Regulations governing the application of medical accelerators

… in 50 minutes ☺.

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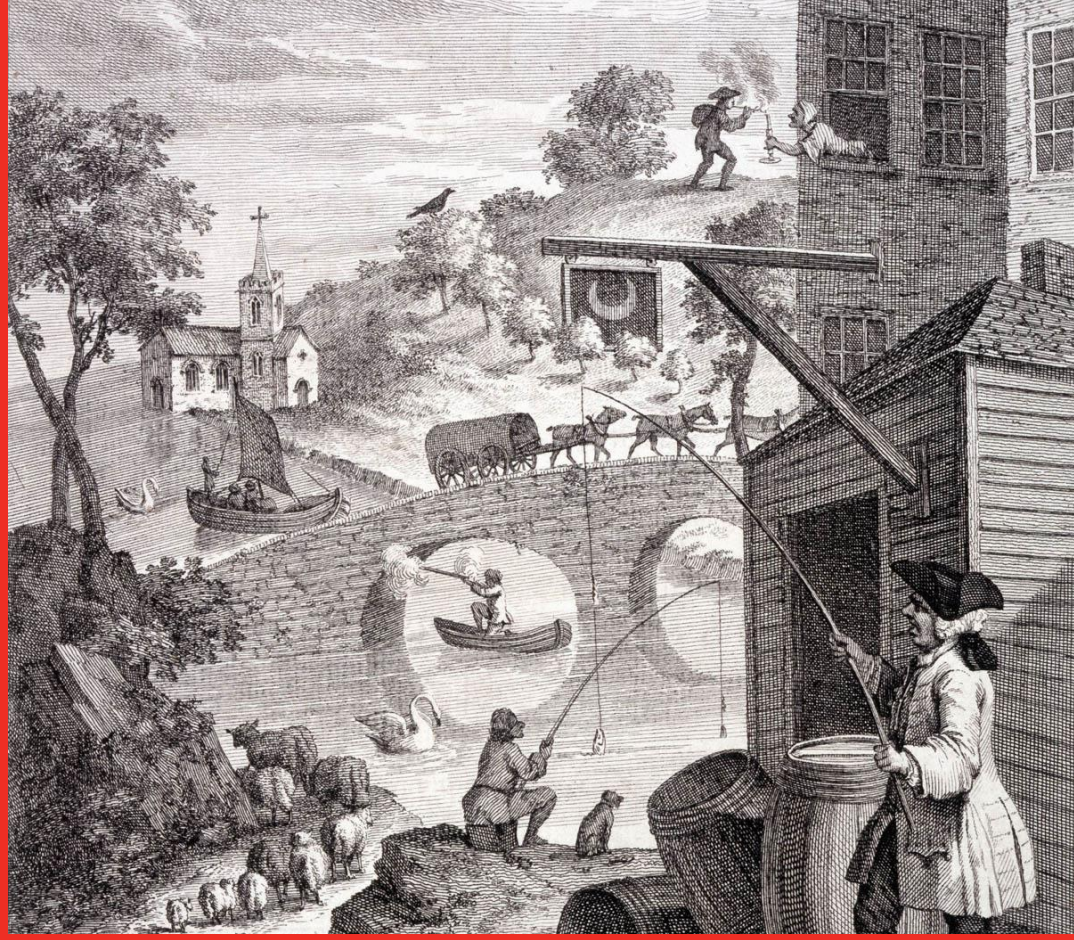

1.The wonderland of

STANDARDS AND REGULATIONS

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Laws and standards

- Medical devices (and systems) are subject to regulations (laws!) – it all starts here.
- …to ensure **safety and effectiveness** of devices on the market.
- Every country/region has its own set of laws/regulations.

- Standards are written by (international, private) organizations.
- In theory, standards are NOT MANDATORY, but…
- In practice, „officially recognized“ standards need to be followed.

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Medical Devices Directive 93/42/EEC* (replaced by new MDR)

- Dev. class I, IIa, IIb and III
- Quality Syst. EN13485
- CE Marking
- Notified Body (private)
- Technical File
- **Harmonized Standards EN**

Code of Fed. Regulations Title 21

- Dev. class I, II and III.
- QMS Title 21 Part 820
- 510(k) or PMA
- FDA clearance
- DHF, DMR and DHR
- Recognized consensus std. AAMI/ANSI

93/42/EEC Contents

Some important contents:

- Definitions.
- Classification into **I, IIa, IIb or III**.
- List of essential requirements for safety and effectiveness for all devices.
- Processes to be followed by manufacturers, such as quality, risk management, post market, etc.
- Instructs manufacturers to create and maintain a Technical File for every device
- Foresees the adoption of „harmonized standards“.
- Legal mechanism for market approval and entitles “notified bodies”.

CE Marking

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1. Intended purpose and classification
2. Identify the essential requirements
3. Establish necessary processes in the organization
4. Develop the device accordingly
5. Verification and Validation
   - Test against requirements (we'll talk about it latter)
6. Clinical evaluation:
   a) Find equivalent device and use available literature route and/or
   b) Clinical investigation route.
7. Finalize technical documentation
8. Contact notified body and perform certification
9. Monitor trough lifecycle

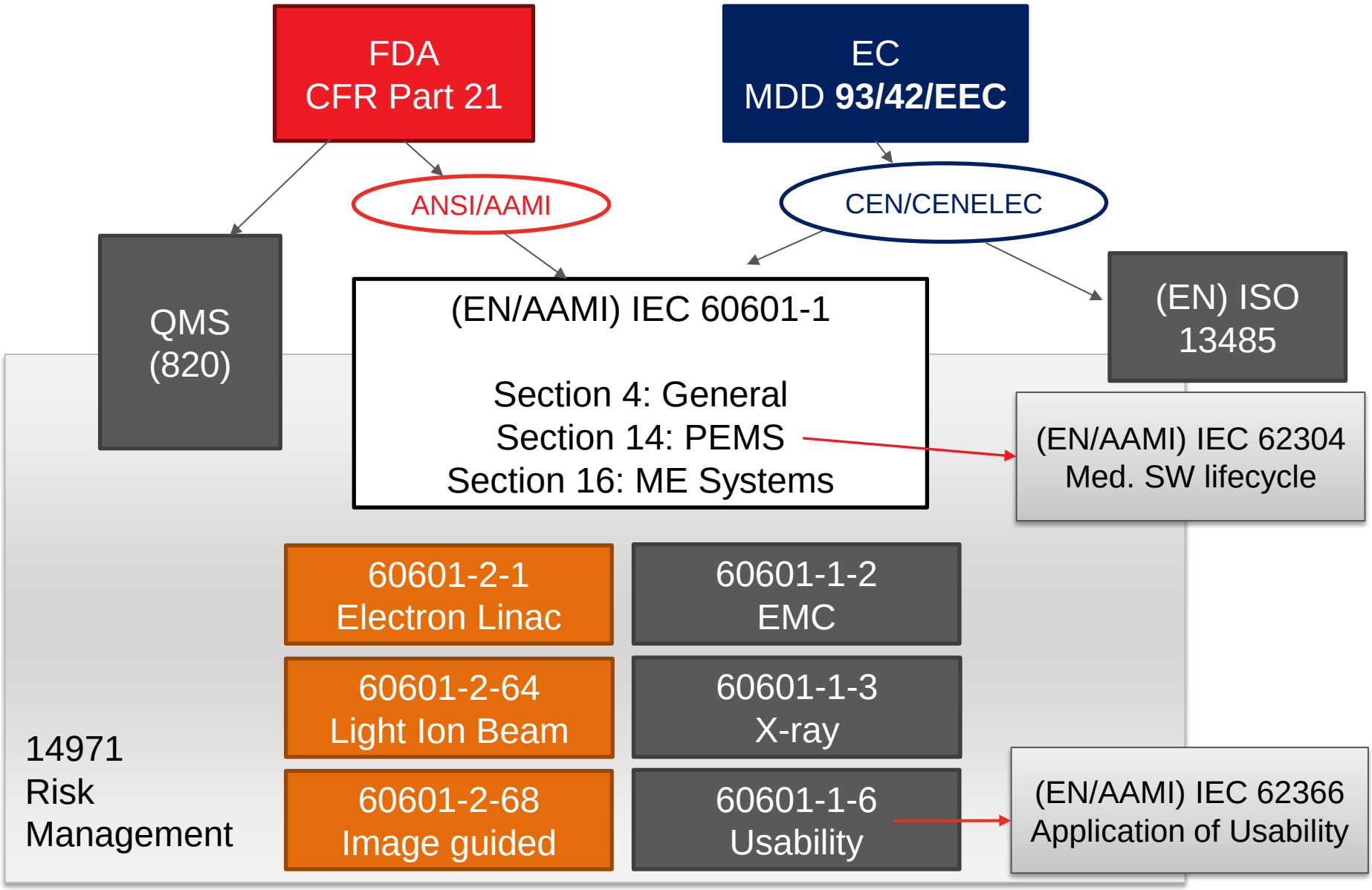
Harmonized Standards

1. **Quality management system** EN 13485:2016
   - Defines organization processes ++
   - Requires auditing the organization (not only the product!)

2. **Risk management** EN 14971:2012

3. **Electrical safety** EN 60601 series (next slide)
4. Software lifecycle EN 62306
5. Usability EN 62366
6. Other standards for specific applications (labeling, packaging, transport, environmental, etc.)

Simplified Standards Ecosystem



Meet the 60601 family

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60601-1:2007

General Requirements

Sections 1 to 17

Collateral Standards

60601-1-2 → EMC
60601-1-3 → X-Ray
60601-1-6 → Usability
60601-1-8 → Alarms
60601-1-9 → Envir.
60601-1-10
60601-1-11 → Home
60601-1-12 → Emergency

Particular Standards

60601-2-1 → Electron ACC
60601-2-3 → Surgical
..
60601-2-8 → therapeutic X-ray
..
60601-2-64 → Light Ion Beam
..
60601-2-68 → Image guided radiotherapy

Risk management: ISO 14971

- Most widely recognized RM standard for medical devices (and required by law).
- Not only design phase => whole device lifecycle.
- Based on the following concepts:
  - **HAZARD** - potential source of harm
  - **HARM** - physical injury or damage to the health of people, or damage to property or the environment
  - **RISK** - combination of the probability of occurrence of harm and the severity of that harm.
- A **„damage-centric“** system => it aims to reduce the risk of harm (contrast with FMEA!)
- Not only failures to devices: also misuse is covered.

Risk Management Process

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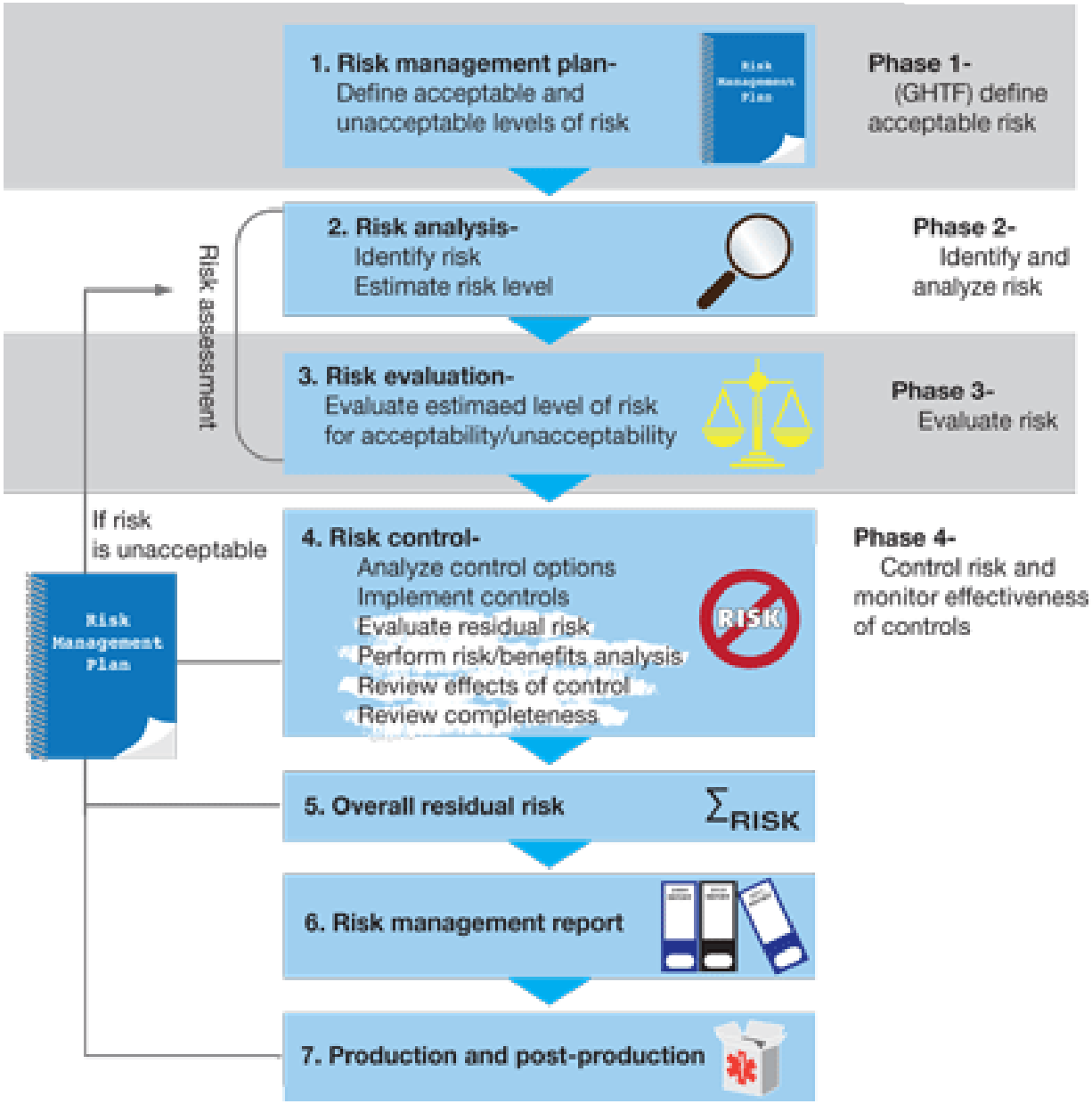

Some important aspects

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- Risk = (Probability, Severity).

- Traceability is Key:
  - Every risk must be identified
  - Every hazardous situation must be evaluated
  - Every risk must be linked to mitigation
  - Every mitigation must be verified (e.g. „tested“)

- Risk Management activities must continue after the product goes to the market **(!!)**
- RM team members must be defined in advance, with proper qualifications/training.

- After each RM cycle, a RM report must be released

How does it look like?

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Risk ID	Element	Hazard / Potential Failure Mode	Cause	Effect	Failure mode	Harm	Who	Probability	Severity	RPN	Partial Probability	Partial Severity	Partial RPN	Final Probability	Final Severity	Final RPN
EIS-HZ-00014	Serial interface with MADAM	Too high voltage on the signal line.	Malfunction on SDS Short circuit with another cable; ESD	Serial interface with MADAM: Input circuit malfunction, can produce incorrect inputs into logical circuit; Other electronic component malfunction	FM-ITS-10	Overdose: undeterminable	Patient	2	5	10	1	5	5	1	5	5
EIS-HZ-00016	Serial interface with MADAM	The cycle list or dose limits in the EVS/ITS are erroneously loaded or corrupted. EVS/ITS status cannot be read out, wrong status read out.	Message corrupted due to EM noise	Serial interface with MADAM: EVS fails to trigger an interlock when the energy is out of limits. ITS fails to trigger an interlock when the dose is out of limits.	FM-EVS-03 / FM-ITS-01	Overdose: undeterminable	Patient	5	5	25	2	5	10	FALSE	FALSE	
EIS-HZ-00016	Serial interface with MADAM	The cycle list or dose limits in the EVS/ITS are erroneously loaded or corrupted. EVS/ITS status cannot be read out, wrong status read out.	Message corrupted due to EM noise	Serial interface with MADAM: EVS fails to trigger an interlock when the energy is out of limits. ITS fails to trigger an interlock	FM-EVS-03 / FM-ITS-01	Overdose: undeterminable	Patient	2	5	10	1	5	5	FALSE	FALSE	
EIS-HZ-00016	Serial interface with MADAM	The cycle list or dose limits in the EVS/ITS are erroneously loaded or corrupted. EVS/ITS status cannot be read out, wrong status read out.	Message corru													
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Risk Evaluation

		Severity 1 Negligible	2 Minor	3 Moderate	4 Severe	5 Catastrophic
Probability of Occurrence	6 Frequent	0	0	1	4	1
	5 Often	4	1	16	7	22
	4 Occasional	2	2	43	16	37
	3 Seldom	0	0	46	32	81
	2 Unlikely	0	0	34	5	8
	1 Incredible	0	0	0	0	0
Risk Evaluation		93				
		84				
		185				
Total		362				

Who	Probability	Severity	RPN	Partial Probability	Partial Severity	Partial RPN	Final Probability	Final Severity	Final RPN		Mitigation ID
Patient	2	5	10	1	5						IS-MI-25800
Patient	5	5	25	2	5	10	FALSE	FALSE			IS-MI-02000
Patient	2	5	10	1	5	5	FALSE	FALSE		Interface with MADAM implemented using differential signals (RS485) for better EMI inmunity.	Inherent safety (by design)	EIS-MI-12900
Patient	1	5	5	1	5	5	FALSE	FALSE		Device and signal lines are not in the vicinity of power cables or high voltage/current devices to reduce EMI and possibility of device misbehavior.	Information for Safety	EIS-MI-02800T
										Data integrity verification mechanisms (parity, CRC) are included on the all serial links (SENSbox, I2M, MADAM). Failed SENSbox and I2M	Preventive/Protective	EIS-MI-34000

Summary (I)

- Laws regulate the market of medical devices.
- Safety and effectiveness.
- Standards are used to demonstrate compliance with the laws.
- In EU, the process is called CE marking. It is about demonstrating fulfillment of „Essential Requirements“. Notified bodies.
- There are many standards; the most important ones are:
  - Quality system 13485
  - Risk management 14971
  - The 60601 family
  - Software lifecycle 62304
- Design process must be documented.

2. Some practical aspects of a

PT MACHINE AS A MEDICAL DEVICE

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What device???

It is quite simple to think of an ECG machine, a thermometer or even an X-ray diagnostic.

According to MDD, a PT system is a class IIb. medical device. But…

- What is the medical device?
- Are the „sub-components“ medical devices on their own? Also class IIb.?
- Do all the same standards apply for all subsystems and components?
- How to aggregate different components into a device with a single purpose?

A complex one…

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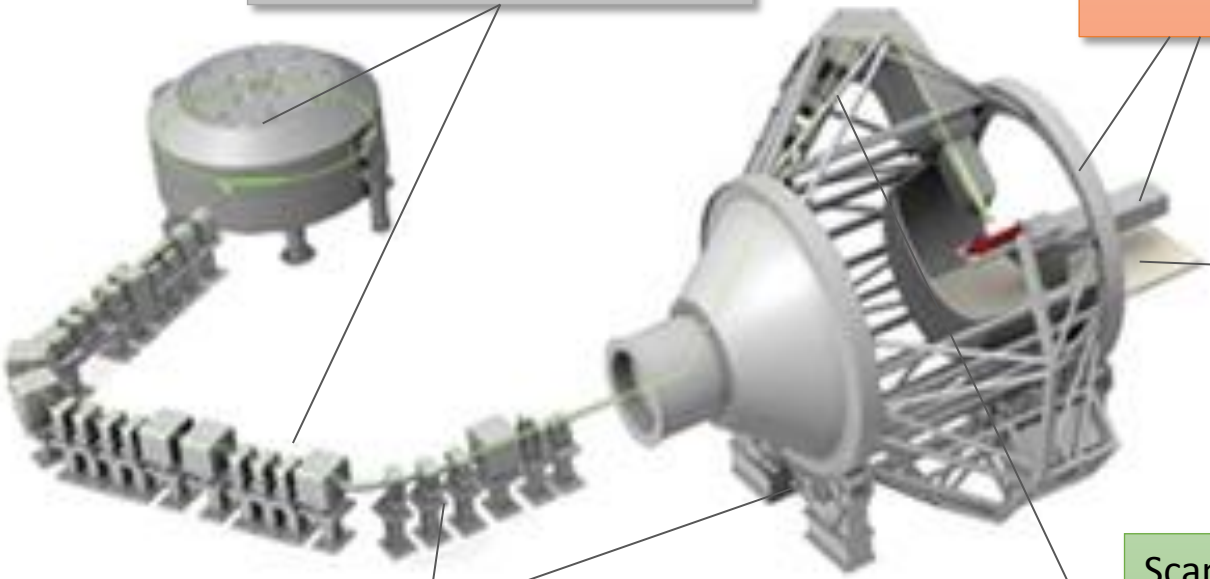
Accelerator
Beamline
Machine Control System
Machine Interlock Syst.
Auxiliary systems
Beam Diagnostics

Patient Couch
Gantry
Positioning Lasers
Nozzle Extender
Collision Avoidance
Control Electronics



Imaging
2D X-Ray / CBCT
Controls for Imaging
Registration Software

Patient protection system
Fast interlocks
Room locking, operator protection

Scanning system
Dose delivery
Treatment Control System
Medical Software,
Interfaces to OIS

ME SYSTEMS

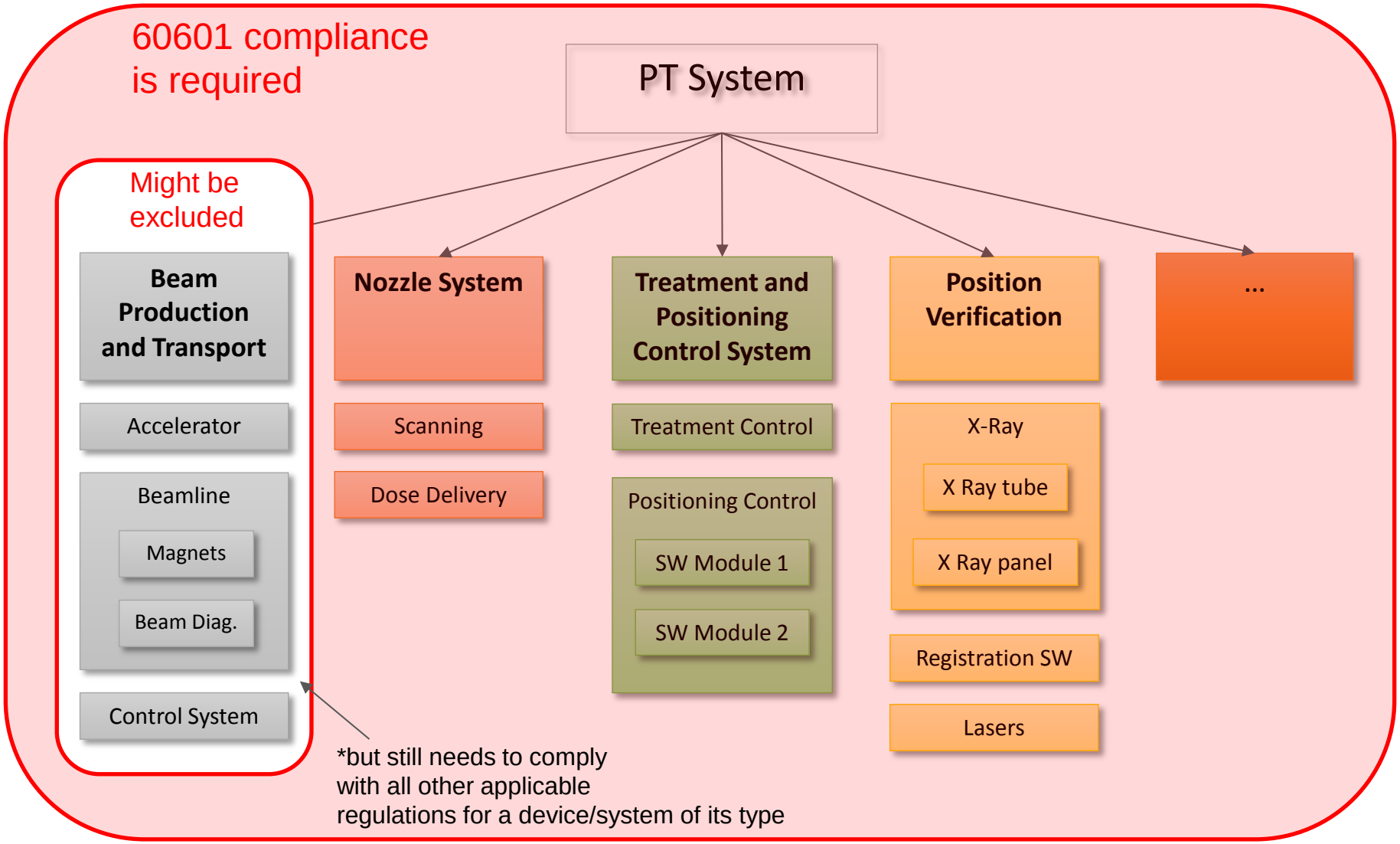
The standard **60601-1**, **section 16** offers an interesting view.

ME system composed of *medical* and *non medical* equipment. 3 Conditions:

- The ME SYSTEM as a whole shall not have unacceptable RISK.
- Within the PATIENT ENVIRONMENT, the level of safety for 60601-1
- Outside PATIENT ENVIRONMENT, the level of safety for applicable standards.

60601-1 allows to exclude some parts of the system from the need to be developed according to medical standards.

System Architecture



Use of Software

Software plays a key role: **system complexity is in fact driven by automation** -> „PEMS“ (60601-1 Section 14.)

1. EN 60601-1

- PEMS clause applies, excepted:
  - No BASIC SAFETY or ESSENTIAL PERFORMANCE*
  - ISO14971 demonstrates no unacceptable risk
- Compliance requires that a development life-cycle be specified and followed

2. EN 62304 -> Software life cycle processes.

Verification and Validation activities need to be conducted.

Goals of System Architecture

- To define a wise system architecture, to group components with similar characteristics and functions in subsystems.
- Risk management is used to determine overall risk and to find what components are „high risk“ and which are „low risk“. Also, risk aggregation.
- Some system components may not need to comply with 60601-1 (and related standards).
- Classify software according to 62304 into classes **A, B and C**.
- Translate User Requirements into Engineering Requirements/Specifications.

Two „types“ of requirements

Product Requirements

- Functional and performance requirements corresponding to the intended use of the product.
- Applicable regulatory requirements

The sources for product requirements are:

- User requirements formulated by clients respect their medical and business goals.
- Requirements known from the market.
- Regulatory requirements imposed or recommended by authority.

System/ Subsystem Reqs

- derived from the product definition requirements (functional, performance and regulatory), translating them onto technical specification.
- Technical requirements for the entire system, potentially with notes for the user manual and service manual.
- Safety relevant requirements
- The sources for translating regulatory requirements into technical requirements are the corresponding standards.
- Safety relevant requirements are derived from risk control measures defined in the risk management process, and applicable safety and essential performance standards for medical devices.

V&V at first sight

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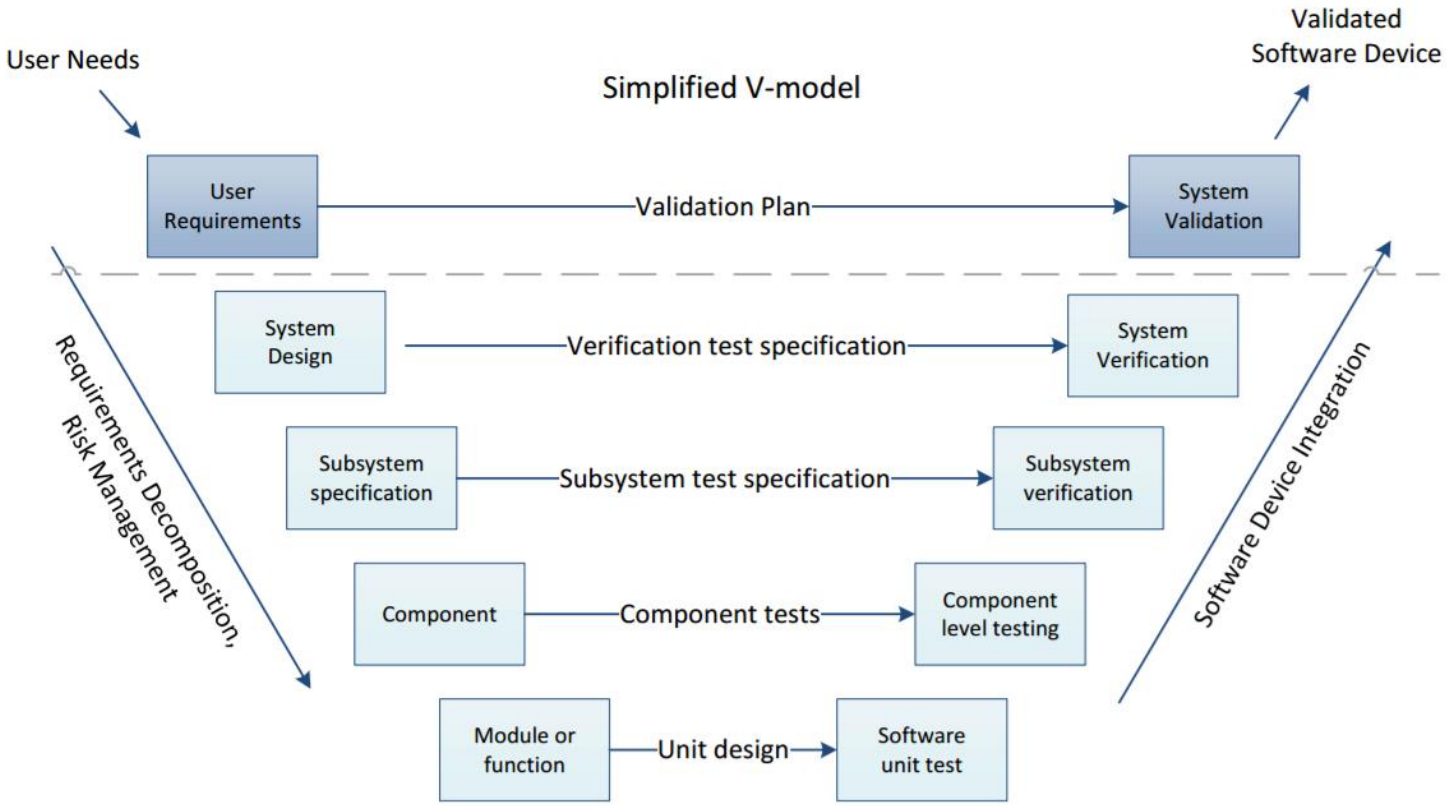
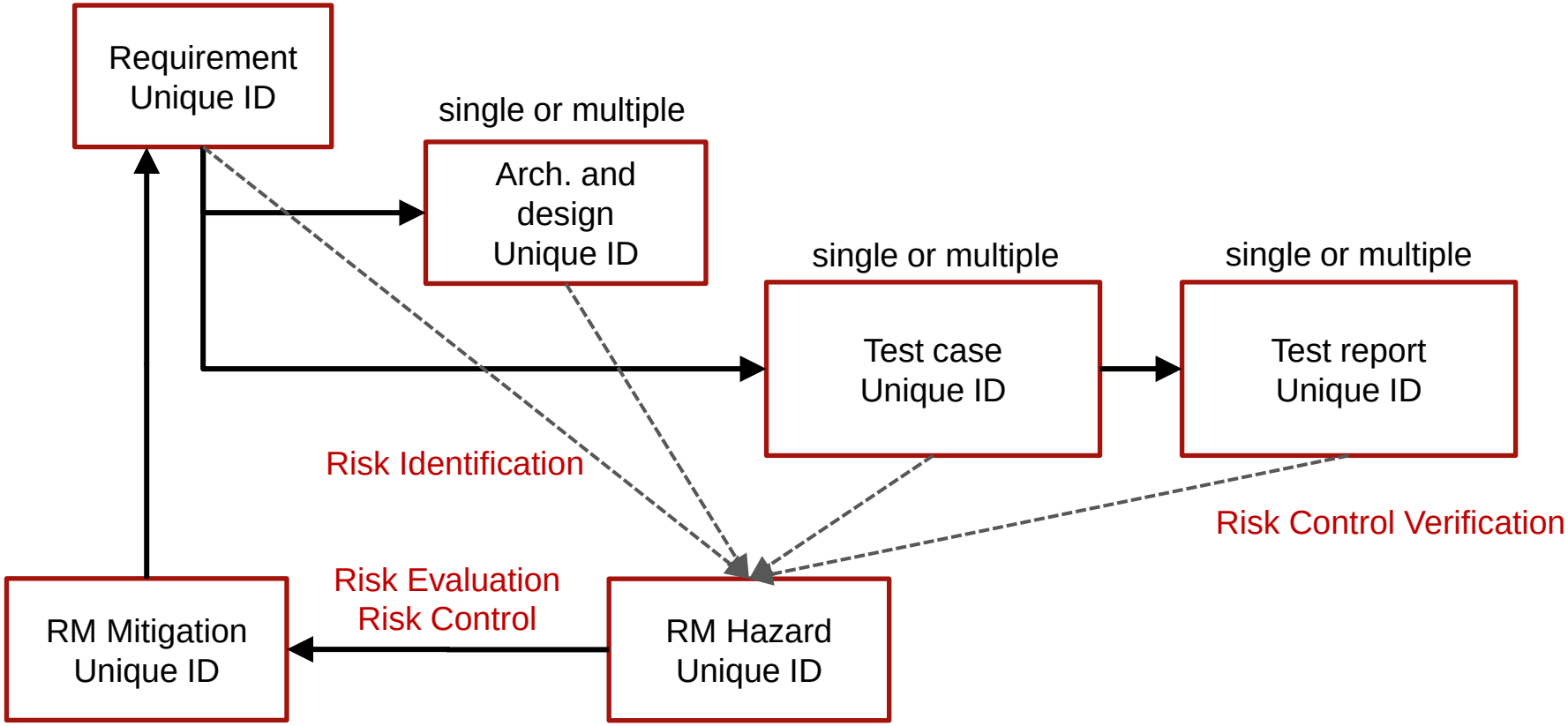
- The infamous „V-model“:



- A concept from the „Software world“
- Building the *thing right* vs. building the *right thing*

Test case traceability

- Every requirement should be covered by single or multiple test cases

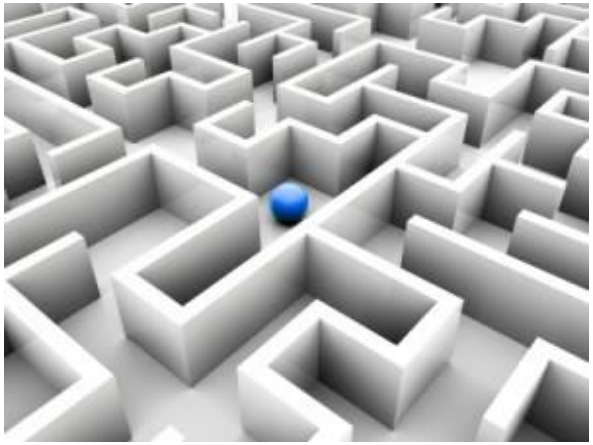


Summary (II)

- A PT System is one of the most complex „medical devices“.
- The regulations and standards are „easier to apply“ to simpler devices; for complex systems sometimes it is necessary to do some magic.
- 3 useful standards:
  - 60601-1, sections 14 and 16
  - Risk Management EN 14971
  - IEC 60601-2-64
- System level architecture plays a major role!
- Write good requirements; start EARLY in the process
- Traceability!

It‘s all about processeses

1. The laws and regulations request it
2. Technical standards require it
3. Good engineering practices recommend it
4. It gives you good tools and maneuvering space when things does not go as planned.
5. It‘s about finding the sweet spot between “too much“ and „too little“:



THANK YOU!

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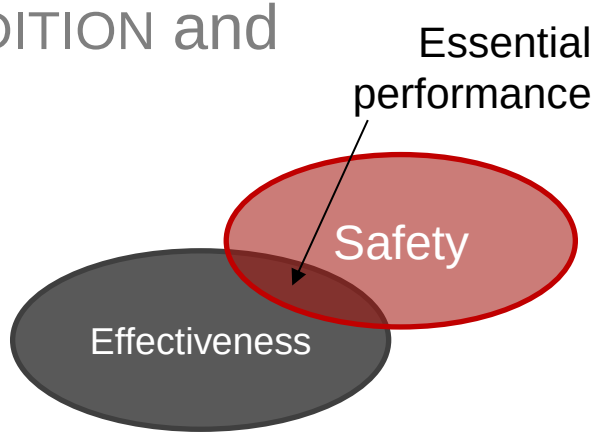
THOSE SLIDES AT THE END…

Basic safety and essential performance

- Originally only safety, Essential Performance is new to the 3rd. Edition
- ESSENTIAL PERFORMANCE: performance necessary to achieve freedom from unacceptable RISK.

  [whether its absence or degradation causes unacceptable RISK.]
- BASIC SAFETY: freedom from unacceptable RISK directly caused by physical HAZARDS when ME EQUIPMENT is used under NORMAL CONDITION and SINGLE FAULT CONDITION.
- Only makes sense in the context of Risk Management!



V&V for FDA

From 21. CFR 820.30 - Design controls

- **Design verification:** […] Design verification shall confirm that the design output meets the design input requirements. The results of the design verification, including identification of the design, method(s), the date, and the individual(s) performing the verification, shall be documented in the DHF.
- **Design validation:** […] Design validation shall ensure that devices conform to defined user needs and intended uses and shall include testing of production units under actual or simulated use conditions. Design validation shall include software validation and risk analysis, where appropriate. The results of the design validation,

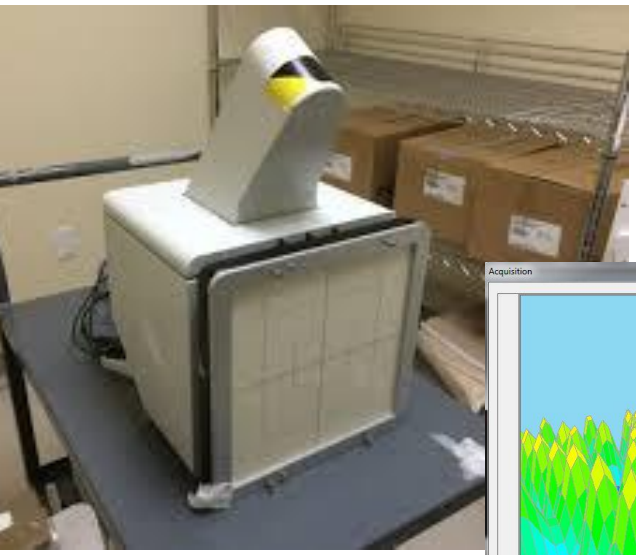
V&V for MDD

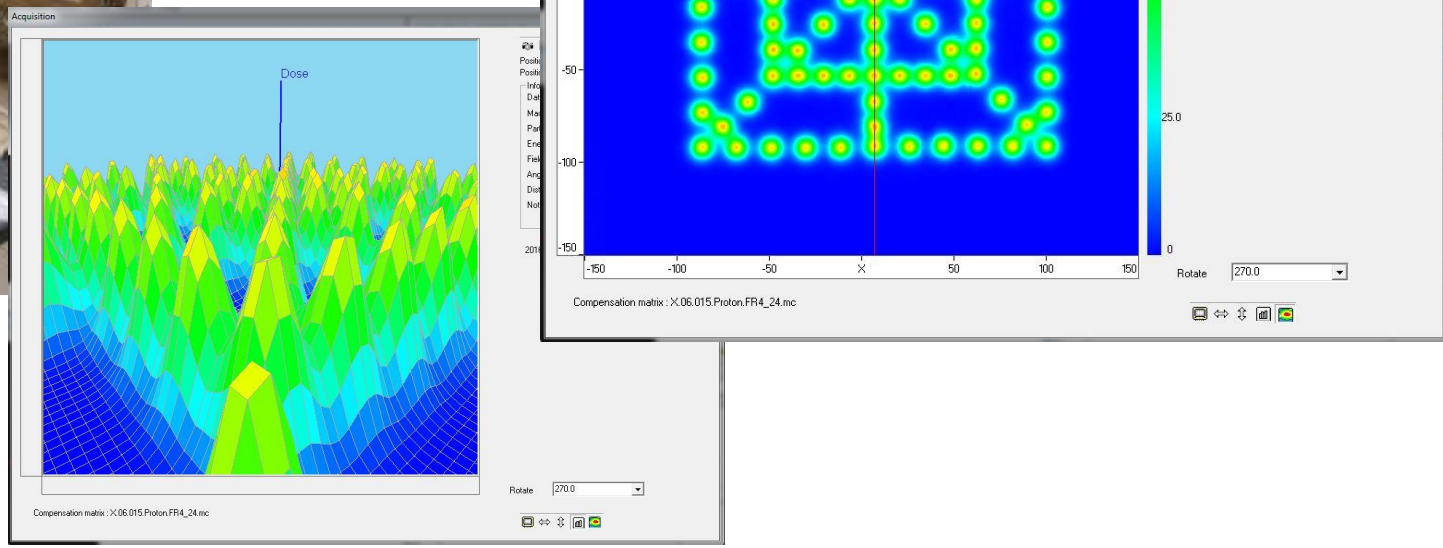
MDD 93/42/EEC, 12.1a:

- „For devices which incorporate software or which are medical software in themselves, the software must be validated according to the state of the art taking into account the principles of development lifecycle, risk management, **validation and verification**.“

Measurement of beam parameters

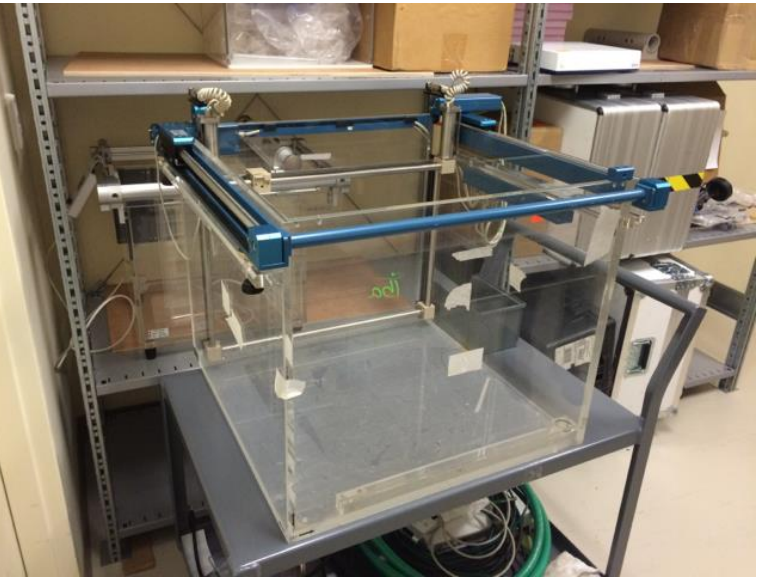
- „The beam size shall be 3mm or less (1sigma) at the isocentre at the highest treatment energy at all gantry angles“ (Verification)

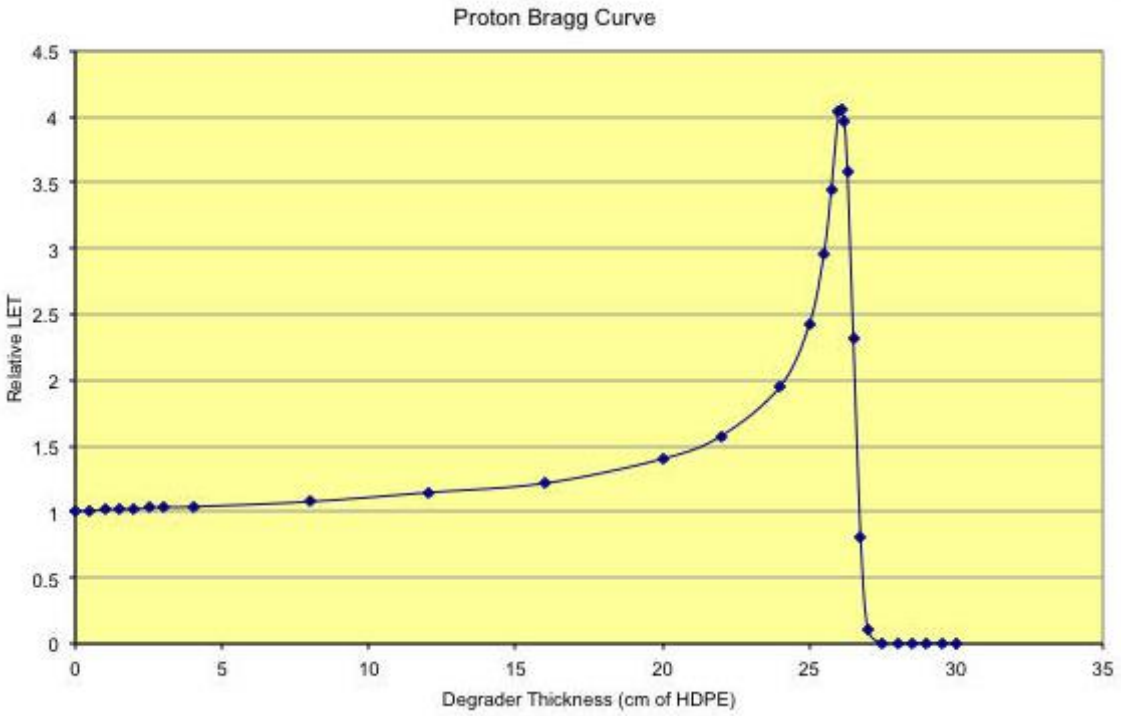




Measurement of beam parameters

- „The maximum range of the beam in water shall be 37 g/cm^2 or greater for treatment, which is defined as 250MeV or greater in a water target.„ (Verification)





Mechanical tests and measurements

- „The PPS shall be aligned with mechanical isocenter ±1mm.“ (Verification)