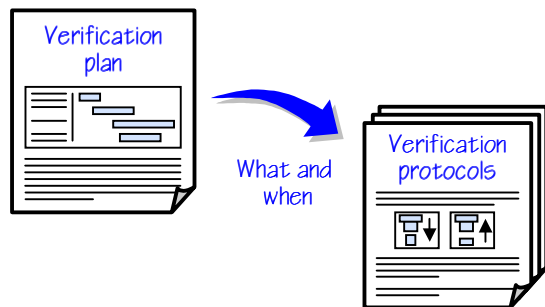
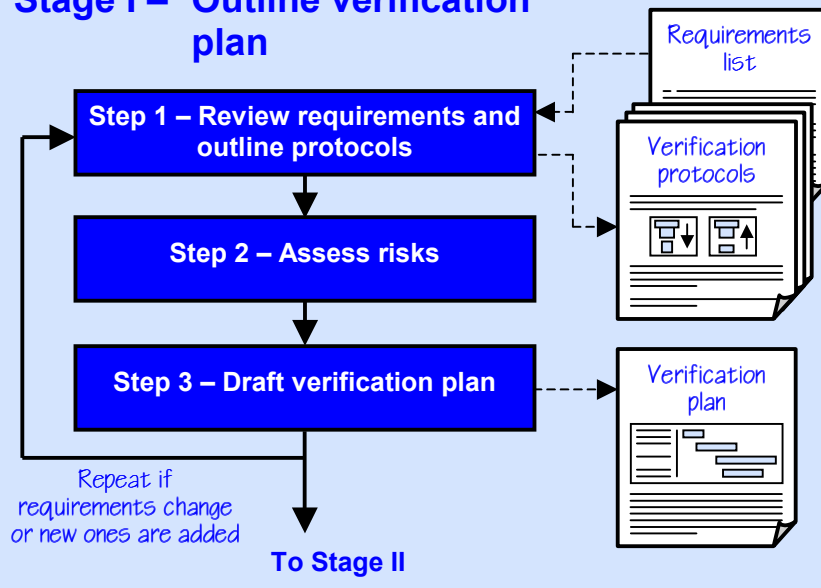


### Stage III – Execute protocols





## Stage I – Outline verification plan



The verification plan defines which protocol to use and when to execute it during design and development.

## STAGE I – OUTLINE VERIFICATION PLAN

*Stage I* focuses specifically upon an analysis of the requirements to assess when verification activity is required during the design process. It is divided into three steps:

- *Step 1.* Review each requirement and draft verification protocols by identifying candidate verification methods and the resources needed.
- *Step 2.* Assess the product development risks to determine the priority of the various design and verification efforts.
- *Step 3.* Draft the plan, by considering the information identified in *Steps 1* and *2*.

### Background to Stage I

The details of each key verification method are laid out in a document called a *verification protocol* (which may also be referred to as a *test protocol* or *test description*).

For a project there may be many of these documents, each containing the details of one or more methods. Each protocol also records:

- any required procedures and equipment for executing the method,
- the data to be collected, the product characteristics, and
- any specific requirements for the verification.

The *verification plan* describes when each protocol should be executed during the design process. It relates closely to the project plan, and may form part of it, depending on the manufacturer's documentation practices. Verification plans are similar to project plans, as they will generally only record the key activities.

## Determining the verification protocol

For many requirements the verification protocol can be determined in outline during requirements capture, early in the design process – even though the details often only come to light later when the design firms up. To do this, each requirement for the device should be reviewed, as described in the next section, and a record made of any candidate verification methods. If this approach is to be effective, a reasonably correct and comprehensive set of device design requirements is needed<sup>3</sup>.

Conducting such a review early in the design process is useful for many reasons. For example, investigating how the design might be verified can help ensure that requirements are stated in verifiable terms. Often this means that they will need to be quantified. A review may also help identify requirements that are difficult to meet through design, and those that are difficult to prove through verification. Such requirements may need their associated design and verification tasks to be prioritised, which may therefore help project planning.

## Resources

Verification activities may incur a significant drain on project resources and significantly impact project budget and timescales.

Where possible, the resources required for verification should be identified up-front to avoid disasters such as that quoted opposite. Knowing how a device may be verified may help design the device so that the proof gathering process is facilitated. Just as this is referred to as *design for testability* in the field of electronics design, more generally it may be referred to as *design for verifiability*.

Details now follow for each step of *Stage I*.

---

<sup>3</sup> For further information on determining requirements, workbook *Good Design Practice for Medical Devices and Equipment – Requirements Capture* may be of assistance.

“What we didn’t do was to allocate a chunk of resource at the end of the prototype phase, to really analyse what we had.”

(Medical device designer)

Design continued regardless, despite a recognised need to build a representative prototype. The final device didn’t work and the redesign took 1 year to complete.

| Requirement   | Method                         | Significant resources                                 |
|---|--------------------------------|---|
| R1 Maximum overall length not to exceed 80.0 mm                                   | Use vernier callipers          |   |
| R2 Corrosion resistance of external parts according to Appendix E of BS 6196:1989 | See Appendix E of BS 6196:1989 | 20g citric acid monohydrate, 2 litres distilled water |
| R3 Dose not to exceed $\pm 10\%$ of label claim                                   | TBD.                           | TBD.  |

Table listing parts of the verification protocol

### The verification protocol:

- verification requirement
- acceptability criteria
- scope of the verification
- characteristics of the model
- verification method and resources required
- references to standard methods

## 1 REVIEW REQUIREMENTS AND OUTLINE PROTOCOLS

A good starting point is to review each requirement and make a note of every candidate verification protocol, including the verification method(s) and any significant resources required. This information may be listed in tabular form, as illustrated opposite.

During this process, several situations could arise:

- For many requirements, a suitable verification method may be obvious and the review may be performed rapidly. For example, proof of meeting a dimensional limit may be demonstrated readily by using standard equipment, such as vernier callipers.
- In other cases, requirements may be verified by standard verification methods, which may also indicate the resources necessary.
- For some requirements, identifying suitable verification methods may be more challenging. This often happens during the early stages of the design of novel devices when little may be known about the final form of the device.

Thus, after this initial review, many of the verification methods (and the details of some of the verification methods that have already been identified) may need to be determined in *Stage II*, which occurs throughout the design process.

Once a candidate verification method has been identified, the corresponding protocol should be drafted, by documenting as many of the components of the protocol, listed opposite, as possible. The details of each component of the protocol are discussed in *Documentation* in *Part 3*.

*It is evident from the above how important it is to formulate requirements that are verifiable during requirements capture.*

## 2 ASSESS RISKS

Once any protocols have been produced in outline, however approximate this may be, the demand for verification should be assessed in terms of its degree of urgency and what it is required to reveal.

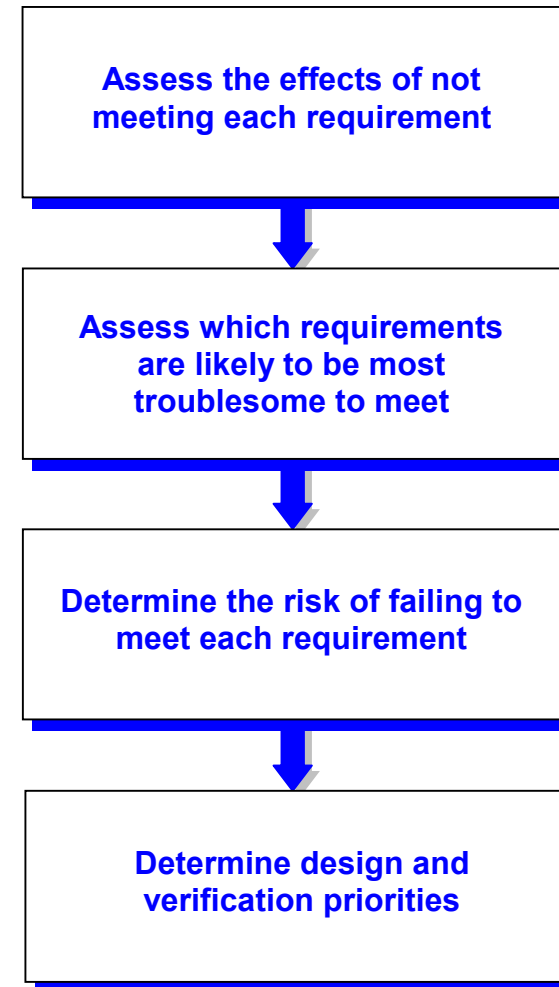
At the requirements capture stage this may be achieved in part by re-reviewing the requirements and considering the risks involved in meeting *each requirement*.

There are four sub-steps:

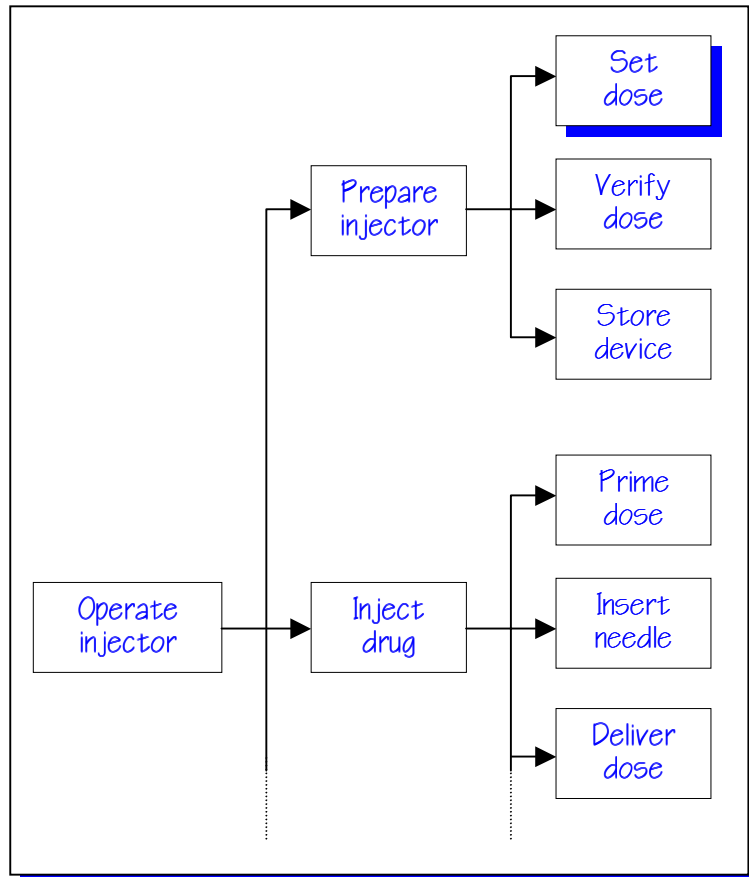
- 2.1 **Assess the effects of not meeting each requirement**
- 2.2 **Assess which requirements are likely to be most troublesome to meet**
- 2.3 **Determine the risk of failing to meet each requirement**
- 2.4 **Determine design and verification priorities**

The sub-steps are described on the following pages.

As development proceeds, it is usually necessary to re-visit the requirements for which the protocols are incomplete and re-assess the overall verification priorities.



Assessing product development risks



FAST diagram for a pen injector - 'Set dose' is highlighted as an example of a critical function

(Source: Requirements Capture workbook)

## 2.1 Assess the effects of not meeting each requirement

During design, the need for verification is largely driven by the effects that a failure to meet each requirement is likely to have on the project. Such effects may be felt anywhere in the device lifecycle – for example, whilst the more obvious post-market consequences might be serious, device development efficiency might be compromised as well. So, the importance – or *criticality* – of each requirement must be assessed.

The FAST (Functional Analysis System Technique) diagram approach, outlined in the *Requirements Capture* workbook, is a good starting point for doing this – an example is shown opposite. It enables the criticality of many requirements to be assessed in terms of their post-market impact.

Whether or not a FAST diagram is used, all requirements should be reviewed and the effects of not meeting them assessed systematically. The effects must be assessed both in terms of their impact during the device lifecycle and their commercial impact by considering how risks propagate, as discussed in *Part 1* of this workbook.

*Consider a company performing subcontract design work. The contract might state that further project funding is conditional upon the successful demonstration of a working prototype by a certain date. Failing to achieve this could be catastrophic for the project, and the commercial impact of project failure could in turn cripple the company.*

*Similarly, failing to identify a fundamental design flaw in a device may necessitate a significant degree of rework once the problem is eventually identified. If the rework occurs late in the design process, the redesign will be expensive and it will be necessary to repeat the verification protocols, incurring additional costs and delay. As in the previous example, the commercial impacts could be very serious.*

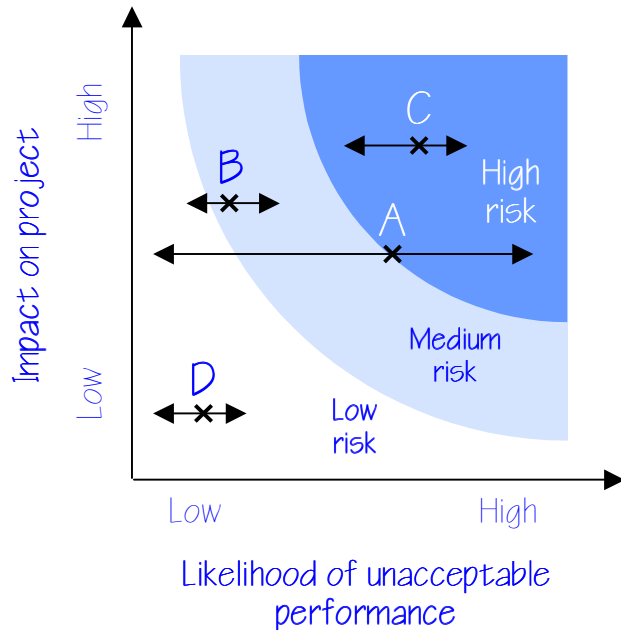
## **2.2 Assess which requirements are likely to be most troublesome to meet**

Once the impact of failing to meet each requirement has been assessed, the likelihood of failure and the uncertainty in this estimate should be considered.

Usually, only very sketchy conceptual designs are available early in the design process, sometimes just a gut feeling that a certain requirement may be difficult to meet. Thus, for some requirements, it may only be possible to guess the likelihood of failure and uncertainty.

The availability of specialist skills, experience and resources also influences the estimates.

*Take the example of a company with considerable expertise in control panel design. They are likely to regard a requirement for an intuitive user interface for a relatively simple infusion pump as easy to meet. A brief review of the concept design would probably reveal there was a high chance of success in meeting the requirement and uncertainty in this estimate would be low.*



Development risks associated with requirements A to D

### 2.3 Determine the risk of failing to meet each requirement

For each requirement, the potential impact of failure and the estimated likelihood of failure can now be combined to assess the risks involved. Development and commercial risks should all be considered. Even though they are different in nature, they may have an equal part to play in dictating any resulting redesign or verification priorities.

Each risk may be recorded in a graphical form to facilitate clarity, although any format, including simple text records, which allows a clear comparison to be made is quite acceptable. It is also helpful to record the rationale behind the rigour of the design and the verification of the device, as this may facilitate liability and regulatory approvals.

The adjacent diagram represents development risks early in a product design. It can be seen that the elements of the design relating to requirements A and C impose the highest risks. The uncertainty in each estimate has also been plotted to indicate the *potential* development risks for each requirement. This is important for making decisions about verification-related and design-related action, which depend not only upon the initial estimate of performance, but on what it *could be*.

Development and commercial risks may vary significantly during the course of design, so all risks should be reassessed and the records updated regularly as the design progresses. Sometimes the effect of two or more low/ medium risks may need to be considered together. For example, when two or more development risks of a low/medium value are combined, the resultant commercial risk is so high that verification action is based on this rather than the individual performance risks for each requirement.

## 2.4 Determine design and verification priorities

Once the risks have been assessed, design and verification activities may be prioritised for each requirement as follows:

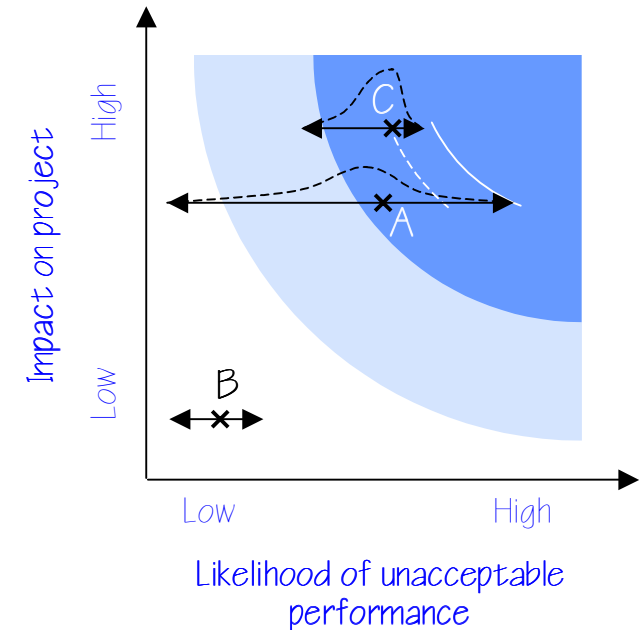
- 1) Start by investigating the performance risks. The elements of the design that relate to the highest risk requirements may need to be prioritised. Prioritisation would be straightforward if it wasn't for the uncertainty in each estimate, which may be considerable at this stage in the design process. This complicates the decision-making process.

In the case illustrated, the white dashed contour line indicates that the initial estimate of the risk in meeting C is higher than that of A. The design of the parts that meet requirement C might therefore be prioritised over that for A if it wasn't for some concern that the performance of A *could* be worse than that of C, as shown by the white solid line. In such ambiguous cases it may be helpful to plot imaginary probability distributions before making the final prioritisation decision. In the example shown, because the distribution for C is skewed, the design for C may be prioritised over that for A.

- 2) The propagation and combination of the performance risks to the other types of risk should be considered next, in a similar fashion. These assessments may change the priority of the original decisions.

The project plan should be updated with the prioritisation decisions and design effort estimates. The timing of verification actions at key stages and at the end of each design phase may then be contemplated.

The design schedule can also be influenced strongly by a variety of issues such as resource availability and the dependence of some parts of the device design upon the design and verification of others.





### 3 DRAFT VERIFICATION PLAN

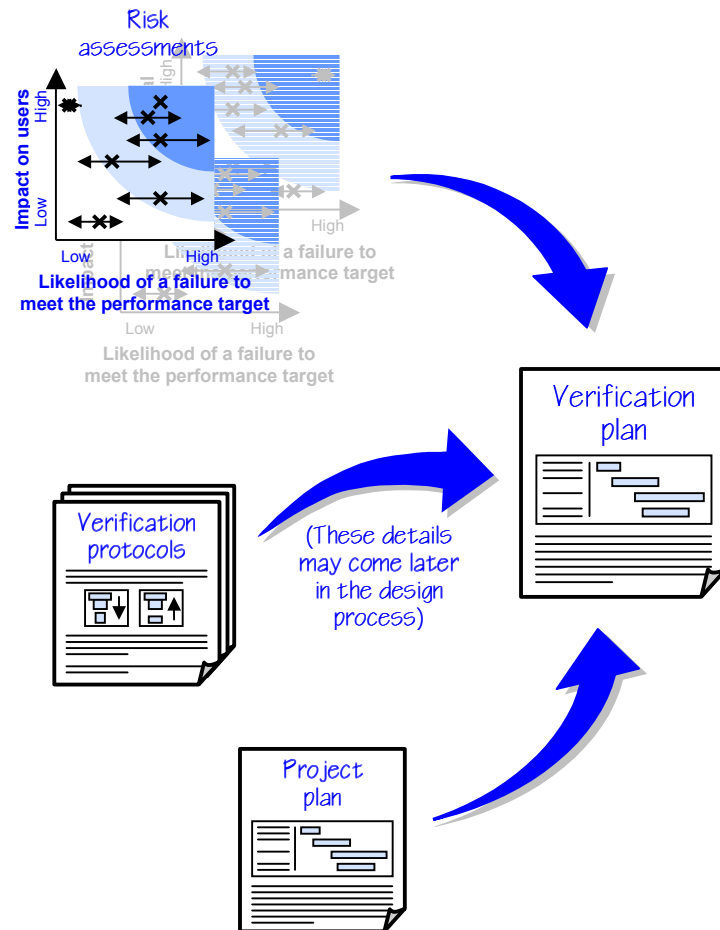
Once design priorities have been identified, an outline of the verification plan may be drafted by considering which protocols should be executed, and when in the design process. Although verification may begin once sufficient design information exists to make a model, the timing of the verification efforts also depends on:

- Key dates in the project plan, such as that targeted to demonstrate a prototype to management, or perhaps a client or sponsor.
- Details within the verification protocols, which will help identify how long some verification activities are likely to take. This may be an issue in the case of life tests, for example, which may be very lengthy. Furthermore, the details of such methods may only come to light later in the design process.

The factors above are only likely to influence the key verification efforts, such as final verification, as the spontaneous regular activities are too ad-hoc and unlikely to be sufficiently resource-intensive to warrant formal planning. These factors may also override any previous decisions regarding the timing of the verification, and the plan should be updated accordingly.

The precise details of the protocols and their timing in the design process will be influenced by other factors, such as the form of the device design. This is particularly true for regular verification. *Stage II* shows how the verification approach can be improved as design progresses, and more is learned about the properties of the device. As opposed to *Stage I*, which focuses on requirements, *Stage II* should commence as soon as an outline has been made of the device design. However, *Stage I* will need to be repeated if new requirements are introduced or old ones are changed.

Although the outline plan may lack detail, it will certainly help with resource scheduling and provide essential early visibility of the extent of the required verification activities.



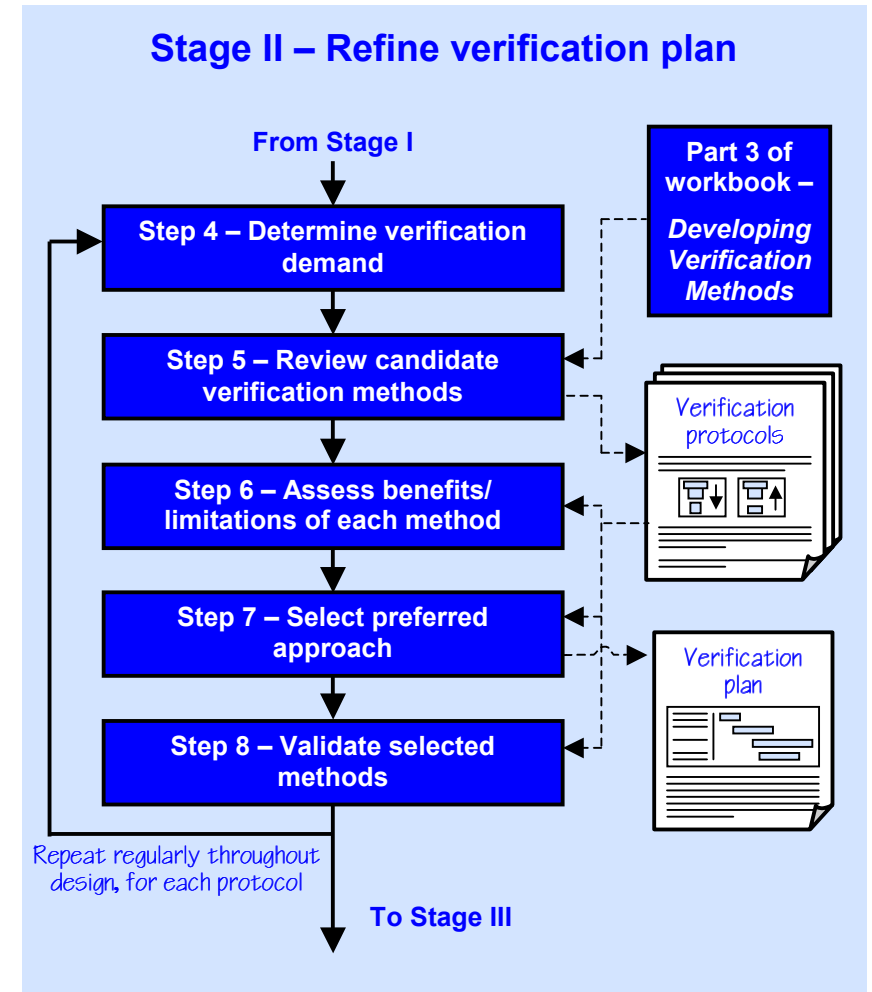
## STAGE II – REFINE VERIFICATION PLAN

*Stage II* starts as soon as the design concept has been chosen and helps to improve the verification plan by:

- detailing the methods for significant regular and final verification activities, and
- determining exactly when they should be used in the design process.

*Stage II* involves an analysis of the device design, rather than the requirements and, as shown in the diagram opposite, is divided into the following five steps:

- *Step 4*. Determine verification demand – how urgently verification is needed and how much the risks need to be reduced.
- *Step 5*. Review candidate verification methods – methods in addition to those already identified under *Stage I* may also be worth considering
- *Step 6*. Assess benefits/limitations of each method, in terms of its ability to reduce risks
- *Step 7*. Select preferred approach – the preferred verification methods and when they should be executed – and update the plan.
- *Step 8*. Validate selected methods, where necessary.



## **Background to Stage II**

The prime purpose of *Stage II* is to determine whether redesign or verification is necessary at any point in the design process. Consideration may also be given to exactly when final verification should occur, if this has not yet been decided.

Fine-tuning the verification plan and the protocols sometimes involves a complex balancing act between a variety of parameters, many of which are likely to change as design progresses. Thus, this stage will need to be repeated more frequently than *Stage I*.

Although the *Stage II* process is rigorously detailed on the following pages, experienced designers will know instinctively when to invoke it and which steps are relevant in a given situation. Consequently, this stage might be regarded as part and parcel of the overall design process ‘philosophy’ and, thus, constantly borne in mind.

For non-key verification activities a quick, cursory review through *Stage II* may suffice whenever new information comes to light that affects the choice and timing of the verification method. Such a review usually incurs minimal resources – for example, a visual check of a “that looks strong enough” nature. If a new candidate method is identified for verifying a non-critical requirement, previous experience may show its immediate benefit, so there may be no need to carry out *Step 6* in depth.

However, for key verification activities, a more systematic walk-through of the method may pay dividends in improving the efficiency and quality of the verification approach. Again, it is intended that discretion should be exercised over how thoroughly the method is followed.

## 4 DETERMINE VERIFICATION DEMAND

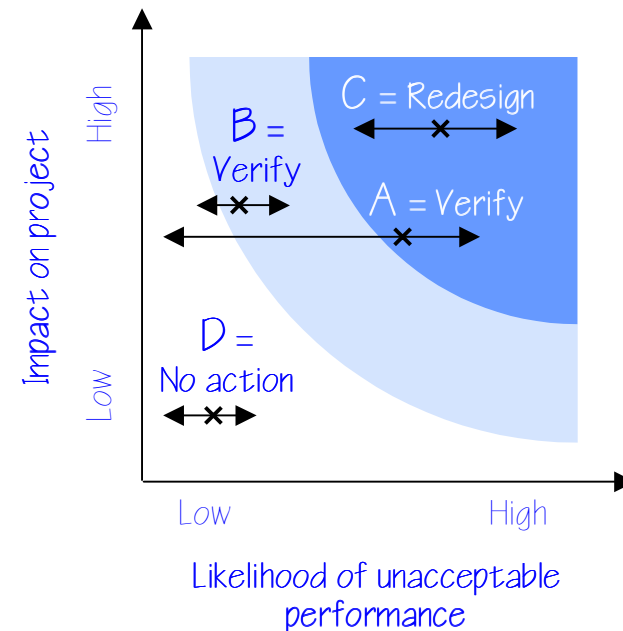
Once a design concept has been chosen, it is important to re-assess verification priorities. This involves repeating the process of reviewing each requirement as described in *Stage I*. As before, all types of risk should be considered. However, armed with more concrete knowledge about the form of the device design, there is an opportunity to perform the risk analysis more accurately.

When the risks have been re-assessed, it is possible to decide upon the need for further action, possibly involving redesign or verification. The timing and priority of such action should be assessed in a similar manner to that for *Stage I* for the various types of risk.

The diagram opposite illustrates the results of such an assessment. The various types of risk can be considered in turn, starting with performance risks and working up to the development and commercial risks. The following observations may be made:

- No action is likely to be required for low risk requirements (as indicated by requirement D).
- Conversely, redesign will almost certainly be required for high-risk requirements (as indicated by requirement C).
- In the cases where risks are unclear, verification may be required in order to learn more about the true performance of the device (as indicated by requirements A and B).

The final decision to take action will always depend upon issues of practicality and business policy. In some cases a medium (or even high) risk may be tolerated, as technological limitations may prevent any form of practical redesign. Such decisions must be made in the light of all types of risk, and are discussed in more detail later in this section.



|    | Requirement                                  | Urgency for verification | Comments                          | Need for uncertainty reduction | Comments   |
|----|--|--------------------------|-----------------------------------|--------------------------------|--|
| R1 | Maximum overall length not to exceed 80.0 mm | 0                        | Confident in performance estimate | 0                              | No action needed at the moment                     |
| R2 | Dose not to exceed $\pm 10\%$ of label claim | 2                        | -                                 | 3                              | Very uncertain and need to prioritise verification |
| R3 | ...  | ...                      | ...                               | ...                            | ...  |

Quantification of the urgency for verification and how much it is required to reduce uncertainty

(R2 represents a situation early in the design process where both the uncertainty in the performance estimate and the urgency for verification may be significant.)

### Re-design or verification?

If re-design is prioritised over verification, *Stage II* should be repeated once the re-design has been completed as the risks and their potential impact may have changed.

However, if verification has been prioritised, it is necessary to determine:

1. the urgency of verification,
2. the need for uncertainty reduction.

### ***Determining the urgency of verification***

The degree of urgency for verification should be considered and, preferably, quantified. As a suggestion, a scale of 0 to 3 may be used – this is usually adequate. 0 indicates minimal need and 3 a highly significant need.

Referring once more to the diagram on the previous page, the development risks for requirement A are likely to be higher than those for B, and so the verification for requirement A should be prioritised over that for B. The need for verification may be recorded in a table such as that shown opposite.

As *Step 4* is repeated during the design process, the verification need will change. Once it reaches a high level, immediate verification may be necessary, hence its timing can be dictated.

### ***Determine the need for uncertainty reduction***

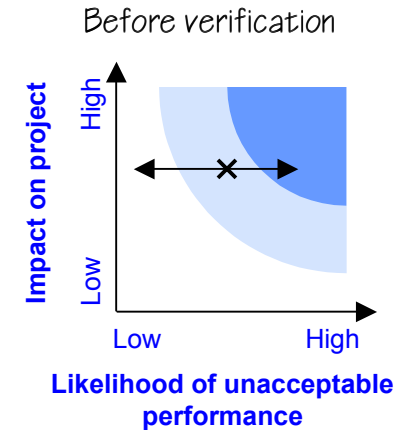
Two further columns are included in the table. These are used to record *how much* the uncertainty should be reduced through verification. Thus, if verification has been prioritised, the degree to which it is required to reduce the uncertainty in the performance estimate – and hence *clarify the risk* – should also be assessed. In other words, it is necessary to consider how much residual uncertainty may be tolerated.

## Reducing uncertainty

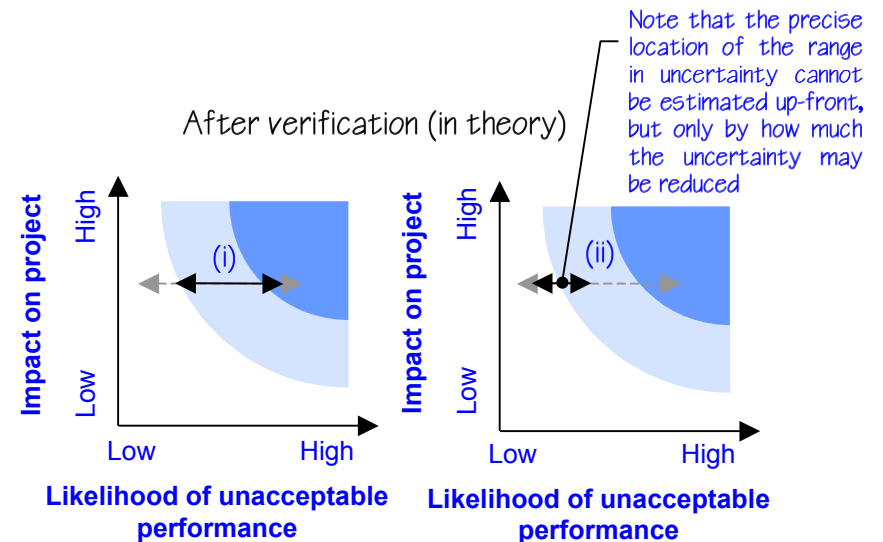
Ideally, the verification method should reduce the uncertainty to zero, but this is simply not possible in practical situations. Generally speaking, the degree to which the verification method can reduce the uncertainty is linked to the cost of its implementation. Thus, the maximum tolerable uncertainty, after verification, needs to be taken into account.

The concept of reducing uncertainty for a single requirement is illustrated on the right. As may be seen in the top diagram, considerable uncertainty exists before verification has been conducted. Diagram (i) below shows that the use of a verification method that is cheap, but only partially effective, may only reduce the uncertainty by a small amount – the risks remain unclear. Diagram (ii) shows the effect of using an alternative verification method that can reduce the uncertainty further. Although this may incur greater cost, it may be preferred. Thus, a verification method should be chosen that is practical to implement and that can reduce uncertainty by a sufficient extent to allow the design process to continue, by ensuring that risks are at an acceptable level.

It follows that if more than one candidate verification method has been identified, considering the tolerance for any residual uncertainty will help select the optimum method.



Before verification the uncertainty in a performance estimate may be considerable



The effect of two different verification methods (i) and (ii) in reducing the uncertainty in the estimate of performance

### **Tolerating residual uncertainties**

For regular verification activities, the degree to which residual uncertainties may be tolerated is likely to vary throughout the course of the design process, as it depends upon the impact of a failure to identify a design problem.

For final verification activities the tolerance of residual uncertainties should be at a minimum, particularly for safety-critical requirements.

For both types of verification the need for reducing uncertainty may be assessed by:

- 1) considering the maximum reasonable tolerance for any residual uncertainty in the ability of the design to meet its requirements, after the verification has been conducted,
- 2) quantifying the need to reduce this uncertainty, thus facilitating a final choice of method using some of the remaining steps in this stage.

As before, any scale may be chosen, but a scale of 0 to 3 is usually adequate, where 0 indicates a minimal need for reduction and 3 a highly significant need. These figures may also be recorded in a table, as shown on the previous page.

The final choice of verification method will be influenced by a number of factors, which are detailed later in *Steps 6* and *7*.

## 5 REVIEW CANDIDATE VERIFICATION METHODS

Although a list of candidate verification methods will have been produced for each requirement during *Stage 1*, the details of many of these may only be refined later in the design process. Further methods may also be identified as the design progresses.

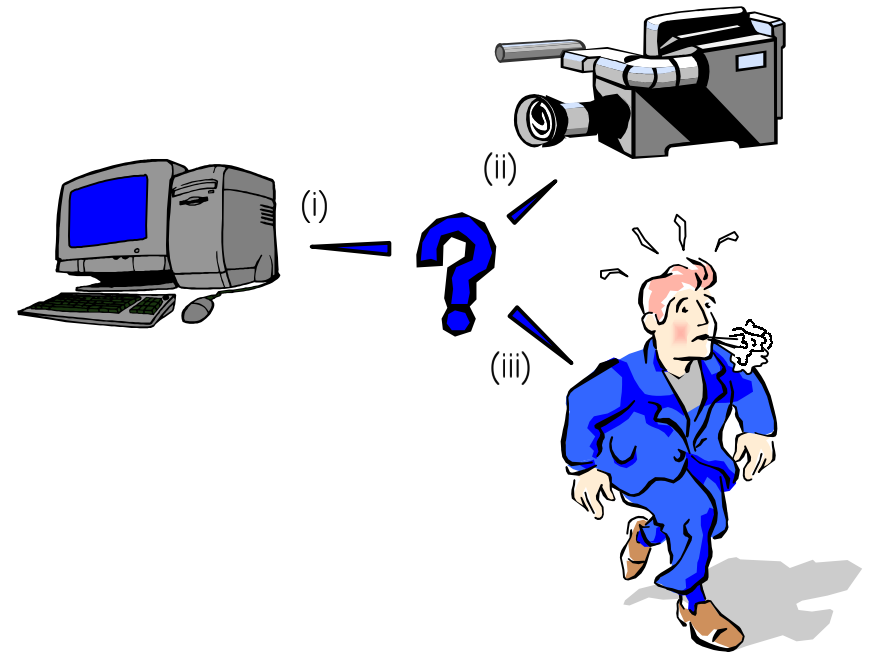
In some cases determining a suitable verification method may be immediately obvious – one method will shine out above all others as easy to implement and capable of providing results of an appropriate quality. Some CAD packages, for example, enable tolerances to be analysed with ease, so there may be little point in seeking an alternative method.

In other cases, although a range of potentially suitable verification methods may exist, determining the candidate list may not be straightforward, particularly if an innovative approach to verification is required.

*Consider investigating the drug flow characteristics (particle size, dispersion and dose) for an inhaler, mid-way through the design process. To do this, several options may be considered, including:*

- i) *modelling the process using computer software,*
- ii) *designing and building a test rig to determine flow rate, perhaps with the help of a high-speed camera,*
- iii) *measuring flow rate with patients – does it relieve the symptoms? (note – this is a validation, rather than verification, method)*

To derive a suitable list of candidate verification methods, the guidance in *Developing verification methods* in *Part 3* may be used. This highlights the need to consider a variety of sources that may influence the choice of method, including the device requirements, any recognised standards and guidance documents. Once this has been followed, one or more verification methods may have been identified and the remaining steps can be taken, to determine the most suitable verification method.



There may be several possible verification methods available.



## **6** ASSESS BENEFITS/LIMITATIONS OF EACH METHOD

If more than one verification method has been identified for a requirement, the results they provide may differ in nature and/or quality. Therefore, the benefits and limitations of each method should be evaluated to make sure that the method chosen is sufficiently sensitive and accurate and capable of producing reliable results.

*For example, a computer simulation for investigating the drug flow characteristics of an inhaler may be difficult to set up using the expertise currently available in a company. Thus, there may be a low confidence that it would produce meaningful results, and hence the estimated degree to which it can reduce the performance uncertainty may be quite limited. In such circumstances, a physical test may appear to be more helpful.*

### **Comparing benefits**

Once the benefits of a method have been assessed, they can be compared with the need to reduce the related uncertainty, previously identified in [Step 4](#). To facilitate this, the benefits of each method may be quantified and recorded in a table, in the same way as that described in [Step 4](#). Each candidate method should be reviewed in turn for each requirement.

Determining the benefits of each candidate verification method may be relatively straightforward, particularly if the methods are already familiar. However, when developing novel methods, there is a real danger that the benefits that verification brings do not match the requirement for reducing the performance uncertainty. In practice, unexpected limitations in the method may be found, perhaps only after executing the verification. Alternatively, the method may be too expensive to be practical, particularly if there is a high chance that it will need to be repeated regularly.

## Comparing the limitations of each method

In addition to the benefits each method offers, costs and practicality issues will constrain the verification approach in terms of the choice of method and when it is used in the design process. These restrictions must be investigated before the optimum timing and rigour of verification can be determined.

### *Directly attributable costs*

Although the costs of spontaneous verification activities may be minimal, key verification activities, for example life testing, may incur costs that represent a high proportion of the overall development budget.

Verification-related activities, such as developing the method<sup>4</sup>, executing the verification and analysing the results, may also incur costs and affect project timescales.

Costs should be estimated for each method listed under *Step 5*. The adjacent diagram lists the main items that need to be considered.

Early in the design process, only an approximate estimate of these costs may be made, as the precise nature of the method may not be known. Nevertheless, even such an approximation of costs may be beneficial in helping determine the verification method of choice. In other cases, for example where previous experience can be used, or when the verification is to be contracted out to a test house and a quotation is given, costs may be estimated more precisely.

Generally speaking, the more concrete the device design becomes the more accurate cost estimates are likely to be. Thus, each time this step is repeated, a clearer picture of the costs will be built up.

### Costs include:

- *Designing the verification method or acquiring a standard verification method*  
(including validation of the method by other means)
- *Setting up the verification*  
(including production of a model such as a rapid prototype, or calibrating measurement equipment)
- *Executing the verification*  
(including labour costs, hire or purchase of equipment, subcontracting tests to dedicated test centres or delays to project whilst results are obtained)
- *Interpreting or analysing the results* (for example, statistical analysis)

Directly attributable costs of verification

---

<sup>4</sup> The development of novel verification methods could be very time consuming

### ***Potentially attributable costs***

Potentially attributable costs arise through and as a consequence of the choice of verification approach. When compared with direct costs these often are considerably more difficult to determine, as a degree of ‘crystal ball gazing’ is necessary.

There are several problem scenarios that could generate potentially attributable costs:

- i) *Obtaining erroneous verification results.* The verification approach chosen may fail to produce a meaningful result or, perhaps more dangerously, produce a result that is so inaccurate that it causes incorrect action to be taken in response. The likelihood and effect of such outcomes should be considered by reviewing the three verification elements. Further guidance may be found in [Check the verification method](#) in [Part 3](#).
- ii) *Design changes.* Changes to the device requirements, the design or the verification method usually incur additional verification-related costs if verification has to be repeated or the verification method changed to reflect the new situation. This scenario is discussed in more detail in [Managing changes](#) in [Part 3](#). Design changes generally place the development project at risk and, in turn, lead to support and commercial risks. This influences the urgency for verification as discussed in [Step 4](#).
- iii) *Failing to carry out verification.* This also places the development project at risk, increases the possibility of re-work being needed at a later stage and may lead to support and commercial risks. The potential impact of these problems again influences the urgency for verification as discussed in [Step 4](#).

### ***Practical limitations – resources***

Verification activities may be severely constrained if appropriate resources are not available to carry out the verification. Resources in this context include expertise and knowledge of verification methods, the time available to carry out verification, test equipment and device design prototypes.

Early in the design process, the device design may not be sufficiently mature to produce a prototype for functional testing. Then, there may be no option but to delay verification until adequate resources become available, or to seek an alternative method.

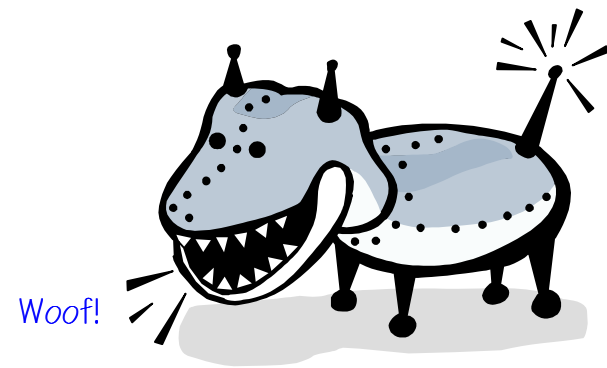
Sometimes, insufficient expertise or test equipment may exist in-house, and it may be necessary to use expert assistance from outside the company. It is common practice, for example, to subcontract the electromagnetic compatibility testing of a device to a specialist test centre.

Practical constraints have a major influence on verification practice and should be considered early in the design process and planned-for proactively.

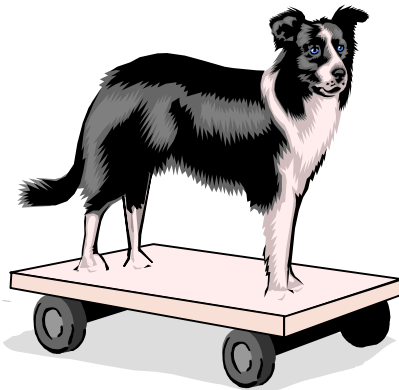
### ***Partial prototypes***

One option, which may be worth considering, is to produce a prototype to test a limited number of the device design features – there may be sufficient information to make a prototype which is either accurate in form (a ‘looks-like’ model) or accurate functionally (a ‘works-like’ model) but not both.

In the example shown opposite, aesthetic features have been ignored entirely in order to produce a purely functional prototype. A contrasting fictional example of a ‘looks-like’ model is shown on the facing page.



Example of a ‘works-like’ model



Example of a 'looks-like' model:

### ***Verification-related inaccuracies***

These may be caused by methods that yield inaccurate results or models that are poor representations of the device design.

For example, early in the design process, because many changes to the device design are expected, inexpensive models may be manufactured and less resource-intensive verification methods may be chosen for economic reasons. However, this will limit the accuracy of the results.

In other cases, it may simply be impossible to use a verification method that represents actual-use conditions to a high degree of accuracy. For example, simulating some physiological conditions can be very challenging.

Problems associated with inaccurate verification results may also be confounded by the complexity of the method and model. Whenever verification is conducted, there is a danger that what is being measured is not what *should* be being measured.

*Consider testing a waterproof seal to failure. Various parameters, such as temperature and humidity, may give rise to misleading test results if ignored. Also, such a model will have several components. Some of these that form part of the model, but do not appear to be related to maintaining the seal directly, may in fact influence the test result – for example, the force provided by screws that clamp the device together.*

Once the details for each verification method are known, the potential for inaccurate results may be assessed by means of the method in [Check the verification method, Step 2 in Part 3](#). This method may also be helpful in the identification of the benefits and limitations of each verification method.

### ***Recording the limitations***

The limitations may be quantified and recorded using a similar method to that set out in [Steps 4 and 5](#). It will almost certainly be necessary to include space for comments because many limitations will be difficult to quantify.

## 7 SELECT PREFERRED APPROACH

The preferred verification approach, that is the final choice of verification method for each requirement and when each method should be used in the design process, may now be determined. Decisions will be based on the demand for verification, *Step 4*, and the benefits and limitations of each candidate verification method, *Steps 5* and *6*.

### Choosing the verification methods

To choose the most suitable method for each requirement, the benefits and costs of each method need to be compared. Samples of comparison tables may be seen on page 53.

For each method, the estimated benefits should be compared with the need for reduction in the uncertainty. It is likely that some verification methods can be eliminated immediately at this point because of their obvious inadequacy or because they are too costly. Comparing the figures in the tables may make this quick and easy.

The remaining methods should then be re-considered and compared in order to decide upon the most suitable verification method at a particular point in the design process.

*Early in the design process when the uncertainty about the device performance needs to be reduced considerably, producing a physical prototype of the device and conducting tests could well provide suitable results. However, when the costs incurred and the likelihood of having to repeat the tests are considered, it may be more prudent to use an alternative, less expensive verification method, or to reduce the accuracy of the model or quality of the testing approach. In contrast, when the final verification activity is to be performed, a more costly but trustworthy verification approach may be chosen.*

To follow Step 7, the following should have been identified, and quantified, where possible:

- 1) The urgency for verification, in terms of the effect of not meeting the requirement (Step 4)
- 2) The degree to which verification is required to reduce the uncertainty in the performance estimate (Step 4)
- 3) Any candidate verification methods (Step 5)
- 4) The benefits of each method and its limitations, in terms of the directly and indirectly attributable costs and the practical constraints (Step 6)

Prerequisites for determining the verification approach

| Method |    |                    | Benefits | Comments                        | Cost | Comments on limitations  |
|--------|----|--------------------|----------|---------------------------------|------|--|
| R2     | M1 | Computer modelling | 2        | Adaptable to new designs        | 2    | Lack of expertise in company                                     |
|        | M2 | Test rig           | 3        | May be the most accurate method | 3    | Hire of camera, cost of model, difficult to adapt to new designs |
|        | M3 | ...                | ...      | ...                             | ...  | ...  |

Quantification of the benefits and limitations for verification

### Assessing the precise timing of the verification

For each requirement, the degree of urgency for verification (*Step 4*) and the limitations of each method under consideration (*Step 6*) will largely determine when verification should occur. When the urgency reaches a medium or high level, where possible verification may be required immediately. Nevertheless, the limitations should still be weighed up.

*Consider the situation when a medium need for verification exists, but a design change is imminent. If the chosen method is costly, it may be worthwhile to wait until the change has been implemented before carrying out the verification, otherwise the method may need to be repeated on the new design model. In other cases the need for verification may be so high that, despite the risk of change, verification should still be conducted.*

### Forming the protocols

Once a suitable verification approach has been selected for each requirement, the chosen verification methods should be entered into a protocol, the contents of which are discussed in *Documenting Plans and Protocols* in *Part 3*.

In certain instances, a protocol may contain more than one verification method. Similarly, a verification method may verify more than one requirement in a single ‘hit’. Although such combinations may result in cost savings, the increase in complexity can result in reduced transparency of the results – in the words of one designer, “It all becomes horribly intertwined.” The previously identified benefits, limitations and risks may be helpful in determining whether such an approach is appropriate.

### Updating the plan

The selected approach should be recorded in the verification plan.

| Requirement |  | Urgency for verification | Comments                          | Need for uncertainty reduction | Comments   |
|-------------|--|--------------------------|-----------------------------------|--------------------------------|--|
| R1          | Maximum overall length not to exceed 80.0 mm | 0                        | Confident in performance estimate | 0                              | No action needed at the moment                     |
| R2          | Dose not to exceed $\pm 10\%$ of label claim | 2                        | -                                 | 3                              | Very uncertain and need to prioritise verification |
| R3          | ...  | ...                      | ...                               | ...                            | ...  |

Quantification of the urgency for verification and how much it is required to reduce uncertainty

(R2 represents a situation early in design, where both the uncertainty in the performance estimate and the urgency for verification may be significant.)

## **8** VALIDATE SELECTED METHODS

It is important to have an especially high degree of assurance that the key verification activities will yield accurate and reproducible results.

This is particularly true in the case of a novel approach when its fitness-for-purpose may need to be proven and the accuracy and reproducibility of the method demonstrated independently against a known benchmark. The verification method may then be said to be *validated*, validation being most critical for the final verification activities.

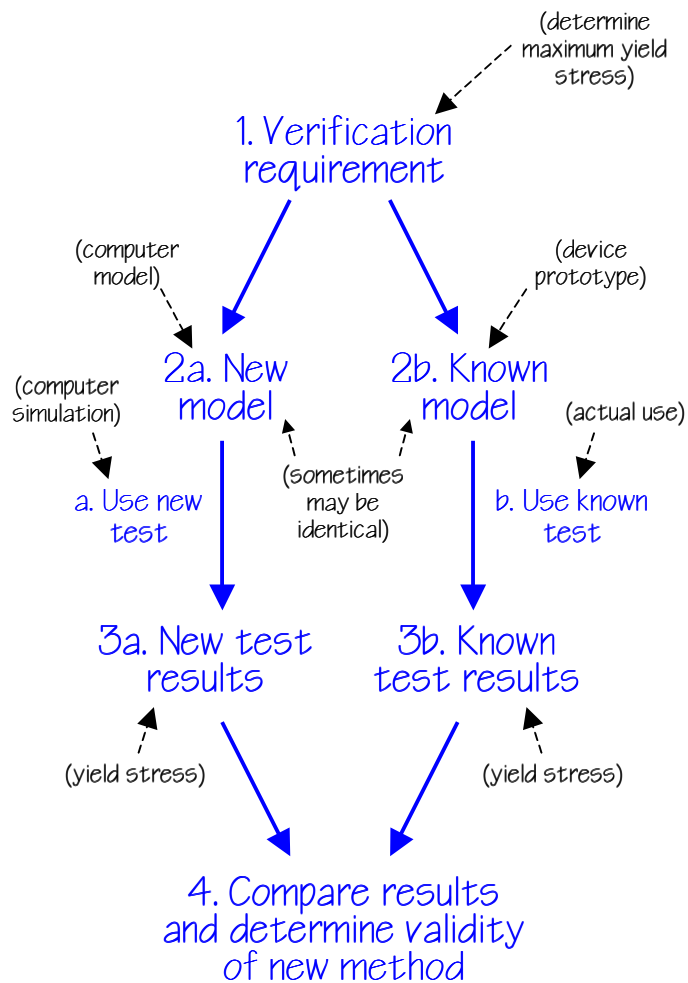
In contrast, the integrity of well-understood verification methods (standardised or very simple methods) may be taken for granted. All that needs to be demonstrated is that the methods have been followed faithfully and, in such cases, this step may be omitted.

### **Is validation necessary?**

The following method can be employed to decide whether validation is necessary.

1. Assess the novelty of each verification method.
2. Assess the level of confidence in each verification method by comparing how well its accuracy matches other standardised methods – if questions are raised about its accuracy, validation may be necessary.
3. Assess the effect of a misleading verification result (as discussed in *Step 2* of *Stage 1*).
4. Determine the risk involved, and how, if the risk cannot be tolerated, the verification method should be validated.





## Validation techniques

Verification methods may be validated by:

- a) executing the method and collecting the results,
- b) comparing the results with ‘known’ results produced by an already accepted method.

Known results include those published in well-recognised scientific literature.

*Consider, for example, how one might validate a new computer simulation for evaluating the strength of various concept designs of a prosthetic knee joint. If the strength of a known design has already been published in a widely respected independently reviewed journal, a model of that knee joint may be used in the computer simulation and the results compared with the published results. If the comparison is sufficiently close, testing may then commence on alternative models using the new method.*

Alternatively, a ‘known’ verification method may be used to test a model of the new device. To validate the new method, the results from the known method may be compared with those produced by the new verification method.

Validation of the new method may also be carried out in stages by breaking down the verification method into its constituent parts, thereby improving the clarity and simplicity of the validation.

*When devising a computer simulation to measure the overall function of a device, separate sub-functions may be validated individually by making comparisons with in-use testing results.*

## STAGE III – EXECUTE PROTOCOLS

### 9 COMPLETE PROTOCOLS

Before executing the protocols it is important to ensure that the procedures to be followed, particularly the test acceptance criteria, are absolutely clear, finalised and approved. In addition, ensuring the existence of a complete list of the protocols and their intended order of execution is, usually, a quality system requirement, and a source of valuable evidence if it necessary to defend the company against postmarket problems. Quite apart from this, failing to complete the verification protocols may necessitate re-work much later, significant unplanned expenditure and late product.

A clear set of verification-related objectives helps provide a focus on the pertinent issues. Without this, there is a temptation to ‘poke’ at the design until the verification is judged to be ‘finished’. A great deal of resources can be wasted in this way, as highlighted by the quotation to the right. A checklist outlining the required contents of each protocol, and other documentation, is presented in *Documenting Plans and Protocols* in *Part 3*.

### 10 CARRY OUT PROTOCOLS

Once the verification approach has been determined, the protocols need to be executed as scheduled in the project plan. However, the likelihood and severity of any impending design changes should be considered beforehand, as detailed in *Managing Changes in the Design Process* in *Part 3*, as these may require verification to be repeated.

Once the protocols have been executed, the results must be documented and any deviations from stated practice noted and justified. The results will then need to be compared with the acceptability criteria and any further follow-up actions noted. Documenting results is discussed further in *Documenting Plans and Protocols* in *Part 3*.

“If you write the protocol before you test, you end up doing about a quarter of the testing you would do if you just get on and design it and then try and test it afterwards. It’s a huge difference.

I’ve seen programmes run late with two engineers working full-time for a couple of months, chasing around. At the end of it they haven’t actually proved anything because they didn’t set out to prove or verify anything.”

(Medical device project manager)

## PART 3 – SUPPLEMENTARY GUIDANCE

*“Test everything.”*

Paul, in a letter to the Thessalonians, ~AD51

## DEVELOPING VERIFICATION METHODS

This section focuses on how the verification methods may be derived.

As shown in the diagram opposite, there are two steps: drafting and checking the verification method.

### Background

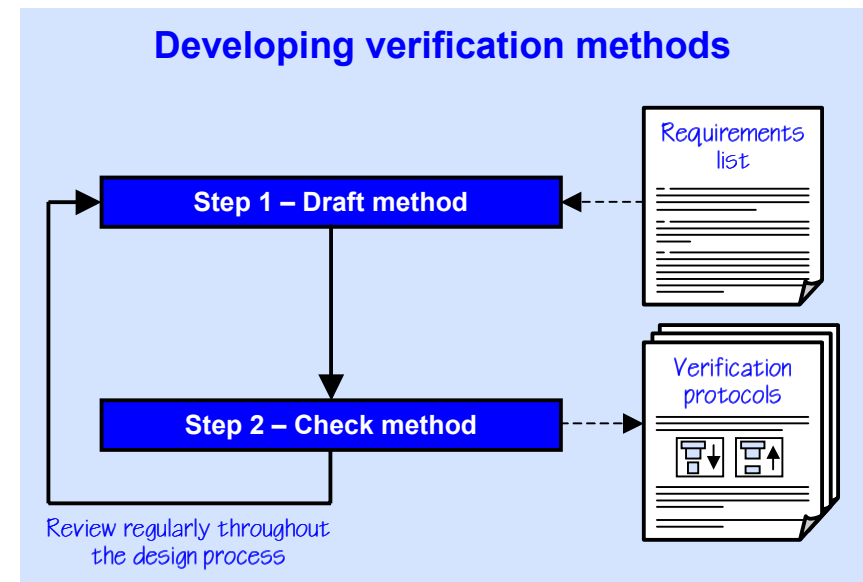
Although the specific details of the verification method may be produced by reviewing the design of the device, as discussed in *Stage II* of *Part 2*, much of its content may often be derived by simply reviewing requirements (see *Stage I* of *Part 2*) and drawing on experience of previous, similar designs. In other cases, particularly for innovative designs, a variety of additional means may be employed. These include consulting:

- standards and FDA ‘Guidance Documents’,
- documentation for previously marketed devices, and
- experts and scientific literature.

Analysing the device design for its potential failure modes may also be highly beneficial in determining the verification approach.

### Requirements and verification

In addition to the form of the device design, requirements also influence verification practice greatly. Requirements help dictate what parts of the design will need to be verified, that is, the set of components and features that meet the requirement, how they will be verified and whether or not the design will be suitable. Consequently, the importance of gaining a comprehensive, clear and correct set of requirements cannot be overemphasised<sup>5</sup>.



<sup>5</sup> See *Good Design Practice for Medical Devices and Equipment – Requirements Capture*

“When non-clinical testing is being conducted or requested, the testing should... use standards or standardized test methods whenever possible...”

*The least burdensome provisions of the FDA Modernization Act of 1997, FDA (2001)*

### ***The use of standardised verification methods***

An advantage of using tried-and-tested verification methods is the fact that their generally-regarded legitimacy usually provides an adequate degree of assurance that they will yield meaningful results. This is helpful from both an industry and regulatory point of view as it reduces work for both parties by limiting uncertainty. Indeed, unless an alternative approach can be justified, the use of standardised methods is expected by regulatory authorities, as shown by the quotation on this page.

When a non-standard verification method has to be used, costs may increase significantly because additional resources are required to derive the method and to assess the validity of the results. Novel verification methods must certainly be checked, as discussed later in [Step 2 – Check verification method](#), and may also need to be validated, as discussed in [Step 8 of Stage II](#).

Consequently, when designing a new device, it is highly advisable to investigate the existence and applicability of standardised verification methods, such as those specified in standards and FDA Guidance Documents. Verification methods that have been approved for relatively new devices for use in the USA may also be identifiable from the documentation associated with the device submission.

The existence and applicability of standardised verification methods is discussed further in [Step 1](#) of this section.

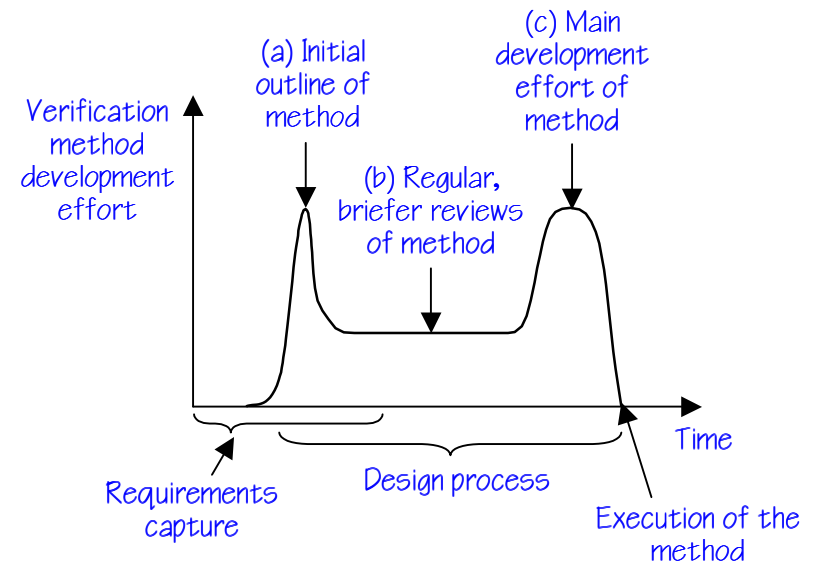
## Using the approach for deriving verification methods

Derivation of the verification method may be split into three steps, as illustrated in the adjacent figure.

1. First, an approximate outline of the method should be formed through a review of the requirements and the concept design, as discussed in *Stage I* in *Part 2*. At this point little may be known about the form of the finished device design, so it may not yet be possible to identify the details of the method.
2. In order to avoid any unpleasant surprises during the design process, the verification method should be reviewed regularly, and may be required to be updated as stated in *Stage II* in *Part 2*. Such reviews may range from token glances at the verification method to ensure that it is on the right lines to a complete rewrite.
3. Depending upon what has already been learned about the device design and how much remaining effort is required to update the method before verification takes place, the remaining parts of the method may be added at this stage. Although a large amount of detail may now be added, it is likely that the overall method will change little, and few surprises should surface regarding the resources necessary for execution, see *Stage II* in *Part 2*.

As details of the verification method are finalised, *Steps 1* and *2* will probably need to be repeated as design progresses, with *Step 1* starting as early as the requirements capture phase.

The method is particularly relevant for novel devices, or with devices that require novel verification methods. In these cases, it may be difficult to identify a suitable verification method at the requirements capture stage.



The verification method may be updated throughout the design process, but two key efforts may be made

**C. Standards**

The following are commonly referenced standards for electrosurgical devices:

1. ANSI/AAMI American National Standard for Electrosurgical Devices HF-18/1993.
2. International Electrotechnical Commission Standard for Electrosurgical Devices, IEC 601-2-2.

The applicant may certify that their device meets the stated standards and maintain documentation of testing showing that the device does meet that standard. Certification to meeting a specific standard may reduce the data requirements for the 510(k) submission.

If a manufacturer wishes to deviate from the test requirements identified in one of the above standards, they need to provide their test protocol and test results to demonstrate that their device design is at least as safe as the cited predicate device.

An extract from FDA's Guidance Document, *General Surgical Electrosurgical Devices*, indicating suggested standards

Note, the additional guidance on testing

## 1 DRAFT THE VERIFICATION METHOD

When deriving candidate verification methods, the first task is to review the device requirements, as discussed in *Part 2, Stage I*. Also, the degree of novelty of the device should be assessed, as this will be an indicator to the presence and applicability of standardised verification methods. This can be quite straightforward if other similar devices have been on the market for some time.

*The following five sub-steps* may be used in the development of both novel and more standard verification methods.

### 1.1 Using standards and Guidance Documents

#### *Where to find standardised methods*

Standardised verification methods may be found through bodies, such as the British Standards Institution (BSI), the American National Standards Institute (ANSI) and the International Electrotechnical Commission (IEC). FDA Guidance Documents may also be consulted<sup>6</sup>.

FDA's web site ([www.fda.gov/cdrh](http://www.fda.gov/cdrh)) contains Guidance Documents ([www.fda.gov/cdrh/guidance.html](http://www.fda.gov/cdrh/guidance.html)) and information on standards for use in the USA ([www.fda.gov/cdrh/stdsprog.html](http://www.fda.gov/cdrh/stdsprog.html)).

---

<sup>6</sup> A list of the various types of standard, and background information about standards in general, is provided in the *Regulatory Requirements Guidelines* section of the *Good Design Practice for Medical Devices and Equipment – Requirements Capture* workbook.

The web addresses of Standards Bodies are given in the Appendix of this workbook.

### ***Content of standards and Guidance Documents***

Standards and Guidance Documents contain various types of information that may be useful for formulating the verification approach. For instance, they may state the criteria for acceptability of various device parameters and, hence, it may not be difficult to identify an appropriate method to measure whether such requirements have been met.

*IEC 60601-2-41, for surgical lamps, specifies appropriate value ranges for the illumination area, diameter and depth of the light beam.*

Standards and Guidance Documents may also reference other potentially relevant standards, or standards that are expected to be followed, as shown in the extracts on the right. These examples also detail procedures for following or deviating from standard practice.

### ***Adaptation of standards and Guidance Documents to the new device***

Particularly in the case of novel devices, when standard verification methods are not applicable directly, they may be combined or modified to tailor them to the specific device design. Sometimes, there may be no directly relevant test method but, by investigating similar devices, suitable methods can be identified and modified accordingly (see right). In other cases, there may be a directly relevant verification method but it may have to be adapted to be compatible with the specific form of the device.

For reasons stated earlier, relevant standards should be reviewed early in the design process to identify candidate verification methods.

*Examination of FDA's Guidance Document for intra-articular prosthetic knee ligament devices highlights the fact that, before conducting tensile tests, the finished device must be pre-soaked in saline solution at 37°C for one month, and that tensile fatigue tests may be discontinued only after  $1 \times 10^7$  cycles have been performed. These statements are likely to have highly significant implications for the scheduling of the verification plan and the resources necessary.*

The following are the types of data required to be provided, if needed, to substantiate the device substantial equivalence claim:

1. Bench/In Vitro Data

a. Engineering

As a minimum the device should meet ANSI/AAMI HF-18/1993. Particular attention should be paid to insulation materials. For laparoscopic/endoscopic devices, include results from a test for capacitive coupling resistance between your device and a conductive material cannula/trocar device under simulated use conditions.

An extract from FDA's Guidance Document, *General Surgical Electrosurgical Devices*, indicating a suggested standard, and particular points for testing

Verification methods for a specific device may be equally applicable for new devices that perform in an equivalent manner in similar environmental and physiological conditions. For example, a test developed for angioplasty catheters may be equally suited for stents, atherectomy devices and minimally invasive bypass products.

Drues, M, "How to meet the new simulation testing requirements"; Medical Device and Diagnostic Industry, 20(3), 1998



[www.fda.gov/cdrh/devadvice/31432.html](http://www.fda.gov/cdrh/devadvice/31432.html)

Where to find documentation for a  
previously submitted device in the USA

## 1.2 Using documentation from previously marketed devices

As well as standards and Guidance Documents, specific device submission documentation for any previously marketed devices may be freely available and a useful source of information regarding accepted methods and procedures for regular, and particularly final verification activities.

Identifying the existence of any devices which are similar to the device under development may save considerable time and effort in following the verification approach, and help present a suitable case for regulatory approval. Even for novel devices that are not identical to previous legally marketed devices, a review of the documentation for any similar devices may also help in determining a suitable verification approach.

### *Where to find documentation for predicate devices*

For devices approved in the USA, the following documentation sources may be of assistance.

- [www.fda.gov/cdrh/foicdrh.html](http://www.fda.gov/cdrh/foicdrh.html) – Contains some downloadable material for previous device submissions, accessible for free from the FDA web site using a ‘Freedom of Information’ (FOI) request. This may be used to search for summaries of safety and effectiveness for previously marketed devices or device families.
- [www.fda.gov/cdrh/devadvice/36g1.html](http://www.fda.gov/cdrh/devadvice/36g1.html) – This lists the types of document that are releasable under an FOI request.
- [www.foiservices.com](http://www.foiservices.com) – This is an example of a commercial web site where much more information can be obtained, at a cost.
- [www.fda.gov/ohrms/dockets](http://www.fda.gov/ohrms/dockets) – Meeting transcripts, minutes and other documents may be viewed by following the ‘advisory committees’ link, choosing the relevant year for searching, and following the link to the appropriate expert review panel for the device. Although the number of transcripts is very limited, this may provide further information about the issues involved in the approval of some devices.

### 1.3 Using expert opinion and scientific literature

Existing practice within the company is not necessarily the best practice. External experts and scientific literature may also be helpful in determining the most appropriate verification approach. The following information sources should be considered:

- clinicians and medical associations,
- regulatory expert review panels, such as FDA Advisory Committees,
- Conformity Assessment Bodies,
- experts from industry and industry literature and
- scientific literature, for example, from journals and institutions.

#### *Methods*

A variety of methods, including interviews, questionnaires, workshops and focus groups, are useful.

Consultation with experts may be beneficial for several reasons. For example, a review before finalising the test protocol may prevent a failure, due to insufficient final testing occurring at the approval stage.

Where the expert is from a Conformity Assessment Body and the verification approach is unclear, early consultation could help to build up mutual confidence that an appropriate and adequate approach to verification will be pursued – this could also help minimise the time to gain approval.

The citation of scientific literature or evidence has similar advantages in terms of streamlining or eliminating some verification activities. The examples on the right demonstrate (a) a case where testing was substituted by the provision of scientific evidence from a previous test and (b) where scientific justification has been provided to support a proposed deviation from expected practice, by conducting a more straightforward bench test instead of running a clinical trial.

(a) “FDA requested a complete test report for “pull-out” testing of the suture anchor. Because the physiological loads in the rotator cuff and ankle ligament are well known and fall within the known loads for the shoulder, we believe that our previous testing adequately addresses your request.”

Example of how a manufacturer might respond to an FDA request for more information - see [www.fda.gov/cdrh/modact/guidance/1195.pdf](http://www.fda.gov/cdrh/modact/guidance/1195.pdf)

(b) “Instead of conducting a clinical trial, we believe that the strength of the device to withstand bending during surgical placement can be adequately assessed by bench testing. The maximum angle of bending during surgical placement is known. Therefore, testing device strength at this maximum angle is adequate to provide valid evidence of the safety of the device.”

Example of how a manufacturer might respond to an FDA request to conduct a clinical trial – see [www.fda.gov/cdrh/modact/guidance/1195.pdf](http://www.fda.gov/cdrh/modact/guidance/1195.pdf)

When performing an FMEA for a novel medical device for preventing urinary incontinence the following failure modes were identified:

- De-bonding between two welded components,
- Puncture of one end of the device through excessive force being applied,
- Excessive bending, buckling or shear failure of a component used to deploy the device,
- Excessive compression during insertion.

Each failure mode highlighted the need for one or more tests to show that it does not occur.

A risk analysis may help determine what should be tested and how it should occur

[www.fda.gov/cdrh/safety.html](http://www.fda.gov/cdrh/safety.html)

[www.fda.gov/cdrh/mdr.html](http://www.fda.gov/cdrh/mdr.html)

[www.fda.gov/opacom/enforce.html](http://www.fda.gov/opacom/enforce.html)

[www.mdsr.ecri.org/index.asp](http://www.mdsr.ecri.org/index.asp)

Where to find reports of problems with previously marketed devices

#### 1.4 Using performance risk analysis

Device risk analysis often plays an absolutely critical part in determining the focus of verification action. In essence, determining how a device can fail – its *failure modes* – helps indicate how failures occur and what should be verified, as shown opposite.

Identifying the failure modes and risks involved is normally accomplished by following a systematic method such as a Failure Mode and Effects Analysis (FMEA). Other systematic methods include Fault Tree Analysis (FTA) and HAZOP. A brief outline of each method is given in Annex F of BS EN ISO 14971, referenced on the following page. Failure modes may also be identified by investigating how similar previously marketed devices have failed in the past. In this respect, the web addresses in the box below opposite may be of assistance.

Identification of the failure modes and the corresponding performance risks should be started early in the design process, and continued throughout. This is to keep in step with the development of the device and any new failure modes that may be identified as the device design takes form.

Once the failure modes have been identified, verification may be used to demonstrate that the design works correctly.

#### ***Risk analysis – different focuses***

Failures – and hence the need to verify – arise from the way in which the device responds to its working environment as well as from within the device itself. Thus, the full range of in-use conditions should be considered throughout the device lifecycle – how *users* use, misuse and abuse the device – and the *environmental conditions* that the device has to operate under. In-use conditions are discussed in more detail overleaf.

#### ***Users***

The FDA's *Medical Device Use-Safety*, referenced on the next page, is an excellent source that describes how to analyse risks from a human usability

point of view. *Task analysis* is one of the methods described – each task is broken down systematically into steps to help further analysis, such as determining which tasks are critical. FAST diagrams<sup>7</sup>, are an example of this approach.

### ***Environmental conditions***

Environmental conditions influence device performance significantly.

*Consider the differences between service in an operating theatre, on a general medical ward, in an ambulance, in a GP's surgery or in the body in the form of an implanted device. These environments may influence the users through affecting their mental workload and their ability to operate the device safely and reliably or the device directly. For example, when testing a balloon catheter, the factors that could interfere with balloon inflation and deflation should be considered. These include blockages or constrictions to the inflation tube, perhaps caused by restrictions or a high degree of tortuosity in blood vessels. Test methods will need to be derived which show that these functions are not adversely affected under 'as-labelled' use.*

When deriving verification methods that are intended to simulate in-use conditions, it is essential to be wary of 'method creep'. Method creep occurs when, for practical reasons, the quality of the verification method is reduced until the method is no longer a reasonable representation of the in-use situation. Using [Step 2](#) should help guard against this.

It should be noted that other medical devices could also adversely influence the operation of the device in question. For instance, light from some surgical, fluorescent and infrared lamps or heaters has been found to influence the measurements made by some pulse oximeters.

### **Risk analysis related references:**

- *BS 6079-3: 2000 Project management – Part 3: Guide to the management of business related project risk*, British Standards Institution, London.
- *BS 8444: Part 3: 1996 / IEC 300-3-9:1995 Risk management. Part 3. Guide to risk analysis of technological systems*, British Standards Institution, London.
- *BS EN ISO 14971:2000 Medical devices – application of risk management to medical devices*, British Standards Institution, London.
- *BS IEC 62198:2001 Project risk management – application guidelines*, British Standards Institution, London.
- *Medical device use-safety: incorporating human factors engineering into risk management*, Center for Devices and Radiological Health, Food and Drug Administration, USA, [www.fda.gov/cdrh/humfac/1497.pdf](http://www.fda.gov/cdrh/humfac/1497.pdf)

---

<sup>7</sup> See *Good Design Practice for Medical Devices and Equipment – Requirements Capture*,

## 1.5 Using both analytical and empirical techniques

### *Risk analysis*

Formal risk analysis techniques are, by nature, systematic. This is an advantage because they help to identify potential device problems in a comprehensive way. Also, because they do not necessarily require a detailed design to yield useful results, they may be used early in the design process. Furthermore, they do not require expensive models of the device design to be manufactured and tested, so they may well be cost-effective. They do, however, suffer from the limitation that they cannot tell you what you do not already know.

### *Empirical techniques*

In contrast, empirical techniques, such as testing, may play a more investigative role and help uncover hidden problems with the device design, but they are generally less systematic and less comprehensive.

### *Combined techniques*

Empirical techniques can be used to assist analytical methods by providing further information for analysis. For example, to complete a fault tree analysis of the device design it may be necessary to quantify some of the likelihoods of failure by testing the relevant components.

Conversely, a critical task may be identified through analysis of the design. Subsequently, empirical tests may be carried out to learn more about the potential failure modes, which may not be identified through pure analysis.

It may be advantageous, therefore, to use a combination of analytical and empirical techniques in the verification of a device if the chance of finding device problems is to be maximised. This is suggested practice by the FDA, as illustrated in the quotation on this page.

“A reasonable amount of both actual testing and failure mode and effects analysis should be done before a device is clinically tested and/or placed into production.”

*Medical device quality systems manual: a small entity compliance guide, Publication No.: FDA 97-4179, FDA (1996)*

## 2 CHECK THE VERIFICATION METHOD

Just as the design should be verified, verification methods should be reviewed to ensure they are likely to produce the intended quality of results.

Such a review may be cursory. However, a more involved review may take place, particularly for more critical verification activities, or when there is a significant degree of uncertainty in the quality of the verification approach. This amount of uncertainty often occurs when a novel verification method has been developed and, for reasons given below, it may be helpful to review the method with individuals who have a special insight into the issues involved for each of the three elements of verification.

### *The requirements*

These are best reviewed with clinical experts, who have a particular insight into the conditions of device usage, and with device engineers, who appreciate how such needs relate to engineering requirements (see opposite).

### *The device model*

The model and its ability to represent the properties of the finished device are best reviewed by the designer, who has responsibility for the design of that part of the device that is to be verified, or by those who have manufactured the model.

### *The verification method*

The method and how it could yield inaccurate results are best reviewed by a person with previous experience of this particular method or similar methods – for example, a test engineer or a representative of the conformity assessment body involved in the approval of the device.

The review of the verification method is similar to a device-based FMEA because it investigates how the verification elements could yield inaccurate

*A company designing a surgical device had to perform a considerable amount of redesign and re-verification because a requirement for waterproofing the device was misleading and led to the wrong test.*

results and what the effects of such a failure could be. In other words, it investigates how verification could fail, by inducing a false positive result or a false negative result. As it focuses on verification, this method is called a *Verification Failure Mode and Effects Analysis* (VFMEA).

### **When to perform a VFMEA**

To determine whether a VFMEA is worthwhile, a preliminary review of the uncertainty in each verification element (requirements, method and model) should take place. Following this, the effect of a false result from the verification should be assessed, as discussed in [Step 2.1](#) in [Part 2](#). A VFMEA may be particularly appropriate for key verification activities, where it is imperative that adequate results are produced.

### **How to perform a VFMEA**

For each verification activity, the modes of failure for each of its three verification elements should be analysed to ascertain whether they could be: *incomplete*, and/or *incorrect*.

Various ‘guide words’ may be used as stimuli for considering whether each element could be incomplete or incorrect in some way. These include the words ‘no’, ‘not’, ‘more’, ‘less’, ‘also (both)’, ‘part of’, ‘reverse’, ‘wrong one’.

For example, when considering the verification method, an incorrect result may occur because the method gives a lower (‘less’) reading than it should.

*When measuring the maximum magnetic field strength in a magnetic resonance imaging (MRI) machine, the location and orientation of the test probe may influence the result. Similarly, the verification method may be incomplete if it records only a proportion of (‘part of’) the parameter to be measured. For example, when testing the maximum field strength of the MRI machine, has the maximum field strength been measured at a single location or throughout the machine?*

The following sections discuss in more detail how each of the verification elements may be considered.

### **Requirements VFMEA**

As already discussed, incomplete or incorrect requirements can create a variety of verification problems, and incomplete requirements will almost certainly result in incomplete verification.

First of all, consideration should be given as to whether all requirements have been identified, perhaps by performing a design review. Next, each requirement should be examined using the ‘guide words’ to assess whether or not it is incorrect.

### **Model VFMEA**

For a variety of practical reasons, models used for carrying out the verification will often behave differently from the final device design. For example, alternative manufacturing methods or materials may be used in order to reduce costs.

Similarly, the device model may not be truly representative of the device design at a particular point in the design process.

*In the case of a finite element analysis for a stress calculation, the fineness of the mesh will affect the accuracy of the results. A coarser mesh may be chosen for practical reasons, at the expense of such accuracy.*

Therefore, for both types of model ‘infidelity’ it is essential to consider the significance of these differences – the ‘guide word’ approach may be helpful in doing this.

“We completely overlooked a critical element of the input. Therefore we didn’t test for it, because we didn’t actually realise that it was so critical.”

(Medical device regulatory affairs manager)

An example of a requirements-related problem

A machine was designed for the processing of a medical device. At the prototyping stage, for reasons of convenience, inexpensive models of the device were used to test the machine. Unfortunately, the models were so insufficiently representative of the final device that a number of key design problems were not identified at this point.

Some time later, when the ‘finished’ machine was tested – this time with the actual medical device – these problems surfaced. An enormous redesign project then took place, at a huge expense and delay to the project.

An example of a poor device model



When testing the corrosion resistance of some medical devices, localised testing may be inadequate, even if the rest of the device is made from the same material. This is the case since the geometry, such as the presence of crevices or pitting, may influence the test result, yet may vary across the device.

An example of a poor verification method

*A finished device may be manufactured from a plastic, which is then sterilised. During design, any testing of a prototype device or component should take into account the fact that the sterilisation procedure may compromise ('less') its mechanical properties.*

Thus, the attributes of each model should be examined systematically to determine if any differences between prototypes and the finished device could influence the verification results significantly.

### **Method VFMEA**

Creating a verification method which yields an accurate result may often be difficult because of the need to appreciate the underlying scientific and engineering principles, as illustrated on the left. Such principles usually need to be incorporated into the design of a good experiment.

*Consider the difficulties of designing an accurate accelerated life test for fatigue testing a hip joint. An attempt to decrease the duration of the test by increasing the cycling frequency may strongly influence the estimate of the true fatigue life if the experiment is not carefully designed.*

In such cases, it is particularly important to involve 'experts' in the review of the verification method.

As well as applying the 'guide words' to review the verification method, malfunctions of equipment involved in the execution of the method should also be considered – a lack of calibration, or miscalibration, of the test equipment may produce misleading test results and invalidate subsequent critically important decisions.

## DOCUMENTING PLANS AND PROTOCOLS

This section focuses on verification-related documentation. It outlines the basics for documenting the verification plans, protocols and results, the objective being to complement any existing company procedures and regulatory and quality system requirements. It is, therefore, not intended as a stand-alone document as it outlines only a proportion of all documentation requirements for medical device design and development.

Documentation is necessary for a variety of reasons, including satisfying regulatory and quality system requirements, helping with liability protection and providing records to pave the way for an efficient design and development process. As may be seen in the adjacent quotation, records may also be required later.

All verification-related activities should be documented to some extent, unless it is clear that they bear no relation to the proof required for the final device design.

However, as may be seen in the quotation on the right, the degree to which the documentation is required will depend greatly upon the premarket and postmarket risks, the regulatory and quality system requirements and company procedures. Early in the design process, non-key verification activities may require only informal documentation in lab books. Later, particularly if design controls are being applied, dedicated (formal) documents may be required.

### **Existing guidance on documentation**

The Global Harmonization Task Force (GHTF) and the Co-ordination of Notified Bodies for Medical Devices (NB-MED) have both produced guidance that discusses documentation in more detail. These sources are referenced in the box on the facing page.

*“The design of the component changed ten times during the course of six months. As you can imagine, they can’t now go back and work out which rack they used for which tests. Consequently it’s quite difficult to know which results are valid for the final process, and there’s quite a lot of re-testing that may now be required.”*

*(Medical device regulatory affairs manager)*

*“The detail and extent of such activities and documentation should be determined on the basis of the classification of the device, its complexity and the outcome of risk analysis.”*

*Summary technical file for premarket documentation of conformity with requirements for medical devices,  
Global Harmonization Task Force (1999)*

### References on documentation:

- *Summary technical documentation for demonstrating conformity to the essential principles of safety and performance of medical devices (STED)*, document number SG1/NO11R16, working draft, Global Harmonization Task Force (2000)
- *Technical Documentation*, document number NB-MED/2.5.1/Rec5, Co-ordination of Notified Bodies Medical Devices (2000)

“Verification... should also be done according to a written protocol(s). The protocol(s) should include defined conditions for the testing.”

*Medical device quality systems manual: a small entity compliance guide*, Publication No.: FDA 97-4179, FDA (1996)

### Documenting the verification plan

This is relatively straightforward since the plan contains only a reference as to when each verification is expected to be carried out during the design process. This is discussed in *Stage I* of *Part 2*.

### Documenting the verification protocols

As discussed in *Stage I* of *Part 2*, a draft of each verification protocol should be made early in the design process. At this stage, there may be many changes to the methods used and therefore, for practical reasons, it is not essential to formalise the documentation. Nevertheless, as stated earlier, it is important that the details are recorded in some manner as these records may form the basis of future verification activities. In addition to simply deriving the method, consideration of the complete protocol during the design process encourages a deeper analysis of the verification approach. This can help ensure that appropriate verification action is taken, and this is particularly important for key verification activities. Formal documentation and the derivation of a protocol are necessary for final verification.

### Verification protocol content

#### *Verification requirement*

This details the purpose of the verification – why it is being conducted and what it should reveal.

*If the performance of a critical seal is in doubt, a prototype may need to be tested to demonstrate that the requirement has (or has not) been met.*

#### *Acceptability criteria*

These must be stated in a format, often quantitative, that allows unambiguous assessment of whether or not they have been met. The criteria should be scientifically relevant, and may be justified through the provision of references to well-recognised published scientific work.

### ***Scope of the verification***

This states what the verification does and does not apply to. For example, the verification may be conducted on devices in fault conditions or in normal operating conditions. The capabilities and limitations of the verification method may also need to be considered, see [Developing verification methods](#) in *Part 3*.

*In order to perform a demonstration test of a catheter for the deployment of stents, a glass model of the vein that the catheter has to pass through may be manufactured. However, despite its transparency allowing easy inspection of stent deployment, this will be a poor representation of the mechanical properties of a real vein.*

### ***Characteristics of the model***

The details of the model of the device should be described or references, such as drawing numbers, made to any documents that define those details. Any differences between test samples, control samples and the final device to be marketed, such as the presence or lack of sterilisation pre-treatment, should also be specified.

### ***Verification method***

The description of the method should include details (possibly a schematic or photograph) of the set-up for the verification and its calibration, discussion of pertinent environmental characteristics – for example, temperature and humidity, and identification of any parameters to be measured. A rationale supporting the choice of method may also be required.

*The cycling rate in accelerated life testing of intra-articular prosthetic knee ligament devices should be justified based on normal use conditions.*

### ***References to standard methods***

Standards must be referenced if used to stipulate the verification method. Deviations from the standard should be highlighted and justified.

### **Verification protocol:**

- verification requirement
- acceptability criteria
- scope of the verification
- characteristics of the model
- verification method and resources required
- references to standard methods

“Designers often make glass models of arteries and then pass catheters through them to study their performance. While the contours of the glass model might be similar to those of an actual artery, the glass itself is rigid and smooth; therefore, a catheter passed through the model will probably not behave like a catheter introduced into a patient.”

Drues, M, “How to meet the new simulation testing requirements”, *Medical Device and Diagnostic Industry*, 20(3), 1998

### Results and conclusions:

- Results
- Analysis of the results
- Conclusions
- Declaration of conformity

| Requirement  | Protocol     | Result & Conclusion | Sign and date |
|--------------|--------------|---------------------|---------------|
| C34-R1-Rev13 | C34-P1-Rev13 | C34-C1-Rev2         | X 02/02/02    |
| C34-R2-Rev2  | C34-P2-Rev2  | C34-C2-Rev1         | X 02/02/02    |
| C34-R3-Rev1  | C34-P3-Rev1  | C34-C1-Rev1         | X 02/02/02    |

An example of a traceability matrix

## Documenting the results and conclusions

The results and conclusions may form part of the documentation for the protocol, or be in a separate document. The following may be recorded:

### *Results*

All data must be recorded, but in many cases a summary of the data will suffice, particularly if the results are presented at a regulatory inspection.

### *Analysis of the results*

This may be required if a statistical evaluation has taken place, for example.

### *Conclusions*

The extent to which the verification results meet the acceptability criteria should be discussed.

### *Declaration of conformity*

If compliance with a standard recognised by the regulatory authority has been claimed, a declaration of conformity to that standard may be required.

All work should be signed and dated.

## Using a traceability matrix

With a large number of verification-related documents to hand and the frequent changes throughout design, it is not difficult to lose track of the location and/or status of each document. A traceability matrix, which records the location and version of all documents, may help to overcome this problem. It can highlight where verification has yet to be performed, and may also help 'trace through' changes to the other relevant documents. For example, if a requirement is changed, it can show which protocol(s) also need to be changed.

In more complex projects computer tools may be used to help manage these documents, but a simple spreadsheet may be equally effective.

## MANAGING CHANGES IN THE DESIGN PROCESS

Changes to any of the three verification elements (the requirements, the model or the method) are everyday occurrences during the design process and quality system requirements for change control management, as set out in ISO 9001 and the FDA Quality System Regulation (QSR) Part 820.30, should be carefully noted.

Changes may occur for a variety of reasons. For example, requirements may be relaxed if they are found to be too difficult to fulfil, or the introduction of a new standard may require a change to the verification method. Changes often have a knock-on effect to other verification elements. A requirements change, for instance, may result in the need to change the design, further repetition of the verification on the new device model and, hence, project delays and overspend.

Many problems with verification are caused by unnoticed changes or a failure to appreciate their full effect. Determining the implications of a change requires an appreciation of the relationships between requirements, the design and the verification method, and a traceability matrix may be of assistance in this area, as discussed in *Documenting plans and protocols* in this part of the workbook.

During the design process, two types of review may be help to manage change and minimise development risks.

### 1. *Before carrying out key verification activities*

The likelihood and severity of any impending changes should be considered, as any changes may require verification to be repeated.

*For example, several components are usually needed to form a hermetic seal. When the seal is tested, these components are usually tested in unison. If a change to one of these components is imminent, there may be little point in carrying out the test before that change has been made.*

“Change is probably the biggest source of verification-related problems that we face.”

(Medical device designer and project manager)

“One of the things that has come up time and time again... The product worked initially, or at least appeared to work, but as the design got finalised it wasn't tested again”

(Medical device regulatory consultant)

## 2. *When a change occurs*

A review of the relevant verification elements, as discussed below, may help determine its effects.

### **Requirements changes**

As the design project progresses, various refinements to the design requirements will often take place. In addition to overt changes, additional requirements may also be identified; particularly as the form of the final design is specified in more detail.

Verification practice should be re-considered in the light of such changes – there might be a need to modify existing verification methods or simply repeat a previous verification activity in order to demonstrate that the device design still meets the revised requirement. Therefore, consideration should be given to the effects of each change on the design, the verification method and the results of any prior verification, which may now be invalid.

### **Design (model) changes**

Early in the design process, when various concepts are being investigated, a great many changes may occur to the device. Even though the changes are numerous, it may still be worthwhile to assess their effects, however brief such assessments may be.

Later in the design process, design changes are more likely to affect key verification activities. Therefore, the potential impact of each change must be assessed more carefully, especially if failure to identify the effects of a change might result in significant development and/or commercial risks.

As design progresses, the form of the model upon which the regular and final verification activities are conducted will inevitably change, and verification may consequently need to be repeated.

*For example, early in the design process an inexpensive prototype, such as a foam model, may be tested. However, even if little further design change takes place, a prototype which represents the final properties of the device design must also be tested. Clearly, such changes are likely to profoundly affect the results.*

For final verification activities, it is important that the model suitably represents the finished production device. There is always a danger that prototype devices behave differently from the finished production devices, even though they have been crafted carefully by personnel who have a good appreciation of the key requirements for manufacture – the prototype may perform better than the mass-produced device.

Furthermore, significant changes may be introduced to the production device as production is scaled up, by the introduction of new manufacturing processes, or by efforts to overcome manufacturability constraints.

*If a device is to be sterilised before use, verification may need to be conducted on sterilised device models, as sterilisation can adversely influence mechanical properties (see adjacent example). Therefore, final verification may need to be conducted on devices that are manufactured in pilot or actual production runs.*

### **Verification method changes**

Verification methods may be modified in response to requirements changes or design changes, as discussed above. External reasons for verification method changes include the introduction of a new ‘industry standard’ test method, which it may be prudent for the manufacturer to adopt. The effects of changes to the verification method should also be reviewed to determine their influence on the requirements or the device design.

“When performing tensile strength tests on prosthetic knee ligament devices in accordance with FDA’s Guidance Document, tests must be conducted on sterilised devices.”

*Guidance document for the preparation of investigational device exemptions and premarket approval applications of intra-articular prosthetic knee ligament devices, FDA (1993)*



## **APPENDIX – WEB-BASED STANDARDS AND REGULATORY INFORMATION**

## SOURCES OF STANDARDS INFORMATION

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

## SOURCES OF REGULATORY INFORMATION ON MEDICAL DEVICES

|                                       |  |
|---------------------------------------|--|
| EU Regulations and Guidance           | <a href="http://europa.eu.int/eur-lex/en/search/index.html">europa.eu.int/eur-lex/en/search/index.html</a> – select by year of issue and document number |
| UK Medical Devices Agency Guidance    | <a href="http://www.medical-devices.gov.uk">www.medical-devices.gov.uk</a> – select ‘Publications’, then ‘Regulatory’                                    |
| FDA Device Advice                     | <a href="http://www.fda.gov/cdrh/devadvice">www.fda.gov/cdrh/devadvice</a>   |
| Index of CDRH Web Documents           | <a href="http://www.fda.gov/cdrh/consumer">www.fda.gov/cdrh/consumer</a> – select ‘Topic Index’  |
| CDRH Guidance Documents & Reports     | <a href="http://www.fda.gov/cdrh/guidance.html">www.fda.gov/cdrh/guidance.html</a>   |
| Good Guidance Practice (GGP) Database | <a href="http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfGGP/Search.cfm">www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfGGP/Search.cfm</a>             |

(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.)

Pages 61 and 63 list sources of guidance that are more specific to verification.

## 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 – a framework*

This workbook, developed through extensive consultation with device manufacturers and an analysis of regulatory requirements, provides real guidance on good design practices for medical device development and a framework for effective validation, since this plays a vital role in defining the success of a product in both technical and economic terms.

---

Jointly published by:



ISBN 1-902546-12-1

Enquiries to: Institute for Manufacturing  
University of Cambridge  
Mill Lane, Cambridge, CB2 1RX, UK  
Tel: +44 1223 766141  
Fax: +44 1223 464217  
Email: [ifm-enquiries@eng.cam.ac.uk](mailto:ifm-enquiries@eng.cam.ac.uk)  
[www.ifm.eng.cam.ac.uk](http://www.ifm.eng.cam.ac.uk)