
Good morning,

My name is Steven Crook and I have been working in Salisbury for over 25 years. Starting as a Medical Physicist I concentrated on microcomputer programming and then became involved in the field I am going to talk about today. Namely, medical device regulations and how you can ensure that they are properly complied with.

## Lecture overview

- Current EC regulatory framework – in detail
- Specific Requirements of the Medical Devices Directive (MDD) – Classify your device, Essential Requirements
- Compliance – who monitors Medical Devices in UK?
- Changes with the new EU Medical Device Regulations
- Motivation for putting a Quality Management System (QMS) in place – do I need it? What does it do for me?
- Complying with other standards
- Areas to be included in the QMS
- Assessment and maintenance of the QMS
- US regulatory framework – overview of 510(k)
- Other regulatory frameworks
- Conclusions

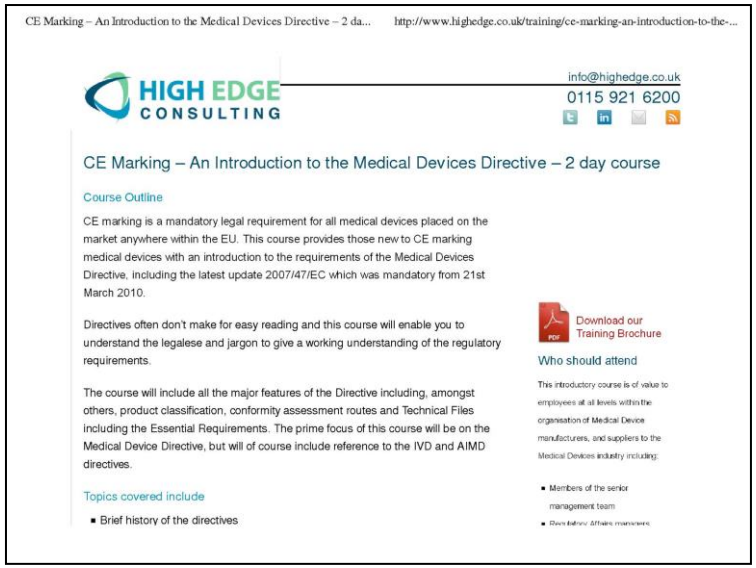
I am pretty sure that very few of you will have signed up to the course here with the thought that you would need to become familiar with European legislation. However, as you have learnt about electronics and medical devices you will have encountered accepted ways of doing things and reasons for following standards and guidance. My aim is to take you through the overarching regulations. Then spend quite a bit of time on the Essential Requirements of the MDD. Following that I will explain why you might need additional guidance and standards to demonstrate that you are doing what you say you do. I will follow this up with specifics from my experience.

This will then lead into specific standards – I will talk about the ones I know about.

If you are dealing with a successful medical device then you will want to export it and therefore come up against other regulatory systems. Of these the most important is probably the US Food and Drugs Administration (FDA). I have put a device through their 510(k) program so I will explain what that entails.

Lastly, I will describe some other countries regulatory systems.

There will be a break after roughly an hour and I am happy to take questions throughout.



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# CE Marking – An Introduction to the Medical Devices Directive – 2 day course

## Course Outline

CE marking is a mandatory legal requirement for all medical devices placed on the market anywhere within the EU. This course provides those new to CE marking medical devices with an introduction to the requirements of the Medical Devices Directive, including the latest update 2007/47/EC which was mandatory from 21st March 2010.

Directives often don't make for easy reading and this course will enable you to understand the legalese and jargon to give a working understanding of the regulatory requirements.

The course will include all the major features of the Directive including, amongst others, product classification, conformity assessment routes and Technical Files including the Essential Requirements. The prime focus of this course will be on the Medical Device Directive, but will of course include reference to the IVD and AIMD directives.

## Topics covered include

- Brief history of the directives

Download our Training Brochure

## Who should attend

This introductory course is of value to employees at all levels within the organisation of Medical Device manufacturers, and suppliers to the Medical Devices industry including:

- Members of the senior management team
- Regulatory Affairs managers

## EC Framework

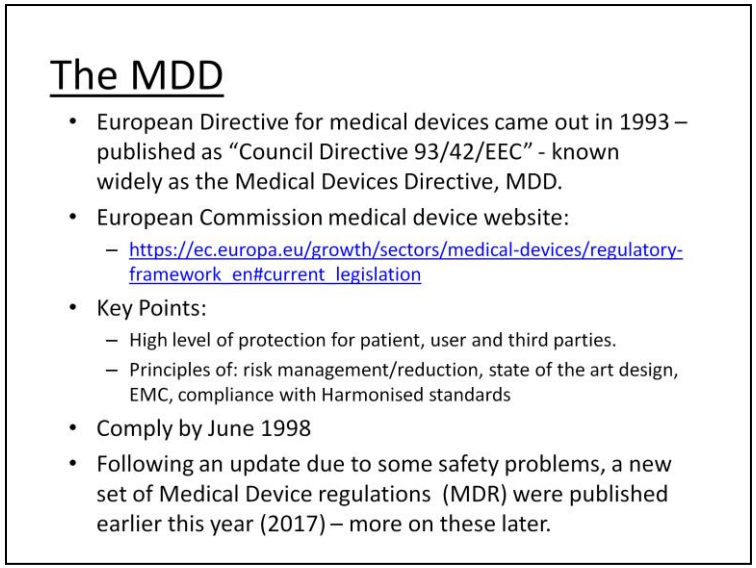
- **EEC - set up to facilitate trade between member states**
- Medical device field – protectionism:
  - Health Ministry's would require that medical devices sold in their territory had to comply to local regulations and safety requirements
  - Might have included specific tests only done by their approved laboratories or clinical trials with a fee payable to the government.
- EEC introduced directives to address this problem - so called 'New Approach'


The UK is a member of the EEC/EC and the main purpose of this organisation is to facilitate trade between the Member States.

[read slide]

The member states are required to implement the EC directives by incorporating them into local legislation. We often hear how UK fully adopts everything coming out of Brussels when other member states are not perhaps as keen to make their laws correspond quite so closely.

By making sure that each state followed the same rules it was intended to remove barriers to trade that would prevent products being sold as widely as possible – this is good for trade. Also the populations in a particular state would not be disadvantaged because of local regulations which meant that it was harder for companies to access their particular market.



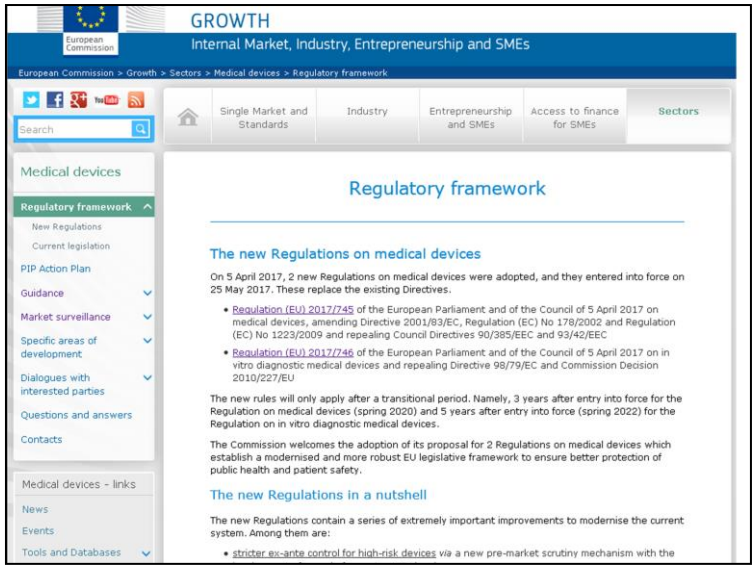

The directive governing medical devices came out in the EC Official Journal in 1993.

If you read it then you can see the angle it is coming from – particularly where it requires a 'high level of protection for patient, user and third parties'.

It also stresses risk management and risk reduction, use of 'state of the art' (design/technology/materials perhaps..), EMC and compliance with other standards.

Manufacturers were given 5 years to comply.

The link in this slide takes you here.. [next slide]




Further down this page there are links to the main directive and also to other directives that cover the higher risk medical devices (active implantable) and in vitro diagnostics.

The Regulations were published this year and will come into force in 2020. So there are three years to comply.

Notice where the legislation sits in the thinking of the EC – within "Growth".

https://ec.europa.eu/growth/sectors/medical-devices/regulatory-framework_en#current_legislation

http://ec.europa.eu/growth/sectors/medical-devices/pip-action-plan_en

## 1996 - The situation in Salisbury Hospital

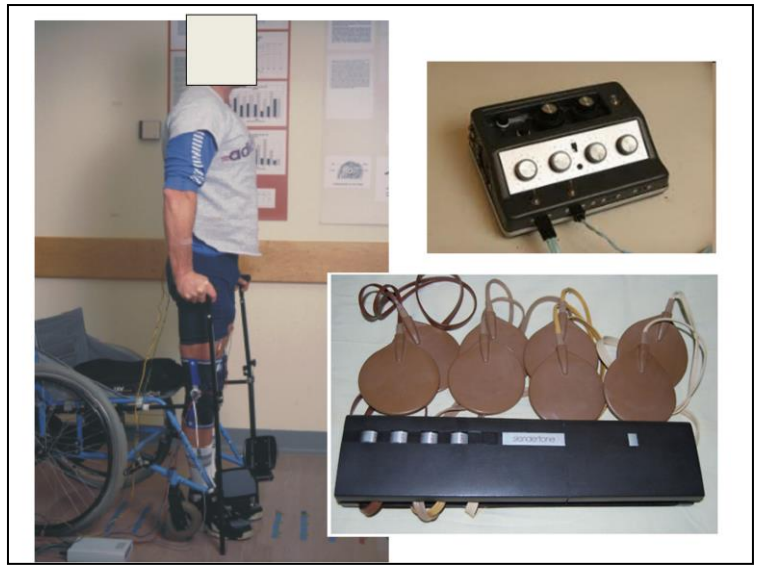
- Working in the field of electrical muscle stimulation. Started with paraplegic standing using modified Slendertone ™ machines.
- developed a dropped foot stimulator (P. Taylor) and a clinical service was developing.
- Other stimulators also being made in lesser numbers (2 and 4 channel exercise plus a 2 channel dropped foot)
- Started to supply other clinics
- Health service changes were encouraging “competition” between hospitals.


So, how did I get myself into this situation.. [run through slide]

Because we were short of money and there were no devices on the market that would do what we wanted we put an appeal in the local papers asking for discarded slimming machines.

Our therapists asked us to help with some incomplete spinal patients – existing equipment was not up to the job..

Outside of a pretty small community, FES had a poor reputation among medics and therapists.



Here are some examples of the devices we used for training paraplegics to stand. The boxes on the right are Slendertone machines that have been adjusted in order to reduce the stimulation frequency and increase the pulsewidth. The brown pads are the electrodes and the other side of the pad is conductive rubber. A layer of wet sponge is used between these pads and the skin and the whole lot is held in place with elastic straps. These machines predate CE marking and may not fall into the category of medical device anyway – can discuss later.

Chap on the left has a closed loop standing system. Much more compact and with self adhesive electrodes. CE marking is looming….

I had just finished my PhD and was assumed to have the time to look into what we needed to do about our electrical muscle stimulators.

1996 - Salisbury Hospital - 2007


Odstock Drop Foot Stimulator (Orthosis)

On the left, the Odstock Dropped Foot Stimulator, ODFS.  Packed with analogue components

On the right, the ODFS Pace, microcontroller based.

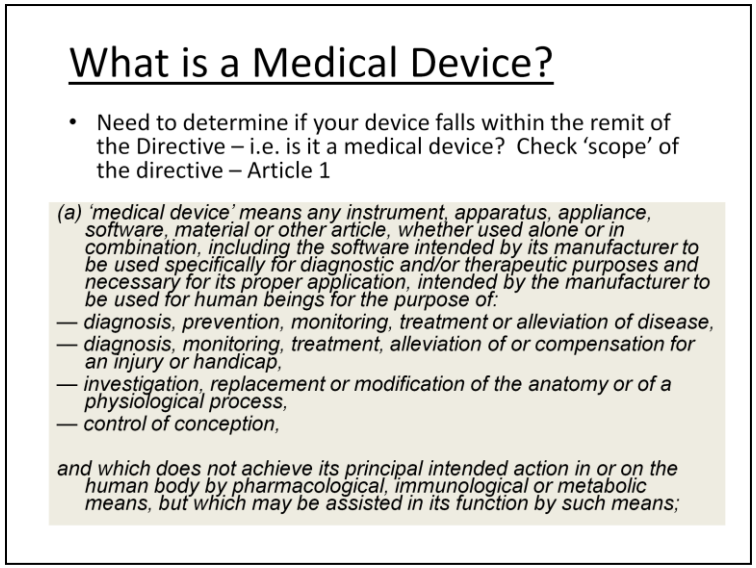
Need to take a look at the MDD…

The MDD is a pretty thin document but you need to read through it a few time to get the overall picture of what it is asking.

Image shows (from the top) quality standard, MDD, quality manual and a Technical File.

The MDR is 336 pages but it incorporates Active Implanted Medical Devices (currently separate – AIMDD)

The MDD starts off with a lot of legal language.  The first section of importance is Article I.



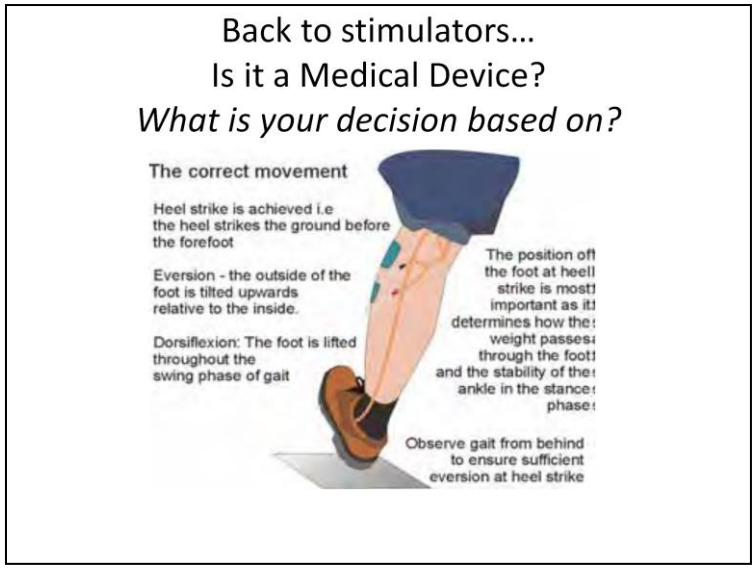

Article 1 is the first crucial part of the MDD. If you are designing a new product then you need to be aware of how it fits into this 'scope' this definition of what constitutes a medical device.

Even if you are sure that your device is a 'medical device' it is still worth looking at the wording here to establish on what basis you will be claiming that this is the case.

The MDD was revised in 2007 and one of the changes was to explicitly include 'software' as a medical device. So, a program on a PC which gives a diagnosis and/or monitoring of a disease will fall into the category of medical device and become subject to the requirements of this directive.

The MDR adds in cosmetic devices, contact lenses and a few other things (Annex XVI, MDR)

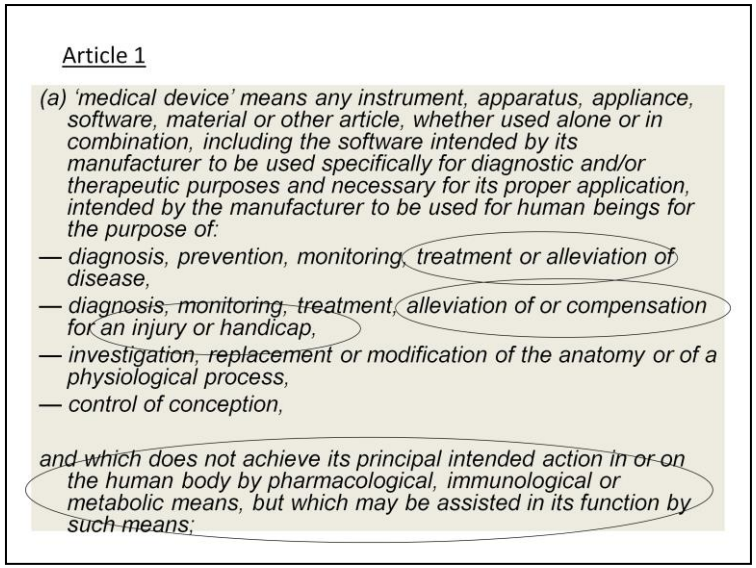
So, is a muscle stimulator a medical device..?




Our Odstock Dropped foot stimulator, what does it do and does that make it a medical device?

Well, it is a neuromuscular stimulator which means it stimulates the nerve in order to get a muscle to contract. By placing an electrode over the common peroneal nerve just below the knee the act of stimulating the nerve actually gets two groups of muscle contractions. Hip flexion and ankle flexion. The stimulation stops when the 'good' leg comes off the ground – this is detected by a thin switch in the shoe.

In order to decide which bit of Article 1 applies we should look at how it is intended to make a difference to the user. Article 1 again..



Article 1

*(a) 'medical device' means any instrument, apparatus, appliance, software, material or other article, whether used alone or in combination, including the software intended by its manufacturer to be used specifically for diagnostic and/or therapeutic purposes and necessary for its proper application, intended by the manufacturer to be used for human beings for the purpose of:*

*— diagnosis, prevention, monitoring, treatment or alleviation of disease,*

*— diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap,*

*— investigation, replacement or modification of the anatomy or of a physiological process,*

*— control of conception,*

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

From a knowledge of our device we can pick out the appropriate terms in Article 1. So this is not just defining our device but it becomes a shortcut to justifying our device as a medical device.

By improving somebody's walking, what are we doing? I would say that we are alleviating the effects of a disease and we are alleviating or compensating for a handicap. We are not really treating a disease – nobody is going to recover from a stroke because they have had treatment from a peripheral nerve stimulator but their quality of life can be improved though making their walking more normal.

Note also the phrase at the bottom, what is this designed to pick up?

- You're reading the wrong directive, should be looking at something to do with drugs.

Article 2 of the MDR – pretty similar, amended for 'reagent' & 'prediction and prognosis'

'medical device' means any instrument, apparatus, appliance, software, implant, reagent, material or other article intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the following specific medical purposes:

— diagnosis, prevention, monitoring, prediction, prognosis, treatment or alleviation of disease,

— diagnosis, monitoring, treatment, alleviation of, or compensation for, an injury or disability,

— investigation, replacement or modification of the anatomy or of a physiological or pathological process or state,

— providing information by means of *in vitro* examination of specimens derived from the human body, including organ, blood and tissue donations,

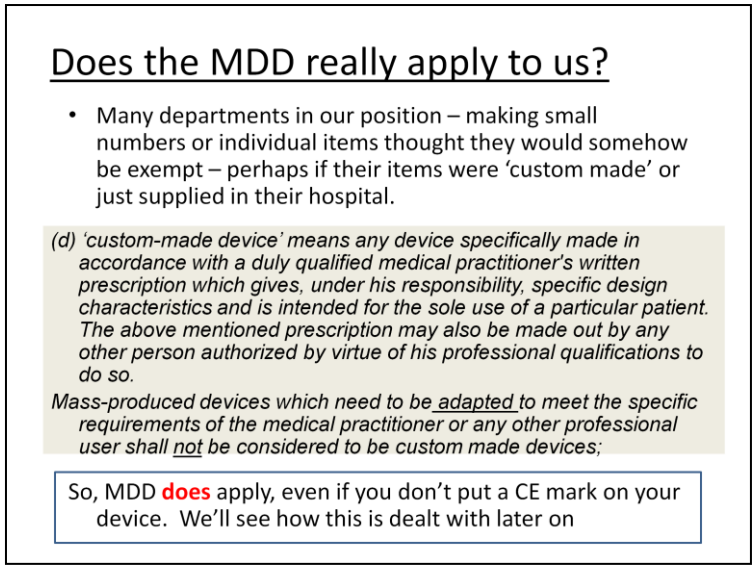
The MDR covers in vivo diagnostics as well.

Back to stimulators…

It is a Medical Device

- Because it ‘treats or alleviates a disease or handicap’


We can now be sure that our device is a medical device and we can borrow some terminology from Article 1 to express this in a compact way.




Article 1 – defining medical devices – goes on to cover custom made devices so the MDD will apply..

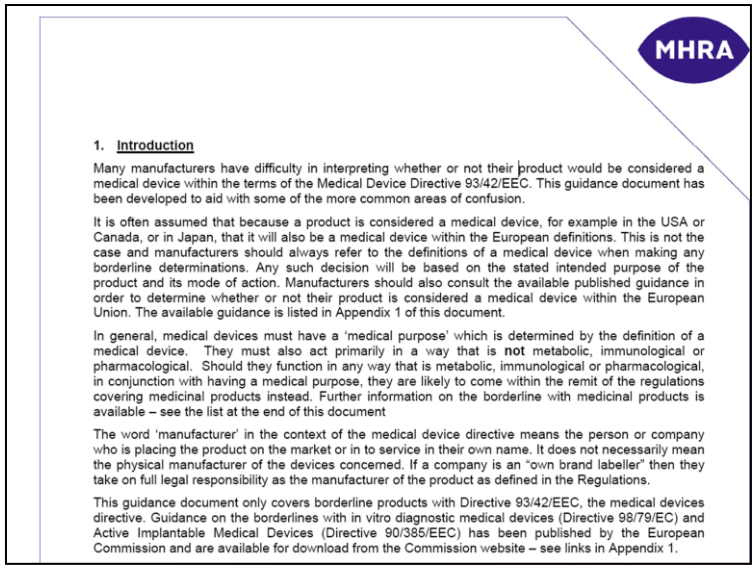
I have underlined 'adapted' as well, so we can think of products that the maker might say were just components and the clinician or technician putting them together in a patient specific way would become the manufacturer. This is covered - components are treated as a medical device. The supplier/maker etc is the manufacturer and takes liability as long as they are used as described in the instructions.

So, you can see the thrust of the MDD and how it would achieve it's underlying purpose. A big clue is in the fact that it has been implemented in UK law as part of the Consumer Protection legislation. SI3017 1994

## Additional Guidance

- The UK Medicines and Healthcare products regulatory agency (MHRA) have publications on their website. These are helpful in interpreting 'grey areas'
- https://www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency/services-information


National bodies have produced their own guidance. In the UK this is the MHRA. In EC jargon the MHRA is the UK Competent Authority, i.e. they are responsible for policing compliance with the MDD in the UK and for receiving and disseminating device alerts from other States Competent Authorities. The jargon for this is *vigilance*. I'll be coming back to that..



MHRA

1. **Introduction**

Many manufacturers have difficulty in interpreting whether or not their product would be considered a medical device within the terms of the Medical Device Directive 93/42/EEC. This guidance document has been developed to aid with some of the more common areas of confusion.

It is often assumed that because a product is considered a medical device, for example in the USA or Canada, or in Japan, that it will also be a medical device within the European definitions. This is not the case and manufacturers should always refer to the definitions of a medical device when making any borderline determinations. Any such decision will be based on the stated intended purpose of the product and its mode of action. Manufacturers should also consult the available published guidance in order to determine whether or not their product is considered a medical device within the European Union. The available guidance is listed in Appendix 1 of this document.

In general, medical devices must have a 'medical purpose' which is determined by the definition of a medical device. They must also act primarily in a way that is **not** metabolic, immunological or pharmacological. Should they function in any way that is metabolic, immunological or pharmacological, in conjunction with having a medical purpose, they are likely to come within the remit of the regulations covering medicinal products instead. Further information on the borderline with medicinal products is available – see the list at the end of this document

The word 'manufacturer' in the context of the medical device directive means the person or company who is placing the product on the market or in to service in their own name. It does not necessarily mean the physical manufacturer of the devices concerned. If a company is an "own brand labeller" then they take on full legal responsibility as the manufacturer of the product as defined in the Regulations.

This guidance document only covers borderline products with Directive 93/42/EEC, the medical devices directive. Guidance on the borderlines with in vitro diagnostic medical devices (Directive 98/79/EC) and Active Implantable Medical Devices (Directive 90/385/EEC) has been published by the European Commission and are available for download from the Commission website – see links in Appendix 1.

If we just pick one bulletin as an example, Bulletin 20, intended to help with 'grey areas'…

You don't have to read very much of it to see that you should be going to the MDD anyway…

## MHRA – Competent Authority

- The MHRA has responsibility for 'policing' the MDD in the UK – vigilance.
- In EU jargon, they are the Competent Authority for the UK

*Article 2*

**Placing on the market and putting into service**

"Member States shall take all necessary steps to ensure that devices may be placed on the market and/or put into service only if they comply with the requirements laid down in this Directive when duly supplied and properly installed, maintained and used in accordance with their intended purpose."

If you encounter a medical device that you know or suspect is not compliant with the MDD despite having a CE mark then the MHRA are the body that you would report this to.

## What does the MDD require you to do?

**Article 3**

**Essential requirements**

"The devices must meet the essential requirements set out in Annex I which apply to them, taking account of the intended purpose of the devices concerned."

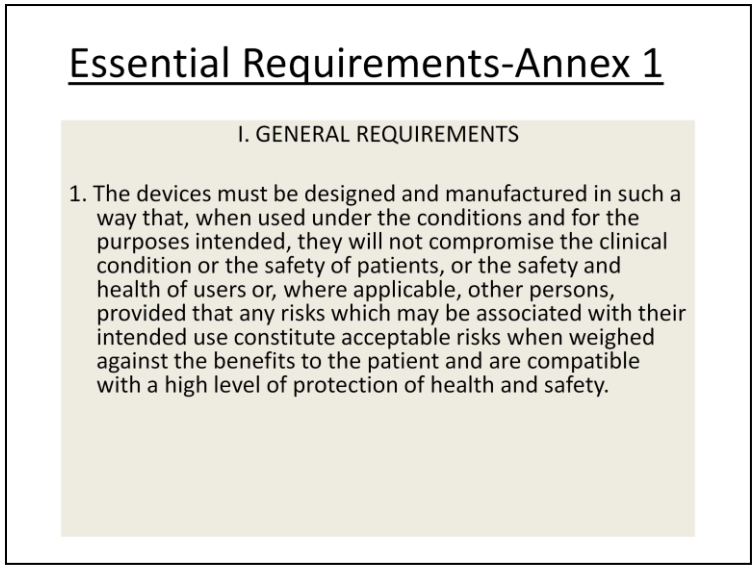
There are a lot of "Essential Requirements" so I will just start with a few of the opening paragraphs and add in more detail later. It won't be complete detail but some specific examples.

## Articles and Annexes

***Articles*** **come first and describe the application of the Directive – may direct you to various *Annexes* – located at the rear of the Directive.**

- Annex I – Essential Requirements, applies to all Medical Devices – *whether you CE mark them or not!*

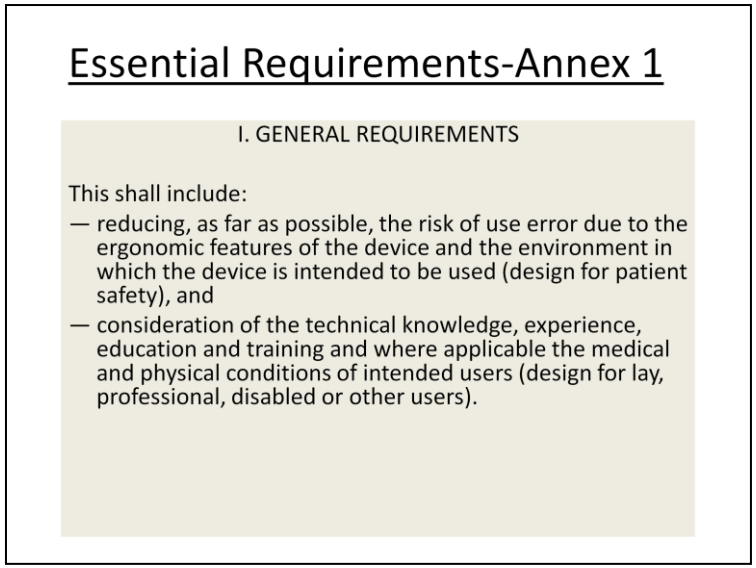
If you are making something that has a medical purpose and you try it on somebody and it injures them then the question is bound to be asked – Did your device comply with the requirements of the MDD. These requirements are the Essential Requirements, Annex 1




What is stated here is pretty much what you would expect – nobody is likely to argue with these requirements.

Placing the emphasis on ergonomics first is not just random – investigations into adverse incidents shows that ergonomics play a primary role, poor ergonomics contribute to user error. Need to think who the 'user' is going to be..

2nd indent – maybe more consideration should be paid to design for older users..

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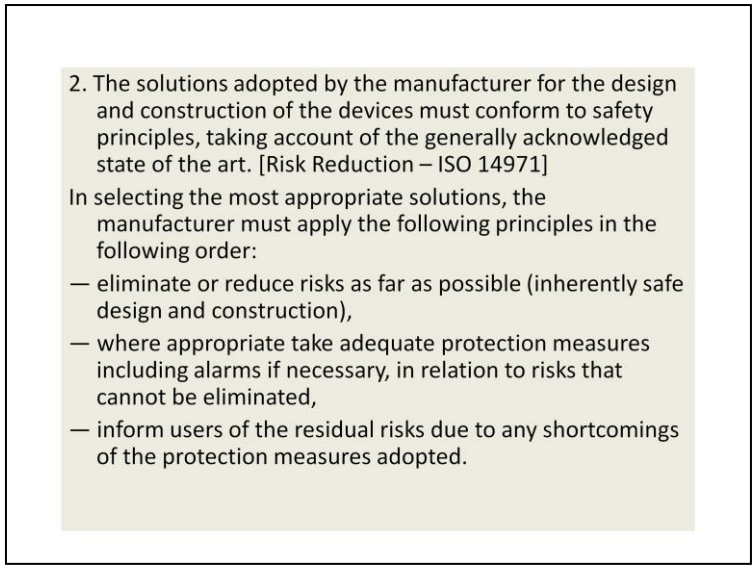
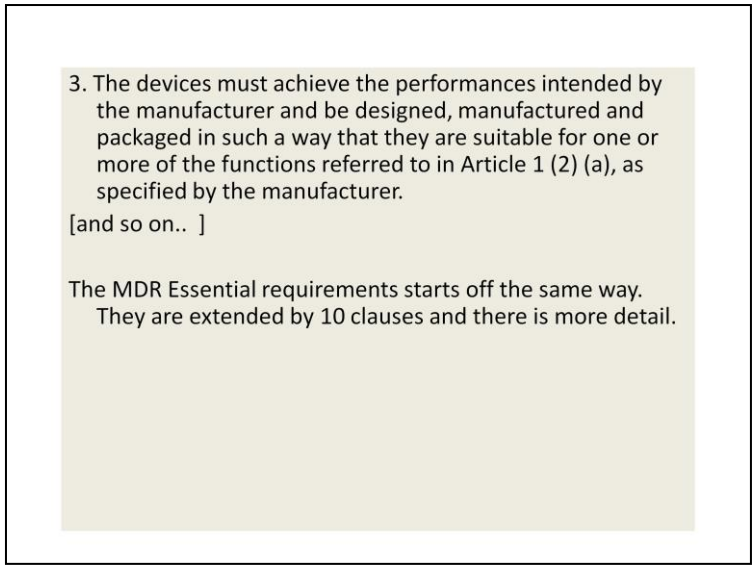


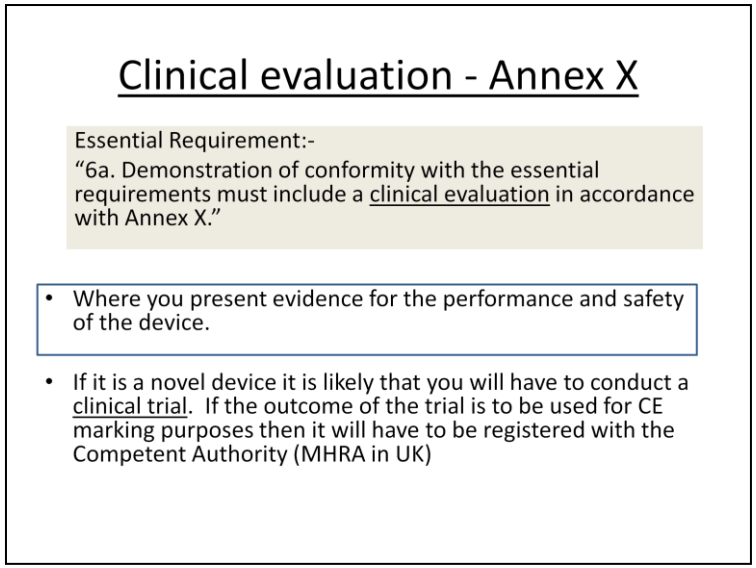

'State of the art'.. i.e. a comparison with other things that are out there..

How do we inform users of residual risks? Labelling, manuals and training..

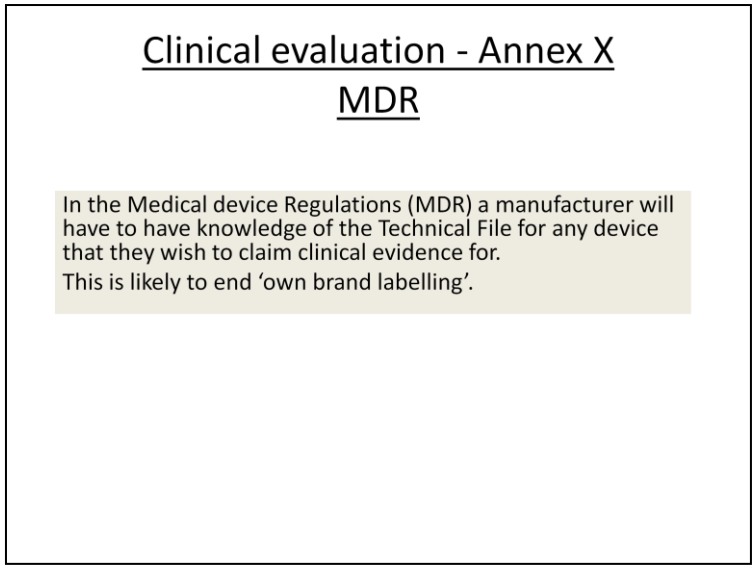
Software..




Designed manufactured and packaged in such a way that they can do their job. Make sure that there is nothing about the delivery or packaging that is going to cause a failure or damage.




Clinical Evaluation is an important section of the Essential requirements. This is where you will present the evidence for the performance and safety of the device. If it is a novel device it is likely that you will have to conduct a clinical trial. If the outcome of the trial is to be used for CE marking purposes then it will have to be registered with the Competent Authority (MHRA in UK)




Clinical Evaluation and post-market clinical follow up is a big change of emphasis in the MDR and manufacturers are already being assessed against the guidance. (MEDDEV 2.7.1 v4)

## *MDD Article 5* - Reference to standards

1. Member States shall presume compliance with the essential requirements referred to in Article 3 in respect of devices which are in conformity with the relevant national standards adopted pursuant to the harmonized standards the references of which have been publishes in the *Official Journal of the European Communities*; Member States shall publish the references of such national standards.
   [snip]

[I'll say more on this when we return to Essential Requirements]

- In other words – If there is a harmonised standard that the EC has adopted and you comply with the standard then you automatically comply with the Essential Requirements.

This is a roundabout way of saying that: If there is a harmonised standard that the EC has adopted and you comply with the standard then you automatically comply with the Essential Requirements.

## *MDD Article 9* - Classification

- Devices shall be divided into Classes I, IIa, IIb and III. In order to determine the class you have to run through the questions in Annex IX.
- Annex IX asks lots of questions.. [p53 MDD]

I've skipped some interim clauses defining how the Commission and Member states should act in various circumstances – e.g. marketed devices not meeting the ER.

Devices shall be split into three classes based on their potential for doing harm. Class II is split into IIa and IIb

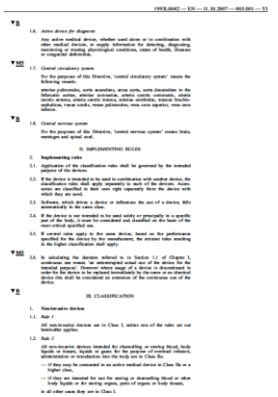
In order to determine the class you have to run through the questions in Annex IX

## If I were a muscle stimulator, which Class would I be?

- Lets step through the rules and see..

  (Double click on picture right to see)

- make sure you go all the way to the end!
- http://ec.europa.eu/consumers/sectors/medical-devices/files/meddev/2_4_1_rev_9_classification_en.pdf



1993L0042 — EN — 11.10.2007 — 005.001 — 53

▼B

1.6. *Active device for diagnosis*

Any active medical device, whether used alone or in combination with other medical devices, to supply information for detecting, diagnosing, monitoring or treating physiological conditions, states of health, illness or congenital deformities.

▼M5

1.7. *Central circulatory system*

For the purposes of this Directive, 'central circulatory system' means the following vessels:

arteries pulmonales, aorta ascendens, arcus aortae, aorta descendens to the bifurcatio aortae, arteriae coronariae, arteria carotis communis, arteria carotis externa, arteria carotis interna, arteriae cerebrales, truncus brachiocephalicus, venae cavae, venae pulmonales, vena cava superior, vena cava inferior.

▼B

1.8. *Central nervous system*

For the purposes of this Directive, 'central nervous system' means brain, meninges and spinal cord.

II. IMPLEMENTING RULES

2. **Implementing rules**

2.1. Application of the classification rules shall be governed by the intended purpose of the devices.

2.2. If the device is intended to be used in combination with another device, the classification rules shall apply separately to each of the devices. Accessories are taken into account for their own right separately from the device with which they are used.

2.3. Software, which drives a device or influences the use of a device, falls automatically in the same class.

2.4. If the device is not intended to be used solely or principally in a specific part of the body, it must be considered and classified on the basis of the most critical specified use.

2.5. If several rules apply to the same device, based on the performance specified for the device by the manufacturer, the strictest rules resulting in the higher classification shall apply.

▼M5

2.6. In calculating the duration referred to in Section 4.1 of Chapter I, continuous use means "an uninterrupted actual use of the device for the intended purpose". However where usage of a device is discontinued to be replaced immediately by the same or an identical device, the use of the device is to be considered as continuous use of the device.

▼B

III. CLASSIFICATION

1. Non-invasive devices

1.1. *Rule 1*

All non-invasive devices are in Class I, unless one of the rules set out hereinafter applies.

1.2. *Rule 2*

All non-invasive devices intended for channelling or storing blood, body liquids or tissues, liquids or gases for the purpose of eventual infusion, administration or introduction into the body are in Class IIa:

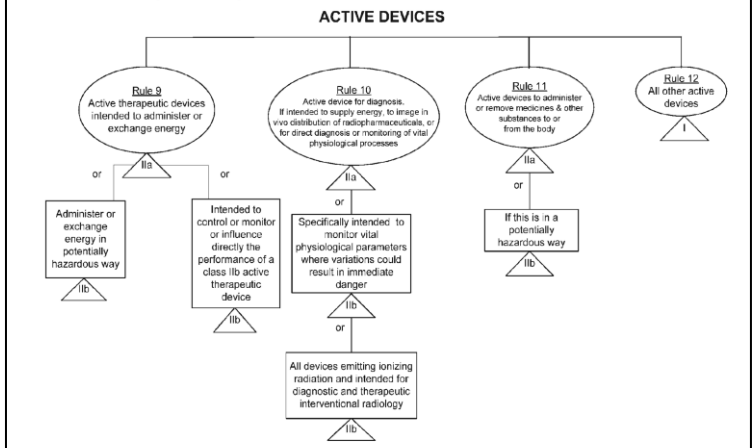
— if they may be connected to an active medical device in Class IIa or a higher class,

— if they are intended for use for storing or channelling blood or other body liquids or for storing organs, parts of organs or body tissues,

in all other cases they are in Class I.

It is quite simple to use the Annex in the Directive in most cases – make sure you go all the way to the end in case there is a twist.

# If I just pick on active devices..



## *MDD Article 10* - Information on incidents

- Adverse Incident reporting:
  - if a device causes harm or something happened with the potential to cause harm then it can be reported to the MHRA by users, patients or manufacturers
- Forms available on MHRA website - excuse for a diversion..

## Revenge of the shower chair!

If you ever doubt the usefulness of MHRA bulletins or device alert notices then this little diversion should make you think.

MHRA

Medical Device **ALERT**

**Ref. MDA/2003/029**
**Issued: 08 September 2003**

## DEVICE:

Examples of bath and shower seating equipment are: bath boards, bath benches, bath seats, bath lifts, bath hoists, shower seats, shower chairs, shower benches, shower stools, shower and changing benches (or stretchers) and foldaway shower seats.

## PROBLEM:

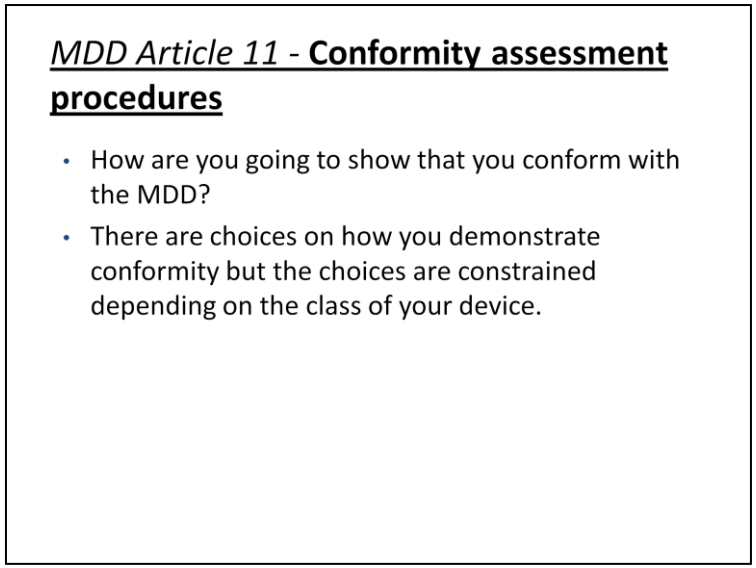
Some bath and shower seating equipment has drainage holes/slots which have the potential to entrap genitalia, leading to serious injury, pain and embarrassment.

The MHRA has received reports of four incidents in the last three months where male genitalia have become entrapped in the drainage holes of a variety of bath or shower seating equipment. These incidents resulted in cuts, lacerations and testicular bruising and in several cases the user had to be freed by the Fire Service. Similarly, an incident was recently reported involving an elderly woman with a rectal prolapse, which became entrapped in the holes of the seat on a bath hoist.

The size, shape and position of the drainage holes/slots influence the risk of entrapment.

The Medical Devices Agency previously highlighted this problem in Safety Notice SN9709, 'Bath and shower seating equipment: risk of injury', issued in May 1997.

Note: British Standard BS EN 12182:1999 'Technical aids for disabled persons - General requirements and test methods' requires that to prevent genitalia traps, holes and clearances between parts shall be less than 8mm or more than 75mm.

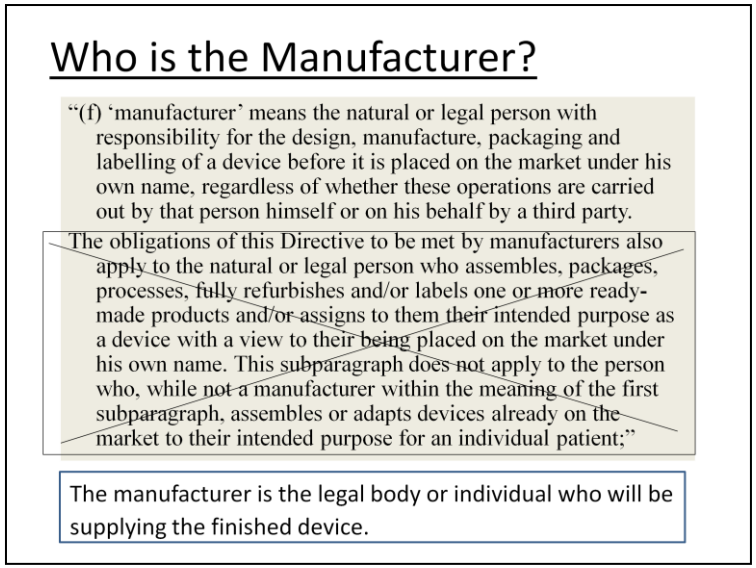



There is some work ahead of us but we should now consider how we are going to demonstrate that we conform to the MDD.

It is worth exploring who is going to be the manufacturer of the device. If you are a small hospital department and you are proposing to develop a high risk device then there could well be significant costs involved. Would it be better to go via NHS Innovations?

If you are working for a large company then they will have put dozens of devices through the regulatory process and you will be generating documentation to fit in with their established requirements.

What was the case with Salisbury/Odstock…??




OK, we have read through the MDD, we have skimmed the Essential Requirements and we are pretty happy that we have a medical device that we can supply to our local patients or place on the market for the benefit of our UK and European customers.

What we should consider now is who will take on the role of the Manufacturer? This is a legal position which doesn't necessarily mean the person who makes or assembles the medical device.

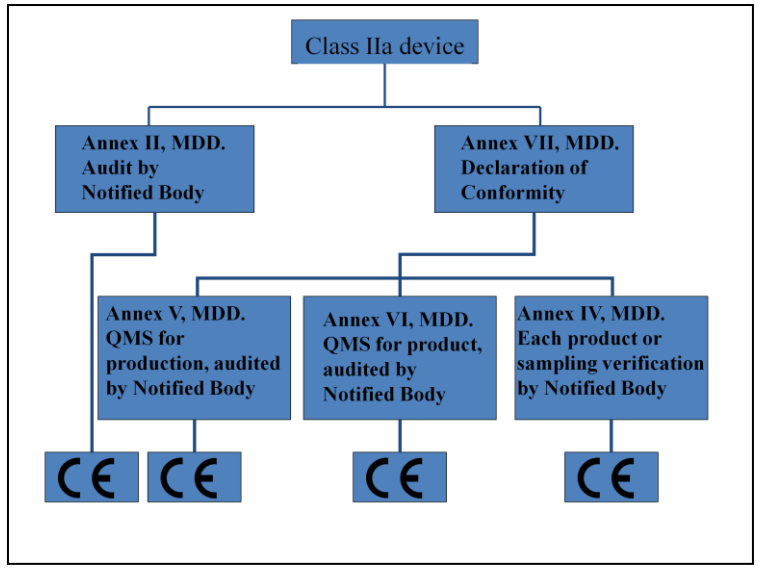
What it does mean is the person or company who is responsible for placing the device on the market. They have to keep all the technical information and take responsibility for the safety and effectiveness of the medical device. This information is kept in the Technical File.

## Stimulators - a route through the MDD (article 11)

- For Class IIa we had a choice of four routes.
- We chose a route that gave us the most flexibility and would allow us to make and CE mark other devices within the scope of our EC Certificate.
- For Class I, Annex VII is required
- Class IIb, Annex II (-point 4) or Annex III +(IV or V or VI)
- Class III, Annex II or III + (IV or V)

At various stages of our work with electrical stimulation we have had rumours and approaches which might have resulted in us selling off our devices but there was always something that made sure this didn't happen. In any case, we couldn't halt our device development and patient treatment as it was bringing in some money. As well as the revenue we were assured that we would have a much more valuable package to sell if the CE marking was all in place.

Ensuring that a research device can be marketed at the conclusion of a study or trial is becoming a requirement of grant applications so it is important that researchers are aware of the need to begin building up a Technical File at an early stage. Also, follow proper design principles..

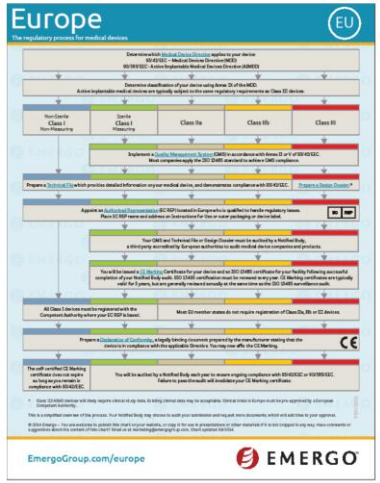



What would make you choose one route in preference to another??

In my experience, this comes down to the kind of device you are selling and the kind of manufacturer you see yourself as being. If you are always going to be making a particular kind of product with reasonable production runs then you may like to avoid each product or a sampled selection being verified by a Notified Body. That would lead you to Annex V or VI. For a smaller number of devices, maybe being made to a customer specification, you may not want to set up a QMS and you would build in the cost of NB involvement to the sale.

Summary of the EU approval process

Emergo also have good resources that summarise the new EU MDR and the latest ISO 13485:2016 (just have to supply your email address)



## What do the Annexes involve?

- **Annex II**
  - Full quality assurance system + notified body inspection of design for Class III
- **Annex III**
  - Type examination – submit documentation and a sample device to a notified body
- **Annex IV**
  - EC verification, final testing by notified body - 100% or sampled (statistical assessment)
- **Annex V**
  - EC Declaration of Conformity + Production quality assurance (A quality management system)
- **Annex VI**
  - EC Declaration + product quality assurance (quality management system needed)
- **Annex VII**
  - EC Declaration of Conformity + assurance provisions based on II, IV, V, or VI

Here is a brief summary of the things that are asked by the different Annexes. [run through slide]

## Additional requirements - Technical File

- Compilation of the documents to do with your device that demonstrate compliance with the Essential Requirements and other aspects of MDD.
- search for “ghtf technical file” for guidance
- Should contain:
  - Descriptions of design and operation of the device
  - Instructions
  - Labelling
  - Demonstrations of effectiveness
  - Risk assessments
  - Statements or certificates showing compliance with other relevant standards, e.g.: ISO 60601.

The Technical File is where everything goes that is linked to a particular device (or family of devices). This can be quite a pile of paper…. For a suggested format look at the GHTF website.

Risk assessment is an important element in the Technical File

## Other additional requirements

- **Declaration of Conformity**
  - Letter by a responsible person saying all requirements have been met and are CE marking your products under the MDD.
- **Annex I**
  - Even if your device is custom made or not to be used outside your legal entity it must meet the essential requirements. Doesn't have to have a CE mark…
- **Compliance with harmonised standards (art 5)**
  - Eg: ISO60601-1 Medical Electrical Equipment, General Requirements for Safety and essential performance

If I jump ahead a little bit to show how the Essential Requirements are addressed (for stimulators) by peeking at a procedure from the QMS

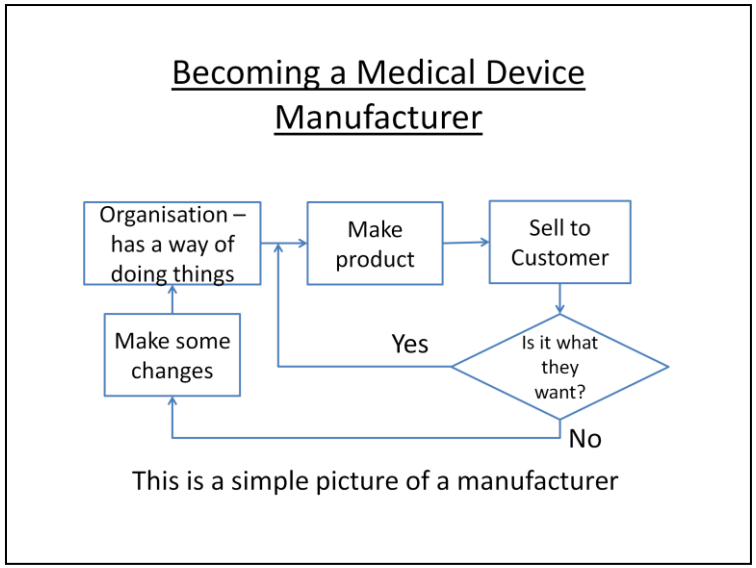
## *MDD Article 5* - Reference to standards

1. Member States shall presume compliance with the essential requirements referred to in Article 3 in respect of devices which are in conformity with the relevant national standards adopted pursuant to the harmonized standards the references of which have been publishes in the *Official Journal of the European Communities*; Member States shall publish the references of such national standards.
   [snip]

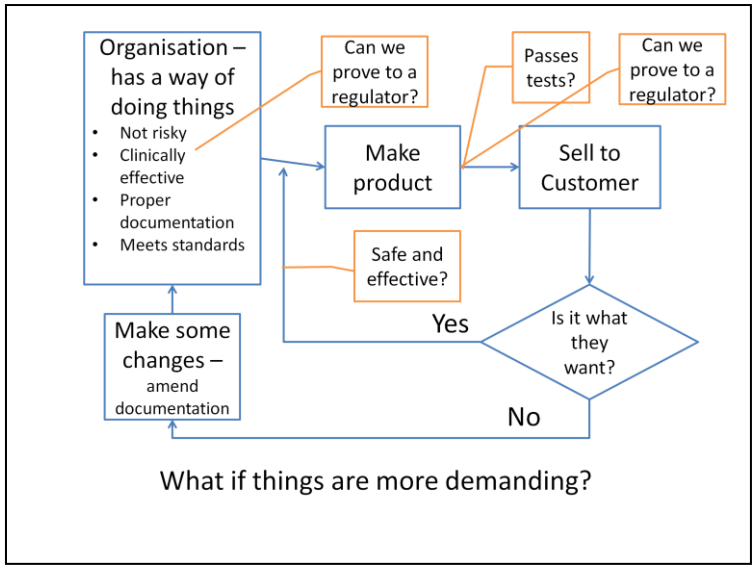
[I'll say more on this when we return to Essential Requirements]

- In other words – If there is a harmonised standard that the EC has adopted and you comply with the standard then you automatically comply with the Essential Requirements.

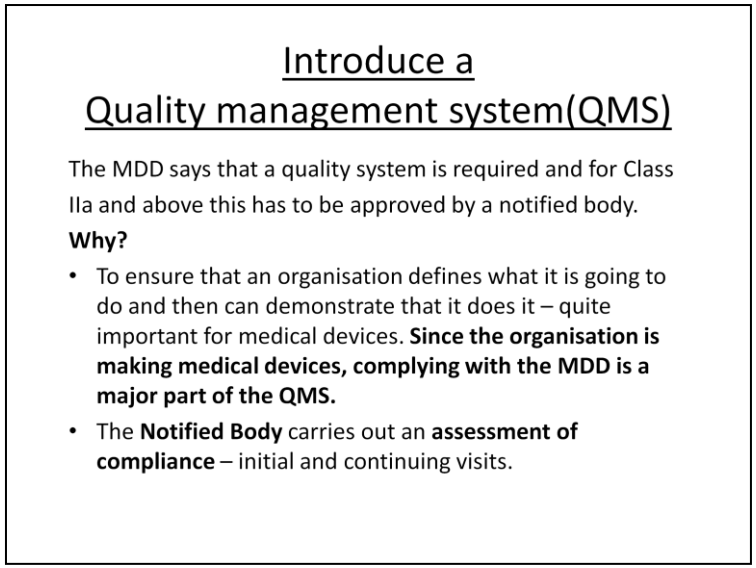
This is a roundabout way of saying that: If there is a harmonised standard that the EC has adopted and you comply with the standard then you automatically comply with the Essential Requirements.




If nobody is checking up on you then this is a workable way of operating.



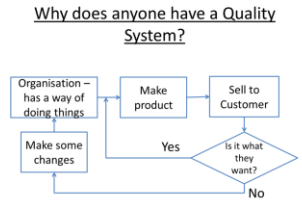

It is the checking by a regulator that means we want to make thing easy for them and ourselves by following a template or structure for how the organisation works. This covers how it keeps information, which records are kept, how it makes sure that changes are not making their product worse instead of better, what involvement management have etc.




So, managing all these thing that have to be done in order to design a medical device and show that it meets the MDD requirements is actually quite a job. The MDD says that a quality system is required. If your device is a Class IIa or above then the QS has to be assessed and approved by a Notified Body. The Quality Management system sets out requirements in a range of areas to ensure appropriate management, planning, resources and record keeping – more later..

# What goes in the Quality system?

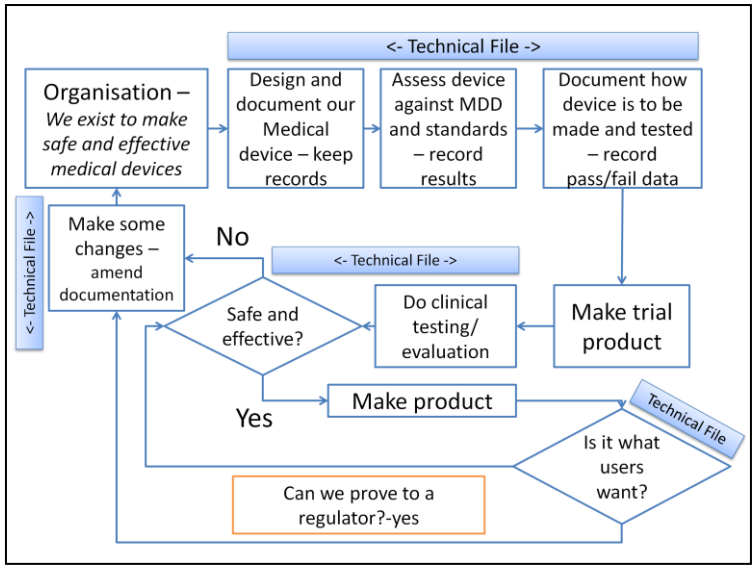
- The quality management system takes a general framework and incorporates the requirements an organisation needs to comply with the MDD



This is a simple picture of a manufacturer

- Since a Notified Body will be involved, it makes sense to use a framework that they are familiar with.

Where to go for this framework…?

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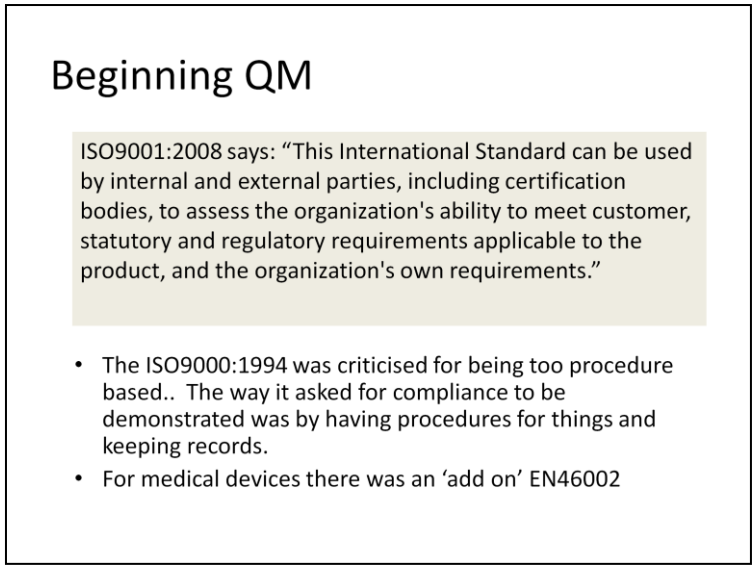
## History of Quality Systems

- Industry has had frameworks or methods for assuring quality for a long time. Probably started with munitions so shells could be interchanged between manufacturers. Also came in for car manufacture.
- Rather than a whole lot of industry specific documents a general standard was written by the International Standards Organisation (ISO)

Standards were not too much of a problem if you bought your guns and shells from one maker but if you wanted to 'second source' your ammunition then it was important that it would fit and fire safely. Later, car manufacturers would insist that their suppliers followed quality systems that were specific to them.




So, there are requirements with the QMS standard and there are requirements in the MDD. If we combine these with what the organisation wants to do – these might be in a company policy – then we have established the full set of requirements that our quality system is going to help us meet. I will just breeze through the numbers and recent history of quality systems for medical devices so you can see why we are where we are.

## Evolution…

- Organisations that were not manufacturing companies had difficulty in making ISO9000:1994 fit into their business. That this was a problem shows that there was a good awareness that ISO9000 meant something in terms of an organisation's quality.
- So, ISO9000:2000 appeared just in time to earn the '2000' suffix. This had some major changes. No emphasis on procedures, much more emphasis on processes.

The first ISO9000 was very much based on how a manufacturing company would do things – lots of mention of suppliers and specifications and that sort of thing. It had to 'interpreted' in order for it to be applied to a service company for e.g. That fact that companies wanted to be certificated to ISO9000 did show that there was a customer awareness and therefore advantage to being able to publicise the fact that you had a quality system. On the other hand – it did only make sure you did what you said you were going to do so if that wasn't very good then ISO9000:1994 wasn't much help. This aspect was recognised and the rewrite in 2000 made some changes. [see slide]

## ISO9000:2000 cont..

- With processes came a requirement to show the linkage between processes and measurement of performance
- Introduced emphasis on 'top management' involvement – there was a perception that some businesses had just appointed a person to get them an ISO9000 certificate
- Emphasis on customer satisfaction and meeting customer requirements

ISO9000:2000 came away from the manufacturing influence of following procedures. Instead processes were the order of the day and the means to measure the performance and linkage of these processes. The information from these measurements should be examined and used to improve the processes and therefore overall performance.

'Top Management' should be involved in the evaluation of the performance and allocation of resources.

The customer should have their requirements met and exceeded to ensure satisfaction with the goods or services.

## Divergence for Medical Devices..

- ISO9000:2000 was looking good but there was a view from the medical device regulators that it was not right for their sector
- By specifying that you would respond to customer requirements you could end up with a production run where a significant proportion of your output had been reworked/altered to meet such requirements
- This was a 'Bad Thing'

We did proceed to change our registration to ISO9000:2000 but our BSI assessor told us that there were developments which pointed to further development in the standards world.

## ‘We’ get our own standard

- ISO 9000:2000 was going to go ahead but by 2003 there was a specific medical device manufacture standard,
- ISO 13485:2003 and now
- ISO 13485:2016

- This has all the good stuff from ISO9000:2000 but none of the requirements that might lead to messing up the smooth production of your medical devices.

Now a specific standard for Medical Devices

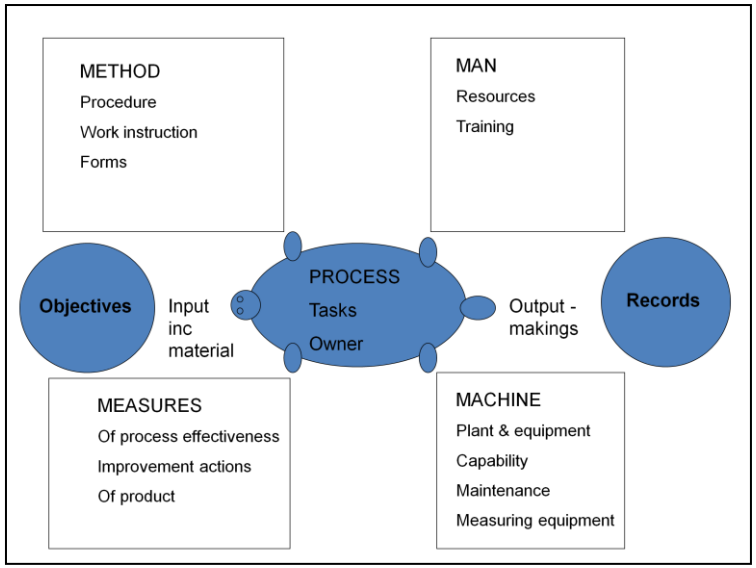
## Processes not procedures..

- Some things can stay as procedures but it is more useful to see things as processes
- The idea is that you can identify the dependencies and redirect your resources to the areas that need them.

We extracted some money out of the hospital to employ a consultant to help us with putting in a quality system. He knew the standard and what was required to demonstrate compliance – came from a background in wound dressings.

The technique he used was to pick an area covered by the standard and assemble the people involved – they knew what was going on now..

Then we worked out what the process was e.g. for taking orders and sending out finished goods. Our consultant put this all up on a flip chart, showed us where we would have to make changes in order to comply and then went off and turned the scribble into a procedure. The major contribution was the points at which records would be needed in order to demonstrate that we were doing the things we said we were.


METHOD
Procedure
Work instruction
Forms
MAN
Resources
Training
Objectives
Input
inc
material
PROCESS
Tasks
Owner
Output -
makings
Records
MEASURES
Of process effectiveness
Improvement actions
Of product
MACHINE
Plant & equipment
Capability
Maintenance
Measuring equipment

## Salisbury 1996
## quality system round up

- MDD is in place and we can't avoid it
- Looking at the MDD we are making a Class IIa device so we need an approved quality system.
- We had some help through use of a Consultant

We extracted some money out of the hospital to employ a consultant to help us with putting in a quality system. He knew the standard and what was required to demonstrate compliance – came from a background in wound dressings.

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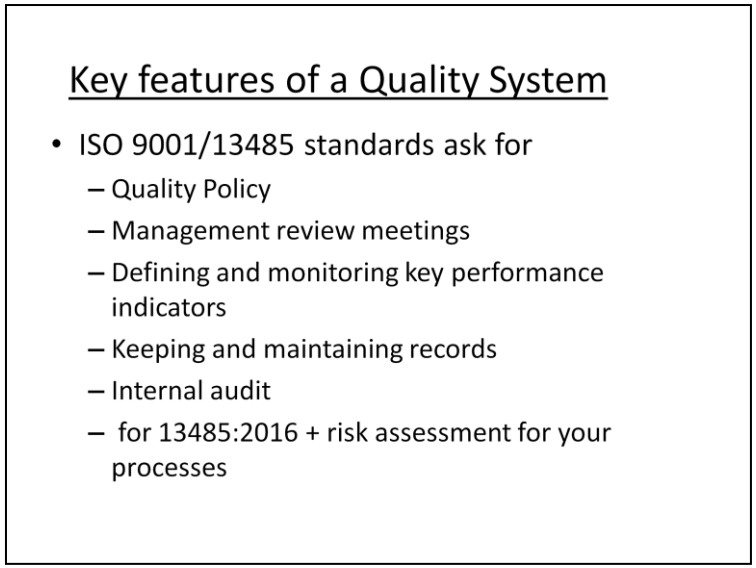
Lets look at some
of ISO13485

Lets look at some
of ISO13485




The first thing to be written is the Quality Policy – this is where you set down the purpose of your quality management system and how far it extends. So you would put in here the activities of the organisation that you wish to have covered by the QMS and also the aims of the company.

You can put in the key activities and who is responsible for them along with the objectives to be monitored to assess performance.

There are some small changes in 2016 but the one that will keep us busy in changing over is adding a risk assessment to all our processes.

Documented procedures required for:

- Control of documents
- Control of records
- Internal audit
- Control of nonconforming product
- Corrective action
- Preventive action

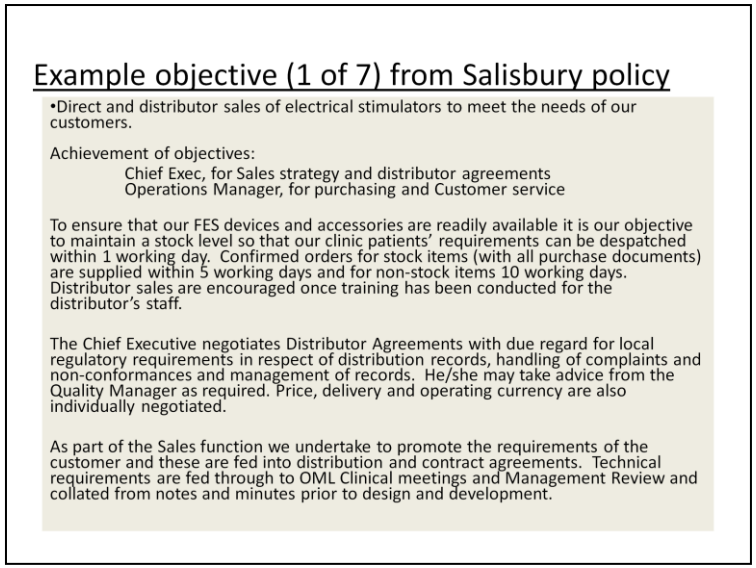
In practice, related areas can be grouped together such as the control of documents and the control of records. Similarly corrective action and preventive action – often seen as CAPA.


Some bullets from our actual Policy. State what the policy is designed to cover and what might be excluded. You may not be involved in sterilising items but you may handle them as accessories or for an unrelated reason.

Everyone needs to follow the policy and other documents so include a statement to this effect.

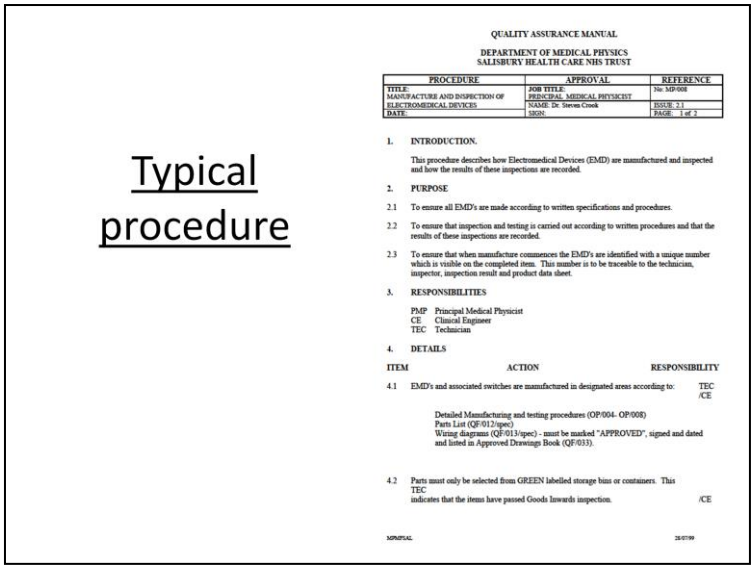
What is the purpose of the organisations activity? This can be one of those lofty aims that businesses like to put on their brochures but it is still a useful reference if a representative proportion of the staff agree. We held a senior management 'away day' and thrashing out this wording was one of the jobs.

Then there are some specific statements or documents that sit well in the policy such as the organisations objectives and associated responsibilities, a commitment to continuous improvement, how the processes link together and a list of the procedures/processes.




From the Policy, here is one of the objectives. This is how I have it written in our manual.. It consists of a top line sentence, who is responsible and what they do: then a bit of detail to help understand the scope.

# Typical procedure



QUALITY ASSURANCE MANUAL

DEPARTMENT OF MEDICAL PHYSICS
SALISBURY HEALTH CARE NHS TRUST

| PROCEDURE | APPROVAL | REFERENCE |
|---|---|---|
| TITLE: MANUFACTURE AND INSPECTION OF ELECTROMEDICAL DEVICES | JOB TITLE: PRINCIPAL MEDICAL PHYSICIST | No: MP/008 |
| | NAME: Dr. Steven Crook | ISSUE: 2.1 |
| DATE: | SIGN: | PAGE: 1 of 2 |

1. **INTRODUCTION.**

This procedure describes how Electromedical Devices (EMD) are manufactured and inspected and how the results of these inspections are recorded.

2. **PURPOSE**

2.1 To ensure all EMD's are made according to written specifications and procedures.

2.2 To ensure that inspection and testing is carried out according to written procedures and that the results of these inspections are recorded.

2.3 To ensure that when manufacture commences the EMD's are identified with a unique number which is visible on the completed item. This number is to be traceable to the technician, inspector, inspection result and product data sheet.

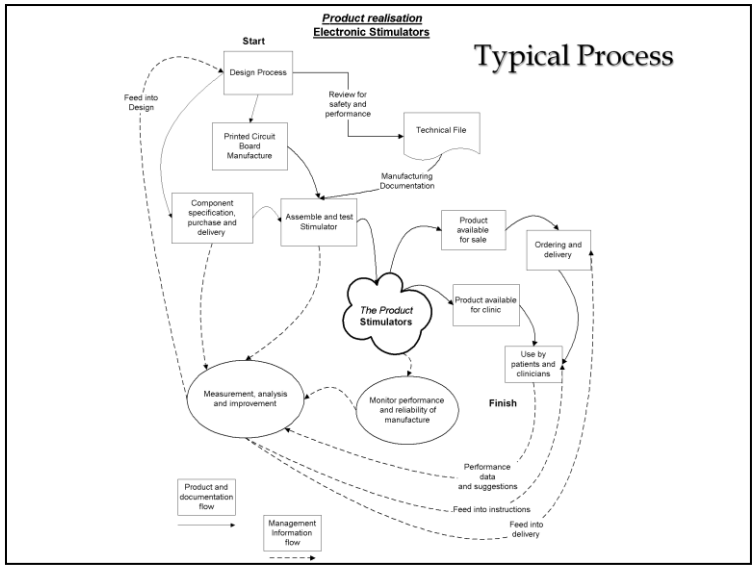
3. **RESPONSIBILITIES**

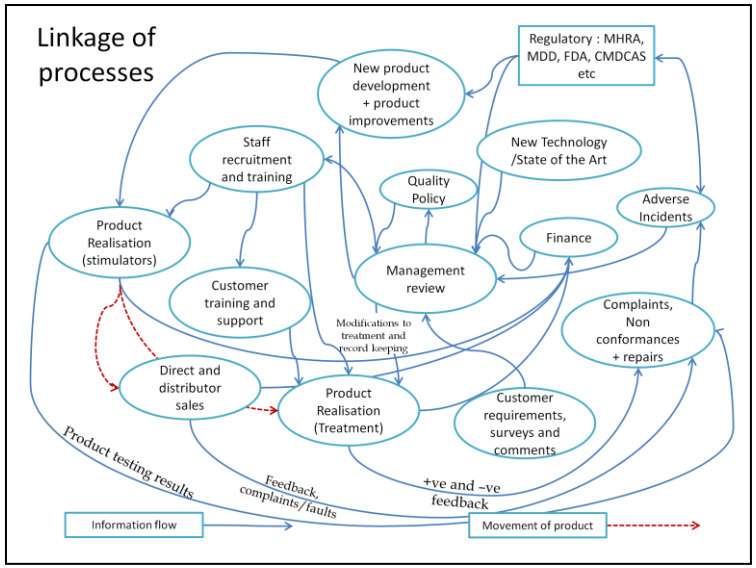
PMP Principal Medical Physicist
CE Clinical Engineer
TEC Technician

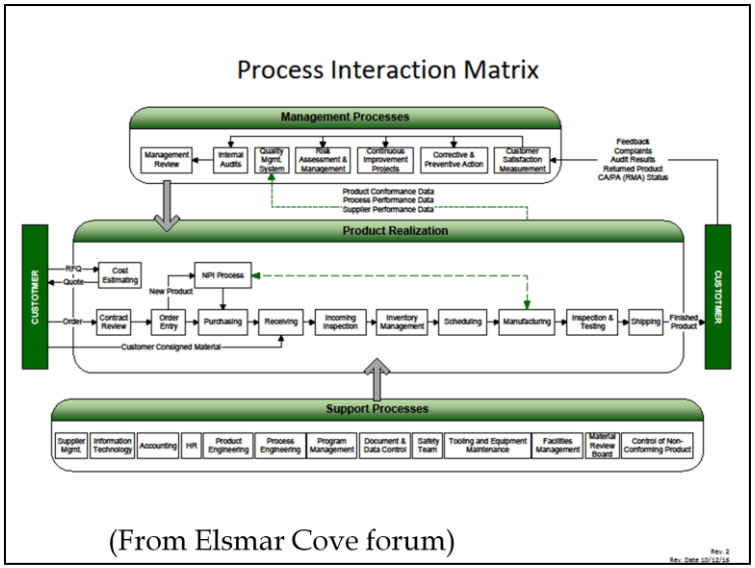
4. **DETAILS**

| ITEM | ACTION | RESPONSIBILITY |
|---|---|---|
| 4.1 | EMD's and associated switches are manufactured in designated areas according to:<br>Detailed Manufacturing and testing procedures (OP/004- OP/008)<br>Parts List (QF/012/spec)<br>Wiring diagrams (QF/013/spec) - must be marked "APPROVED", signed and dated and listed in Approved Drawings Book (QF/033). | TEC /CE |
| 4.2 | Parts must only be selected from GREEN labelled storage bins or containers. This indicates that the items have passed Goods Inwards inspection. | TEC /CE |

MP/MP2AL 28/07/99

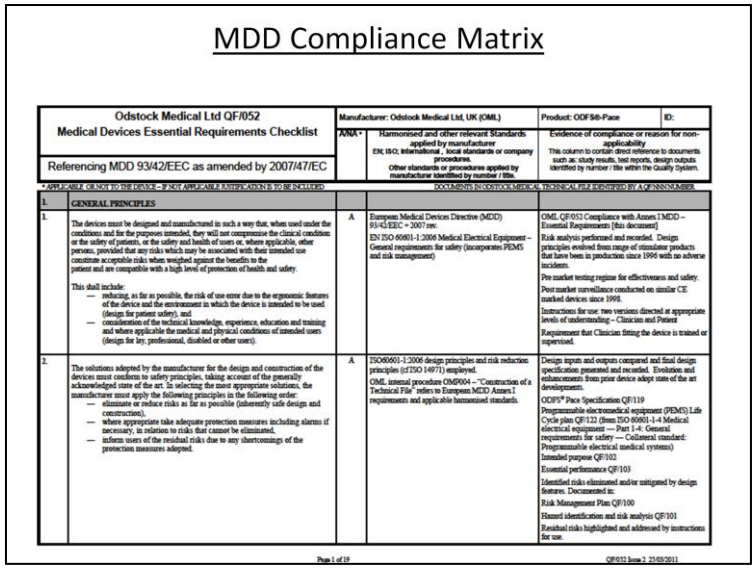

Product realisation
Electronic Stimulators
Typical Process
Start
Design Process
Feed into Design
Review for safety and performance
Technical File
Printed Circuit Board Manufacture
Manufacturing Documentation
Component specification, purchase and delivery
Assemble and test Stimulator
Product available for sale
Ordering and delivery
The Product Stimulators
Product available for clinic
Use by patients and clinicians
Measurement, analysis and improvement
Monitor performance and reliability of manufacture
Finish
Performance data and suggestions
Feed into instructions
Feed into delivery
Product and documentation flow
Management Information flow


Linkage of processes
Regulatory : MHRA, MDD, FDA, CMDCAS etc
New product development + product improvements
Staff recruitment and training
New Technology /State of the Art
Quality Policy
Adverse Incidents
Product Realisation (stimulators)
Finance
Management review
Customer training and support
Modifications to treatment and record keeping
Complaints, Non conformances + repairs
Direct and distributor sales
Product Realisation (Treatment)
Customer requirements, surveys and comments
Product testing results
Feedback, complaints/faults
+ve and –ve feedback
Information flow
Movement of product




(From Elsmar Cove forum)

## MDD Compliance Matrix



| Odstock Medical Ltd QF/052<br>Medical Devices Essential Requirements Checklist | Manufacturer: Odstock Medical Ltd, UK (OML) | | Product: ODFS®-Pace | ID: |
|---|---|---|---|---|
| Referencing MDD 93/42/EEC as amended by 2007/47/EC | ANA * | Harmonised and other relevant Standards applied by manufacturer<br>EN; ISO; international , local standards or company procedures.<br>Other standards or procedures applied by manufacturer identified by number / title. | Evidence of compliance or reason for non-applicability<br>This column to contain direct reference to documents such as: study results, test reports, design outputs identified by number / title within the Quality System. | |

* APPLICABLE OR NOT TO THE DEVICE – IF NOT APPLICABLE JUSTIFICATION IS TO BE INCLUDED DOCUMENTS IN ODSTOCK MEDICAL TECHNICAL FILE IDENTIFIED BY A QFN9XXNUMBER

| | | | | |
|---|---|---|---|---|
| 1. | **GENERAL PRINCIPLES** | | | |
| 1. | The devices must be designed and manufactured in such a way that, when used under the conditions and for the purposes intended, they will not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons, provided that any risks which may be associated with their intended use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety.<br><br>This shall include:<br>— reducing, as far as possible, the risk of use error due to the ergonomic features of the device and the environment in which the device is intended to be used (design for patient safety), and<br>— consideration of the technical knowledge, experience, education and training and where applicable the medical and physical conditions of intended users (design for lay, professional, disabled or other user). | A | European Medical Devices Directive (MDD) 93/42/EEC + 2007/xxx.<br><br>EN ISO 60601-1:2006 Medical Electrical Equipment – General requirements for safety (incorporates PEMS and risk management) | OML QF/052 Compliance with Annex I MDD – Essential Requirements [this document]<br><br>Risk analysis performed and recorded. Design principles evolved from range of stimulator products that have been in production since 1990 with no adverse incidents.<br><br>Pre market testing regime for effectiveness and safety.<br><br>Post market surveillance conducted on similar CE marked devices since 1998.<br><br>Instructions for use: two versions directed at appropriate levels of understanding – Clinician and Patient<br><br>Requirement that Clinician fitting the device is trained or supervised. |
| 2. | The solutions adopted by the manufacturer for the design and construction of the devices must conform to safety principles, taking account of the generally acknowledged state of the art. In selecting the most appropriate solutions, the manufacturer must apply the following principles in the following order:<br>— eliminate or reduce risks as far as possible (inherently safe design and construction),<br>— where appropriate take adequate protection measures including alarms if necessary, in relation to risks that cannot be eliminated,<br>— inform users of the residual risks due to any shortcomings of the protection measures adopted. | A | ISO60601-1-2006 design principles and risk reduction principles (cf ISO 14971) employed.<br><br>OML internal procedure OMD004 – "Construction of a Technical File" refers to European MDD Annex I requirements and applicable harmonised standards. | Design inputs and outputs compared and final design specification generated and recorded. Evolution and enhancements from prior device adopt state of the art development.<br><br>ODFS® Pace Specification QF/119<br><br>Programmable electromedical equipment (PEMS) Life Cycle plan QF/122 (from ISO 60601-1-4 Medical electrical equipment — Part 1-4: General requirements for safety — Collateral standard: Programmable electrical medical systems)<br><br>Intended purpose QF/102<br><br>Essential performance QF/103<br><br>Identified risks eliminated and/or mitigated by design features. Documented in:<br><br>Risk Management Plan QF/100<br><br>Hazard identification and risk analysis QF/101<br><br>Residual risks highlighted and addressed by instructions for use. |

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As a useful tool for the organisation and also to show any assessor that you have covered everything there should be a compliance matrix to show what is applicable, how you meet those requirements and where the evidence is located.

## MDD Assessment

- Although it is a bit like an exam, the assessor wants to you pass. In fact there is a pre-assessment visit for 'new' organisations to make sure that they are close enough to warrant a full assessment.

- For us (Salisbury), it is one assessor for a whole day.
- Bigger organisations - could be longer and involve more than one person

## Assessment of your devices

- The assessment looks at two aspects:
  - Have you documents and processes in place to meet the requirements of the quality standard and the MDD?
  - Are you using them appropriately to manage your organisation?
    - Are your staff trained?
    - Have you kept records throughout the process?

So, you go through the MDD and ISO13485 and make sure that all the aspects of what needs to be done are covered by things you say that you do. Then you get up from the desk and walk around checking that what you say you do is actually what is going on. This is why you have trained staff and this is why you keep records at certain point in the process.

## Internal auditing

- There is a requirement for an organisation to do its own auditing – internal audit.
- A complete ‘cycle’ should be completed before your first assessment and then again every year.
- If you have procedures then you can step through them ticking off each point. But you get a lot of overlap.
- With processes you can follow them through with their linkages.

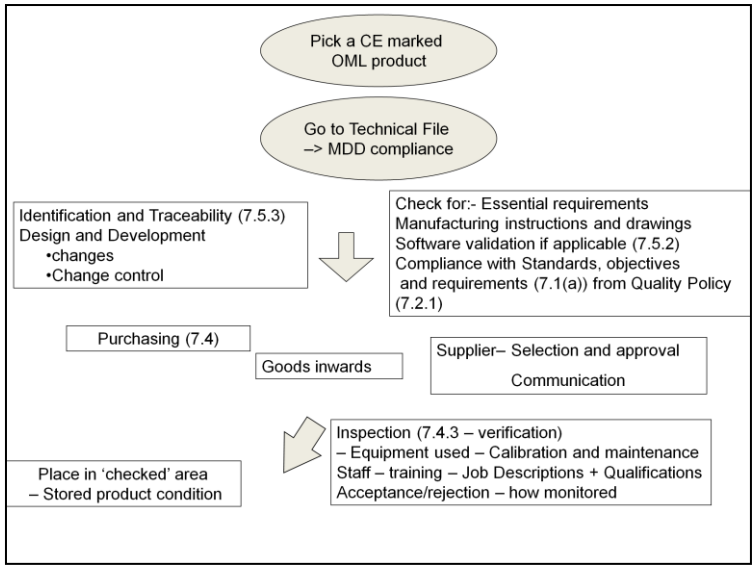
## Audits - documentation

- Documentation and records are the key to a successful assessment and audit.
- You also need to have them well organised otherwise you will make extra stress for yourself and your assessor.

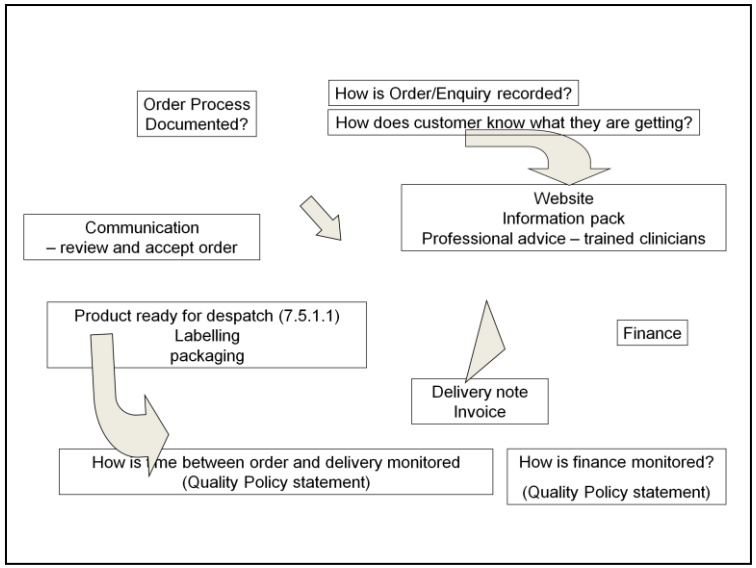

On this pile is a technical file and then above that is the binder full of procedures and the red covered document is the MDD with the ISO 13485 on top. So you can see that even the thin MDD has generated quite a bit of paper. Our latest stimulator has two binders worth of technical file as we had to add in more complicated risk management along with customer tests and software documentation.

## Plan for auditing

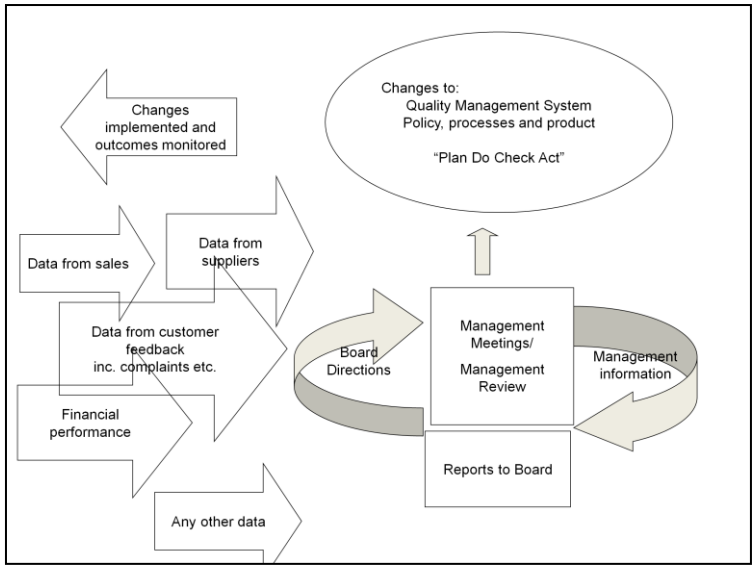
- Have your own plan [required]
- Follow it, using someone who is not involved in the operation of the QMS.
- Something which is tricky to extract is the effectiveness of what you are doing. Which is a shame as this is probably the most useful thing you want to know.
  - Criticism of quality management systems in general




Here is a diagram that can be used to guide the audit process – looking at devices with a CE mark. The MDD compliance can be checked and also the QMS (are all the clauses met and is there documentation to show this)



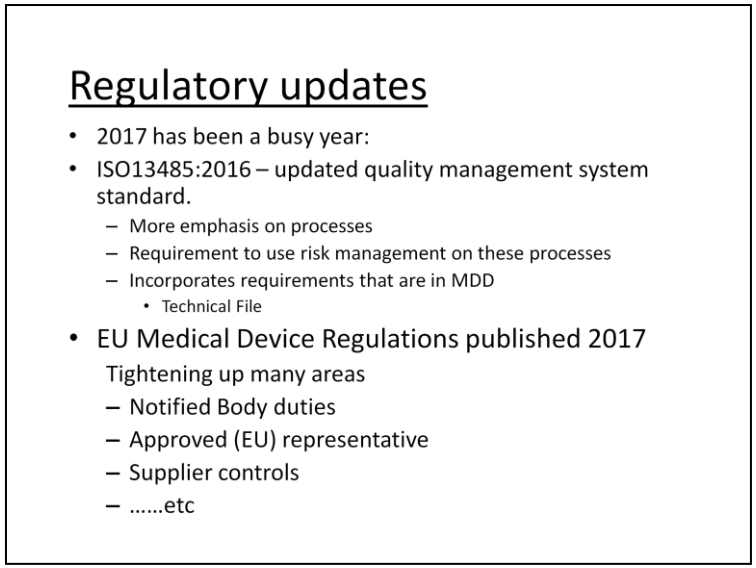

Continuation of above…


Changes to:
Quality Management System
Policy, processes and product
"Plan Do Check Act"
Changes implemented and outcomes monitored
Data from sales
Data from suppliers
Data from customer feedback inc. complaints etc.
Financial performance
Any other data
Board Directions
Management Meetings/ Management Review
Management information
Reports to Board

# Other considerations

- For Class I devices you need to register with the MHRA. They also produce some useful Bulletins. (web site)

- Tell them which devices you are involved with from their list..
  - **Walking Aids and Wheelchairs**
    - **I 1** Crutch/Walking Stick
    - **I 2** Walking Frame/Multi-Leg Walking Aid/Standing Frame
    - **I 3** Rollator/ Mobilator
    - **I 4** Wheelchairs (Non-Powered) and Accessories
    - **I 5** Wheelchairs (Powered) and Accessories
    - **I 6** Mobility Aids for the Visually Impaired
    - **Z168** Rehabilitation Tricycles/Mobility Carts(Technical Aids for Disabled Persons)




Why was the MDR brought in?

From Wikipedia:

**Poly Implant Prothèse** (PIP) was a French company founded in 1991 that produced silicone gel breast implants. The company was preemptively liquidated in 2010 following the revelation that they had been illegally manufacturing and selling breast implants made from cheaper industrial-grade silicone since 2001.

When the regulators visited (prearranged visits) , they were shown containers and documentation relating to 'proper' medical grade silicone. The CE approvals were therefore maintained. The PiP implants were found to have a higher than usual incidence of leakage – up to 35% - where other makes were around 1 - 10%.

So, despite these actions being deliberate fraud, changes have been made to increase unannounced inspections and also require more frequent post-market clinical follow-up.

An EU wide database of reportable incidents will be set up (EUDAMED). Manufacturers will no longer be able to claim that their products are equivalent to another similar product unless they have access to the technical information. If they have no access then a clinical trial is required.

Other measures are a high level review (EU panel of experts) for high risk devices to ensure they are safe and effective and the regulatory officer having suitable qualifications.

# US Food and Drug Administration (FDA) 510(k)

- The US has a system for approving devices that are developments of existing devices. This is a short cut to their market because it means that you don't need to register a clinical trial in the US. Called 510(K)
- Need to determine a pre-existing (*predicate*) device or devices.
- Submit an application which contains the information about your device and the predicate device showing that they are '*substantially equivalent*'
- Some device family guidance available (e.g. for muscle stimulators)

## Other places..

Europe

- Pretty straight forward – some countries still have extra hoops, e.g. Italy, France, Germany – MDR supposed to level this out too

- South Africa, Australia and New Zealand
  - Health Ministry maintains a list of registered devices – accept CE standards

- Also coming – Medical Device Single Audit Program - MDSAP

MDSAP is a scheme where a single regulatory inspection will cover the requirements of a number of countries and so reduce the number of regulatory inspections and documents that a Manufacturer has to deal with.

# Conclusions - I

- We are able to sell our products in UK (and Europe)
- We manage things better than before.
- We have documentary evidence of the way we do things. (See you in Court!)
- There is slightly more work day to day.
- There is quite a lot of work to audit the system and prepare for each assessment.
- There is an annual cost to our Notified Body.

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# Conclusions-II

- We have seen how to check that your device is a Medical Device and where to determine the risk level (Class)
- Brief look at the MDD Essential requirements.
- The way of making sure that all the devices produced meet requirements and the manufacturer is meeting other MDD requirements -> use a quality management system such as ISO 13485
- Evidence assembled into a Technical File
- Everything self-checked (internal audit) as well as externally assessed (class II and above)

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