Medical Devices Regulation
Impact on Resources

Suzie Halliday & Jay Katta
26 July 2016
Impact on Resources

1. Routes of Conformity
2. Certificate Requirements
3. Clinical Evidence
4. Post Market Surveillance
   1. Periodic Safety Update Report
   2. Summary of Safety and Performance
5. Unique Device Identification

bsi.

Suzie Halliday
Jay Katta
Routes of Conformity
Classification & Conformity Assessment – Directive

- Competent Authority Assessment
- Notified Body Conformity Assessment
- Self-Certification

Risk
- Class IIa
- Class Im /Is
- Class I
- Custom Made
Classification & Conformity Assessment – Regulation

Commission Assessment

Competent Authority Assessment

Notified Body Conformity Assessment

Self-Certification

Risk

Class III

Class IIb

Class IIa

Class I

Custom Made

Class IIa – more sampling

Class IIb Implants

Class III Implants & Class IIb active – delivering medicines

Animal tissues, human tissues, medicinal substances, absorbable

Custom Made Class III Implants
Custom Made Devices

Annex XI
Technical Documentation

Annex XIII
PMS / PMCF / Incidents

Name of Person Authorised to make out prescription, Name of Healthcare Institution & Name of Particular Patient + Meets Requirements of Annex I
Class III Implantable – Custom Made Devices

Annex XI
Technical Documentation

Annex VIII
QMS

Annex X – Part A
Production
Quality Assurance

Name of Person Authorised to make out prescription, Name of Healthcare Institution & Name of Particular Patient + Meets Requirements of Annex I

Article 42 Point 7a
Class I Device
(non-sterile / no measuring function / not reusable)

Annex II
Technical Documentation

Declaration of Conformity (Annex III) & CE Marking (Annex IV)
Class I Device
(sterile / measuring function / reusable)

Annex II
Technical Documentation

Annex VIII*
QMS

Annex X – Part A*
Production Quality Assurance

* Only aspects related to sterility / metrology / reuse
* cleaning, disinfection, sterilization, maintenance, functional testing and related IFU

Declaration of Conformity (Annex III) & CE Marking (Annex IV)
Class IIa Device

Annex II
Technical Documentation *each Category

Annex VIII
QMS

Annex X – Part A
Production Quality Assurance

Annex X – Part B
Product Verification

Declaration of Conformity (Annex III) & CE Marking (Annex IV)
Class IIb Device

Annex II
Technical Documentation *each Generic Device Group

Annex VIII
QMS

Annex IX
Type Examination

Annex X – Part A
Production Quality Assurance

Annex X – Part B
Product Verification

Declaration of Conformity (Annex III) & CE Marking (Annex IV)
Class IIb Implantable Device

* sutures, staples, dental fillings & braces, tooth crowns, screws, wedges, plates, wires, pins, clips & connectors

Annex VIII
- Technical Documentation

Annex VIII
- QMS

Annex IX
- Type Examination

Annex X – Part A
- Production Quality Assurance

Annex X – Part B
- Product Verification

Declaration of Conformity (Annex III) & CE Marking (Annex IV)
Class III Device

(including those with medicinal substances, human tissues or animal tissues)

Annex VIII
Technical Documentation

Annex IX
Type Examination

Annex VIII
QMS

Annex X – Part A
Production Quality Assurance

Annex X – Part B
Product Verification


Declaration of Conformity (Annex III) & CE Marking (Annex IV)

bsi.

Article 42 Point 2
Class III Implantable Device & Class IIb Active Devices intended to administer medicinal products* (including those with medicinal substances, human tissues or animal tissues)

Annex VIII
Technical Documentation

Annex VIII
QMS

Annex IX
Type Examination

Annex X – Part A
Production Quality Assurance

Annex X – Part B
Product Verification


Consultation Procedure – Annex VIII or Annex IX Section 6.0

Declaration of Conformity (Annex III) & CE Marking (Annex IV)
Annex VIII – Clause 6 / Annex IX – Clause 6

Notified Body Review

21 days

39 days

Notified Body Review

Implantable Class III & Class IIb Active – Administer Medicines

Article 44:
- Manufacturer’s Clinical Evaluation
- NB Clinical Evaluation Report
- PMCF Plan
- IFU
- Summary of Safety and Performance

EU Commission

- Benefit:Risk Determination
- Consistency with indications
- PMCF Plan

No ‘scientific opinion’

NB Further Review

- Restrict indications
- Limit duration of certificate
- Undertake specific PMCF studies
- Adapt IFU or Summary of Safety and Clinical Performance
- Impose other restrictions

- Duly justify if advice not followed

Notified Body Certificate

Complete Conformity Assessment

Notified Body Certificate
Certificate Requirements
Annex V:
A new UDI-DI shall be required whenever there is a change that could lead to misidentification of the device and/or ambiguity in its traceability, in particular any change of one of the following UDI database data elements require a new UDI-DI:

a) Brand Name or Trade name
b) Device version or model
c) Labelled as single use
d) Packaged sterile
e) Need for sterilization before use
f) Quantity of devices provided in a package
g) Critical warnings or contraindications: e.g. containing latex or DEHP
Scope and Definitions – Article 2 – Clinical Evidence

Clinical Evidence
• the clinical data and clinical evaluation report pertaining to a device
• sufficient amount and quality to allow a qualified assessment of whether the device achieves the intended clinical benefit(s) and safety, when used as intended by the manufacturer

Clinical Evaluation
• a systematic and planned process to continuously generate, collect, analyse and assess the clinical data pertaining to a device
• to verify the safety and performance, including clinical benefits, of the device when used as intended by the manufacturer

Clinical Data
• clinical investigation on the device concerned
• clinical investigation reported in the scientific literature, of a similar device for which equivalence to the device in question can be demonstrated
• peer reviewed scientific literature on other clinical experience of either the device in question or a similar device for which equivalence can be demonstrated
• data from the manufacturer’s post-market surveillance system, in particular post-market clinical follow-up
Technical

- be of similar design
- used under similar conditions of use
- have similar specifications and properties (e.g. physicochemical properties such as intensity of energy, tensile strength, viscosity, surface characteristics, wavelength, software algorithms, porosity, particle size, nanotechnology, specific mass, atomic inclusions – nitrocarburising, oxidability)
- use similar deployment methods (if relevant)
- have similar principles of operation and critical performance requirements

Biological

- use same materials or substances in contact with the same human tissues or body fluids
- for a similar kind and duration of contact and similar release characteristics of substances
- including degradation products and leachables
- Exceptions can be foreseen for devices in contact with intact skin and minor components; in these cases risk analysis results may allow the use of similar materials taking into account the role and nature of the similar material. Evaluators should consider biological safety (e.g. ISO 10993) as well as other aspects necessary for a comprehensive demonstration of equivalence. A justification explaining the situation should be provided for any difference.

Clinical

- used for the same clinical condition or purpose (including similar severity and stage of disease)
- at the same site in the body
- in a similar population (including age, gender, anatomy, physiology)
- have same kind of user
- not foreseen to deliver significantly different performances
- have similar relevant critical performance according to the expected clinical effect for a specific intended purpose
Equivalent devices

The notified body should clearly document its assessment of clinical data presented from an equivalent device as part of a clinical evaluation. This should critically review and conclude on the equivalence or not of the device under assessment to the devices presented as equivalent in terms of their technical, biological and clinical characteristics. The relevance of each dataset from an equivalent device should be clearly evident and assessed by the notified body.

The notified body should also assess and document the level of access to the technical and clinical data from an Equivalent device that the manufacturer has.

Relevant information may be commercially sensitive / confidential and not available to the manufacturer. The notified body should challenge the ability of the manufacturer to access information that are relevant to the demonstration of equivalence.

Demonstration of equivalence might be difficult or impossible in case of limited access to the technical documentation of the devices.
• **Other products**

• For hazard identification and when assessing the benefit/risk profile of the device, the notified body should consider *current knowledge / the state of the art*.

• The notified body should assess the appropriateness of the use of data from *benchmark devices, other devices*, and *medical alternatives*. 

• These characteristics shall be similar to such an extent that there would be no clinically significant difference in the clinical performance and safety of the device.

• Considerations of equivalence must always be based on proper scientific justification.

• Manufacturers must be able to clearly demonstrate that they have sufficient levels of access to the data on devices to which they are claiming equivalence in order to justify that claimed equivalence.
Clinical Evaluation and Investigation – Article 49 – Clinical Evaluation

- In the case of implantable devices and devices falling within class III, clinical investigations shall be performed except if:
  - the device has been designed by modifications of a device already marketed by the same manufacturer
  - the modified device has been demonstrated to be equivalent and this has been endorsed by the Notified Body (Annex XIII) and
  - the clinical evaluation is sufficient to demonstrate conformity with the relevant safety and performance requirements.

- In this case the notified body shall check that the PMCF plan is appropriate and includes post market studies to demonstrate the safety and performance of the device.

- Clinical investigations need not be performed in the following cases – sutures, staples, dental fillings, dental braces, tooth crowns, screws, wedges, plates, wires, pins, clips or connectors for which the clinical evaluation is based on sufficient clinical data and is in compliance with the relevant product-specific common specification, where such a common specification is available...

... in view of similar well-established technologies – Delegated Act – add or remove to this list ...
• A manufacturer of a device demonstrated to be equivalent to an already marketed device not manufactured by him, may not need to perform a clinical investigation provided that the following conditions are fulfilled in addition to what is required in the paragraph above:

• the two manufacturers have a contract in place that explicitly allows the manufacturer of the second device full access to the technical documentation on an on going basis, and
• the original clinical evaluation has been performed in compliance with the requirements of this Regulation, and
• the manufacturer of the second device provides clear evidence thereof to the notified body.
Clinical Evaluation and Investigation – Article 49 – Clinical Evaluation

- The requirement to perform clinical investigations shall not apply to implantable devices and devices falling into class III:
  
  a) which have been lawfully placed on the market or put into service in accordance with Directive 90/385/EEC or Directive 93/42/EEC and for which the clinical evaluation is based on sufficient clinical data and is in compliance with the relevant product-specific common specification for the clinical evaluation of that kind of device, where such a common specification is available;

  or

  b) and is in compliance with common specification for the clinical evaluation, if available.
• Except for class III and implantable devices, where demonstration of conformity with general safety and performance requirements based on clinical data is not deemed appropriate, adequate justification for any such exception shall be given based on the results of the manufacturer’s risk management and on consideration of the specifics of the interaction between the device and the human body, the clinical performances intended and the claims of the manufacturer.

• The adequacy of demonstration of conformity with the general safety and performance requirements based on the results of non-clinical testing methods alone, including performance evaluation, bench testing and pre-clinical evaluation, has to be duly substantiated in the technical documentation referred to in Annex II.
Post Market Surveillance

- SSCP
- PSUR
Identification and Traceability of Devices – Article 27 – European Databank

EUDAMED

Electronic System on Registration / Conformity Assessment
Applications + Summary of Safety and Clinical Performance

Electronic System on Certificates
(issued, reissued, refused, suspended, withdrawn)

Electronic System on Vigilance
(incidents, FSCA, FSN)
+ Periodic Safety Update Report

Electronic System on Market Surveillance
(measures taken by Member States)

Electronic System on Clinical Investigations
(sponsors, description of investigational device, comparators, purpose, status)

Electronic System on UDI

Electronic System on Registration – Manufacturers & Authorised Representatives – SRN
Post-market surveillance, vigilance and market surveillance – Article 60 C – Periodic Safety Update Report

- Per device and where relevant per category or group of devices, manufacturers of devices in class IIa, IIb and III shall prepare a **periodic safety update report** summarising the results and conclusions of the analyses of the gathered post-market surveillance data according to Annex IIa together with a rationale and description of any preventive and corrective actions taken.

- Manufacturers of class IIb and III devices shall update the report at least annually.

- Manufacturers of class IIa devices shall update the report when necessary and at least every two years.

- Manufacturers of devices in class III or implantable devices shall submit reports by means of the electronic system to the notified body. The notified body shall review the report and add its evaluation to the database with details of any action taken. Such reports and the notified body evaluation shall be available to competent authorities through the electronic system.

**Throughout lifetime:**

- Conclusions of the benefit risk determination
- Main findings of PMCF
- Volume of Sales
- Estimate of the Population that use the device
- Where practicable usage frequency of the device
Identification and Traceability of Devices
– Article 26 – Summary of Safety and Clinical Performance

• In the case of devices classified as class III and implantable devices, the manufacturer shall draw up a summary of safety and clinical performance.

• It shall be written in a way that is clear to the intended user and, if relevant, to the patient and shall be available to the public via EUDAMED.

• The draft of this summary shall be submitted to the notified body and shall be validated by that body. After validation the notified body shall upload this summary report to Eudamed. The manufacturer shall mention on the label or instructions for use where the summary report is available.

• Manufacturer + SRN
• Device + UDI
• Intended Purpose, Indications, Contra-indications
• Description, previous variant(s), differences, accessories, other products intended to be used in combination
• Possible diagnostic or therapeutic alternatives
• Harmonised Standards / Common Specifications
• Summary of the Clinical Evaluation Report + PMCF
• Suggested profile and training for users
• Information on residual risks, undesirable effects, warnings & precautions

Article 49 – Clinical Evaluation
For devices classified as class III and implantable devices, the PMCF report and, if indicated, the summary of safety and clinical performance shall be updated at least annually with these data.
4. The UDI carrier shall be placed on the label of the device and on all higher levels of packaging. Higher levels of packaging do not include shipping containers.
Article 24 – UDI

*not commercially available on its own

*unique @ all levels of packaging

*if significant space constraint on the unit of use package the UDI may be placed on the next higher package level
Article 24 – UDI

4. The UDI carrier shall be placed on the label of the device and on all higher levels of packaging. Higher levels of packaging do not include shipping containers.

- The UDI shall be used for reporting serious incidents and field safety corrective actions in accordance with Article 61.
- The Basic UDI device identifier (‘Basic UDI-DI’ as defined in Annex V Part C) of the device shall appear on the EU declaration of conformity referred to in Article 17.
- The manufacturer shall keep up-to-date a list of all applied UDI as part of the technical documentation referred to in Annex II.
4. The UDI carrier shall be placed on the label of the device and on all higher levels of packaging. Higher levels of packaging do not include shipping containers.

- The UDI shall be used for reporting serious incidents and field safety corrective actions in accordance with Article 61.

- The Basic UDI device identifier (‘Basic UDI-DI’ as defined in Annex V Part C) of the device shall appear on the EU declaration of conformity referred to in Article 17.

- The manufacturer shall keep up-to-date a list of all applied UDI as part of the technical documentation referred to in Annex II.
Article 24 – UDI

4. The UDI carrier shall be placed on the label of the device and on all higher levels of packaging. Higher levels of packaging do not include shipping containers.

- The UDI shall be used for reporting serious incidents and field safety corrective actions in accordance with Article 61.
- The Basic UDI device identifier (‘Basic UDI-DI’ as defined in Annex V Part C) of the device shall appear on the EU declaration of conformity referred to in Article 17.
- The manufacturer shall keep up-to-date a list of all applied UDI as part of the technical documentation referred to in Annex II.

The technical documentation and, if applicable, the summary thereof to be drawn up by the manufacturer shall be presented in a clear, organised, readily searchable and unequivocal way and shall include:

1. DEVICE DESCRIPTION, SPECIFICATION, VARIANTS & ACCESSORIES
   - Device description and specification + UDI
   - Reference to previous / similar generations of the device

2. INFORMATION SUPPLIED BY THE MANUFACTURER

3. DESIGN AND MANUFACTURING INFORMATION

4. GENERAL SAFETY AND PERFORMANCE REQUIREMENTS

5. RISK/BENEFIT ANALYSIS AND RISK MANAGEMENT

6. PRODUCT VERIFICATION AND VALIDATION
   - Pre-clinical and clinical data
   - Additional information in specific cases
Annex I – Safety & Performance Requirements

- **SPR# 19.2. Information on the label**
- The label shall bear the following particulars:
- Many new requirements ...

- (h) the unique device identification (UDI) carrier according to Article 24 and Annex V Part C.

- (fa) SPR #7.4.5 – list of carcinogenic, mutagenic, toxic to reproduction, having endocrine disrupting properties >0.1% weight by weight
Article 24 – UDI

5. **Economic operators** shall store and keep, preferably by electronic means, the UDI of the devices which they have supplied or they have been supplied with, if they belong to:
   - class III implantable devices;
   - the devices, categories or groups of devices determined by a measure referred to in point (a) of paragraph 7.

- **Health institutions** shall store and keep preferably by electronic means the UDI of the devices which they have supplied or they have been supplied with if they belong to **class III implantable devices**.

- For devices **other than class III implantable devices**, Member States shall **encourage, and may require**, health institutions to store and keep, preferably by electronic means, the UDI of the devices which they have been supplied with.

- Member States shall **encourage, and may require**, health care professionals to store and keep preferably by electronic means, the UDI of the devices which they have been supplied with.
Article 16 – Implant Card

The manufacturer of an implantable device shall provide together with the device the following:

- device name
- serial number
- batch code or lot number
- Unique Device Identification
- device model
- manufacturer name, address and URL of the website
- any warnings, precautions or measures to be taken by the patient or a healthcare professional with regard to reciprocal interference with reasonably foreseeable external influences, medical examinations or environmental conditions;
- any information about the expected lifetime of the device and any necessary follow-up;
- any other information to assure a safe use of the device by the patient
- including the information in Annex I, Section 19.3 – Instructions for Use
Questions & Answers

1. Routes of Conformity
2. Certificate Requirements
3. Clinical Evidence
4. Post Market Surveillance
   1. Periodic Safety Update Report
   2. Summary of Safety and Performance
5. Unique Device Identification