.....the practical approach

The last 'clinical' elements of implementation before DoA

Paul van Geffen, PhD

Sr. Consultant & EU MDR Lead

Qserve Group

Outline

- Introduction
- Clinical evidence scrutiny, harmonization and transparency
- Common Specifications
- Consultation procedure
- Expert Panels
- Summary of Safety and Clinical Performance (SSCP)
- State of the art methodology – Meddev 2.7.1
- What you still can and should do

Regulation EU 2017/745

Transitional dates	
5 April 2017	Adopted
5 May 2017	Published
26 May 2017	Entry into force
26 May 2020	Date of application

< 8 months

5.5.2017 EN Official Journal of the European Union

I

(Legislative acts)

REGULATIONS

REGULATION (EU) 2017/745 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL
of 5 April 2017
on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC
(Text with EEA relevance)

THE EUROPEAN PARLIAMENT AND THE COUNCIL OF THE EUROPEAN UNION,

Regulation EU 2017/745

Key objectives
- Improve level of health & safety protection for EU citizens
- Enhance free and fair trade of medical devices throughout the EU
- Adaption to significant technological & scientific progress

Key elements
- Expansion and clarification of scope
- Better supervision on/by Notified Bodies
- Better supply chain control and responsibilities
- Increased clinical evidence scrutiny, harmonization and transparency

Before placing a device on the market…

- A device shall meet the General Safety and Performance Requirements (GSPRs)
- Demonstration of conformity with the GSPRs shall include a clinical evaluation and shall be based on clinical data providing sufficient clinical evidence.
- Clinical evaluation is required for all medical devices
- Clinical evidence must be of a sufficient amount and quality.

Before placing a device on the market…

- Clinical evaluation of Class III devices and implantable devices must include a clinical investigation (except in case of modifications to own equivalent device on market and for with the clinical evaluation demonstrates conformity with GSPR)
- Clinical evaluation consultation procedure required for Class III implantable devices and Class IIb active devices that are intended to administer and/or remove a medicinal product (Rule 12 devices).
- For Class III device and for Class IIb Rule 12 devices, the manufacturer may consult an expert panel for advice on clinical investigation strategy.

More scrutiny, harmonization and transparency

- Common Specifications
- Clinical evaluation consultation procedure
- Designation of Expert Panels
- Summary of Safety and Clinical Performance (SSCP)
- EUDAMED

Common Specifications

The Commission, after consulted the MDCG, may adopt Common Specifications by means of Implementing Acts where

- Harmonized standards are insufficient or do not exist, or
- Where there is a need to address public health concerns

Manufacturers shall comply with applicable Common Specifications unless they can duly justify that they have adopted alternative solutions to ensure safety and performance

MEDDEV 2.7.1 should be used as state-of-the-art methodology for clinical evaluation until adoption of Common Specification

Clinical evaluation consultation procedure

- Required for Class III implantable devices and Class IIb Rule 12 devices except if:
  - Certificate renewal;
  - Modification to own equivalent device (no affect on RBD); or
  - Clinical evaluation according applicable Common Specification.
- Notified Body submits clinical evaluation assessment report together with the clinical evaluation documentation to the Commission.
- Commission submits those documents to an expert panel to provide their scientific opinion (within 60 days).

Clinical evaluation consultation procedure (cont'd)

The expert panel shall judge:

- Level of evidence;
- Benefit risk determination; and,
- Consistency of evidence with intended purpose and PMCF plan.

In case of a negative expert opinion, the NB may impose a limit on duration of certificate validity, and shall advice the manufacturer to:

- Restrict the intended purpose,
- Undertake specific PMCF studies, and/or
- Adapt the IFU or SSCP.

Expert Panels

- Provide the Commission, MDCG, MS, NB and/or manufacturers with up-to-date scientific, technical and clinical advice in a range of relevant fields.
- Implementing Decision 2019/1396 of 10 September 2019 on rules and procedures on the designation, coordination and work of expert panels.
- Advisors shall declare interest which may compromise their independence, impartiality and objectivity.
- Public call for expression of interest later in 2019.

Summary of Safety and Clinical Performance (SSCP)

- SSCP for implantable devices and for class III devices
- Recent guidance MDCG 2019-9, with suggested template
- Publicly available in EUDAMED
- Validated and uploaded to EUDAMED by NB.
- Link in IFU to SSCP in EUDAMED; state value of Basic UDI-DI
- Full consistency with TD, including IFU, CER, PMCFR and PSUR
- Controlled doc. Revision history and NB validation status/ language
- Periodic review/ update if needed; align with PMCFR/ PSUR updates
- To enhance readability and to facilitate printing, separated parts for:
  - Healthcare professionals (medial terms) and,
  - Patients, if relevant (laymen's terms).

SSCP patient information

- Patient information relevant especially for:
  - Implantable devices that require an implant cart
  - Class III devices to be used directly by patients
  - Annex XVI devices eligible for SSCP
- Considerations for patient information:
  - No assumption of any knowledge of medical/ clinical terminology
  - Readable in terms of layout, font size, language, terminology, etc.
  - Understandable in terms of unambiguity and by avoiding or explaining abbreviations, acronyms and professional terminology.
  - Validation by means of tests with lay persons

SSCP elements

Element	Main section *Medical terms*	Patient section *Laymen's terms*
1 Device identification and general information	**X**	**X**
1.1 Device trade name(s)	X	X
1.2 Manufacturer; name and address	X	X
1.3 Manufacturer single registration number (SRN)	X	-
1.4 Basic UDI-DI	X	X
1.5 Medical device nomenclature	X	-
1.6. Class of device	X	-
1.7 Year of initial CE	X	X
1.8 Authorized representative name and SRN	X	-
1.9 Notified Body name and id no.	X	-
2 Intended use of the device	**X**	**X**
2.1 Intended purpose	X	X
2.2 Indication(s) and target population(s)	X	X
2.3 Contraindications and/or limitations	X	X
3 Device description	**X**	**X**
3.1 Description of the device	X	X
3.2 Previous generation(s)/ variants, description of and highlighting differences	X	-
3.3 Accessories or other devices to be used with the device	X	X

SSCP elements (cont'd)

Element (cont'd)	Main section *Medical terms*	Patient section *Laymen's terms*
4 Risks and warnings	**X**	**X**
4.1 Residual risks and undesirable effects	X	X
4.2 Warnings and precautions	X	X
4.3 Other aspects such as FSN or FSCA	X	X
5 Summary of clinical evaluation and PMCF	**X**	**X**
5.1 Summary of clinical data related to equivalent device; incl. name and Basic UDI-DI	X	-
5.2 Summary of clinical investigations related of the device; link to EUDAMED	X	-
5.3 Summary of other clinical data related of the device	X	-
5.4 An overall summary of the clinical performance and safety	X	X
5.5 Ongoing or planned post-market clinical follow-up	X	-
6 Possible diagnostic or therapeutic alternatives	**X**	**X**
7 Suggested profile and training for users	**X**	**X**
8 Reference to any harmonized standards and CS applied	**X**	-
9 Revision history	**X**	-
9.1 Revision no.	X	-
9.2 Revision date.	X	-
9.3 Change description	X	-
9.4 NB validation status; validated language	X	-

State-of-the-art methodology for clinical evaluation

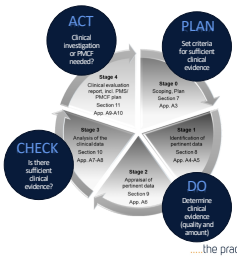
Meddev 2.7.1 until adoption of Common Specification(s)


EUROPEAN COMMISSION
Health Technology and Cosmetics

MEDDEV 2.7/1 revision 4
June 2016

GUIDELINES ON MEDICAL DEVICES

CLINICAL EVALUATION:
A GUIDE FOR MANUFACTURERS AND NOTIFIED BODIES
UNDER DIRECTIVES 93/42/EEC and 90/385/EEC

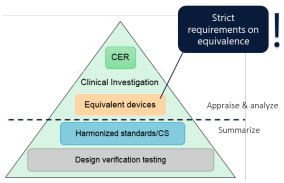


.....the practical approach

Identify clinical data

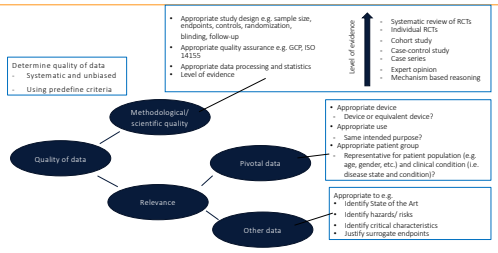
Data held by manufacturer
Pre-clinical studies (V&V, harmonized standards/ CS)
Pre-market clinical investigations
Data from PMS/PMCF activities

Data not held by manufacturer
Clinical literature - Based on systematic review principles - Carefully devised research questions - Systematic methods to identify, appraise and analyze clinical data - Thorough, objective, non-biased, using favorable and unfavorable data



.....the practical approach

Appraise clinical data



.....the practical approach

Analyse clinical data

Does the appraised data sets collectively provide sufficient clinical evidence to demonstrate conformity with the relevant GSPRs?

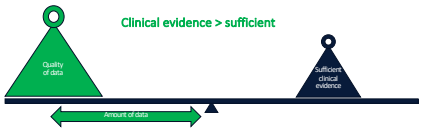
The level of clinical evidence depends on the amount and quality of the data.

Depends on device nature, characteristics, classification, risks, intended purpose and claims

Analyse clinical data

Does the appraised data sets collectively provide sufficient clinical evidence to demonstrate conformity with the relevant GSPRs?

Clinical evidence > sufficient

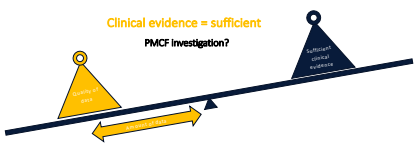


Analyse clinical data

Does the appraised data sets collectively provide sufficient clinical evidence to demonstrate conformity with the relevant GSPRs?

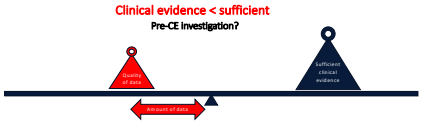
Clinical evidence = sufficient

PMCF investigation?



Analyse clinical data

Does the appraised data sets collectively provide sufficient clinical evidence to demonstrate conformity with the relevant GSPRs?



More need for clinical investigation?

Most likely, because:

1. Greater need for clinical evidence
   - Due to stricter criteria e.g. on equivalency
2. Up-classifications (e.g. into class III devices) to adapt to the technological and scientific progress. Some examples:
   - Rule 14 – The classification of devices incorporating a medicinal substance no longer depends on whether the substance is liable to act on the human body
   - Rule 11 – The classification of software intended to provide information for decision making depends on the impact of the decision
   - Rule 19 – The classification of devices with nanomaterials depends on the level of potential for internal exposure
   - Rule 21 – Applicable for substance based devices that are absorbed by or locally dispersed in the human body

What you still can and should do

1. Consider making use of 'soft' transition period
2. Update clinical evaluation process according MDR rules
3. Implement process to allow MDR compliant new product development
4. Re-assess legacy evidence following MDR rules
5. In case of gaps and/or uncertainties:
   - Restrict the intended purpose
   - Undertake specific PMCF studies, and/or
   - Adapt the IFU (and SSCP)

Summary

Increased need for clinical evidence
- Stricter criteria, re-classifications into Class III

Increased scrutiny on clinical evidence
- Clinical evaluation consultation procedure

Increased harmonization and transparency of clinical evidence
- Expert panels, SSCP, EUDAMED

Time is running out…

… but there are still things you can and should do!

Thank you for your attention

Paul van Geffen, PhD

Sr. Consultant & EU MDR Lead
Qserve Group

Your Global Medtech Partner for **Clinical, Quality and Regulatory Compliance**

Europe – The Netherlands - Germany | USA – Massachusetts - California | China – Nanjing