Clinical Evaluation and Clinical Investigation update

MDR

December 5th, 2017

Carine Cochereau, Cardinal Health
• **Directives:** obligation for Member State (MS) to implement provisions into their national legislation – slight implementation differences between MS possible

• **Regulations:** directly applicable in each Member State & obligation to repeal conflicting national regulations

• **Guidance Documents & “Soft law”** (MEDDEVs, Interpretative documents, Consensus statements) -not legally binding
• MDR for:
  – 28 Member states of the EU (27 + UK)
  – European Economic Area (Iceland, Liechtenstein and Norway)

• Under negotiation:
  – Switzerland
  – United Kingdom
MDR – A significant impact ...

- Scrutiny
- Clinical Requirements / new Clinical Equivalence approach
- UDI & Labelling updates
- Up-classifications from Class IIb to III
- New reprocessing rules
- Increased checking by Notified Bodies
- Capacity / Volume of Dossiers (Notified Bodies / CA / Ind)
- Registration Database / Eudamed
- Systems changes, validations and training
- Fees
MDR is an opportunity

- Enhanced patient safety and product performance
- Transparency
- New strategic decisions are possible
- Fast movers = marketing edge
- Improved portfolio management
- Early scientific advice
Clinical evaluation and device lifetime/ cycle

Clinical evaluation

- Pre-clinical
- Clinical
- Conformity Assessment
- Clinical use
- PMS / PMCF
- Vigilance / Post market surveillance

Risk analysis
Clinical Evaluation

Equivalency
Narrowed pathway/Data access and exemptions

Publication
Peer reviewed Journal

Scope of Studies
EU regulation/Globalization

CI Strategy

Extent of clinical data
Well established Technologies / PMS and PMCF

Consistency
Definitions interpretations

Expert Panel
Pre-meeting/Conformity assessment and scrutiny

December 5-6, 2017
Hilton Orlando, Orlando FL, USA
Existing devices
- Clinical Evaluation and PMCF plan shall be reviewed asap (Equivalency/Literature/Studies)
- Robustness of the clinical data
- Establish the PMS and CI plan
- Monitor Common Specifications and new guidances
- Compliance with MDD 93/42/EC/Iteration of medical devices

New Product Introduction
- Clinical Roadmap shall be established as early as possible in the product development
- Establish whether a CI shall be conducted and whether an expert panel consultation may be necessary
- Equivalency and data access
- Establish the PMS and CI plan
Article 61 (4)

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 by the manufacturer to be equivalent to the marketed device, in accordance with Section 4a of Part A of Annex XIII and this demonstration has been endorsed by the notified body, and
- the clinical evaluation of the marketed device is sufficient to demonstrate conformity of the modified device with the relevant safety and performance requirements.

Article 61 (5)

A manufacturer of a device demonstrated to be equivalent to an already marketed device not manufactured by him, may also rely on paragraph 4 in order not to perform a clinical investigation provided that the following conditions are fulfilled in addition to what is required in that paragraph:

- 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 ongoing 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.

Article 61 (6)

The requirement to perform clinical investigations pursuant to paragraph 2a 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;

(b) That are sutures, staples …
Continuous innovation and patients’ Health
Cross Functional

- Risk management
  hazard identification list and identified clinical risks

- Design Dossier/Technical files

- Literature

- PMS and Vigilance

- Clinical Investigation

- Clinical Development Plan
Key ongoing information and set up

- Common Specifications: Format / process / categories of devices unknown
- Implementing act and delegated act
- Eudamed
- SAE’s reporting for ongoing studies
The Regulatory framework surrounding MDR

• Meddev 2.7.1 revision 4
  • Transition
  • CER Model

• ISO 14155 under revision
  • Global perspective
  • Clinical Investigation strategy
  • Registries
  • Statistical considerations
The Regulatory framework surrounding MDR

- Data Privacy law : 2016/679
  Protection of natural persons with regard to the processing of personal data and on the free movement of such data (May 25, 2018)
  - Informed consent Form
  - Data usage
  - Retrieval of consent
  - Clinical research definition

- Implementation at country level

- Global acceptance of the new regulatory system of Europe?
Initial needed clarifications for implementation

Need clarity for industry to effectively plan and comply in time:

- Insufficient detail on extent of data expected
- Incoherent definitions and terminology, overly complex text
- How to practically demonstrate equivalence
- The practicalities of addressing post-market clinical follow-up and annual reporting requirements
Progress is impossible without changes

G. Bernard Show
### Case Study: guidewire

<table>
<thead>
<tr>
<th>Category</th>
<th>Device Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class</td>
<td>Class III</td>
</tr>
<tr>
<td>Intended purpose</td>
<td>Intended for use in the percutaneous introduction of catheters.</td>
</tr>
<tr>
<td>Device description</td>
<td>Guidewire with stainless steel shaft. The shaft is PTFE coated. Radio-opaque markers</td>
</tr>
<tr>
<td>Clinical Performance</td>
<td>For procedure in the treatment of stenosed lesions</td>
</tr>
<tr>
<td>Contra-indications</td>
<td>No</td>
</tr>
<tr>
<td>Sterilization</td>
<td>Eto</td>
</tr>
<tr>
<td>Claims</td>
<td>PTFE coating intends to minimize friction on the proximal end for smooth device delivery</td>
</tr>
<tr>
<td></td>
<td>One-Piece stainless steel core wire design optimizes the transmission of torque to the distal tip of the wire for optimal control</td>
</tr>
<tr>
<td></td>
<td>Precise positioning with the radio-opaque markers</td>
</tr>
<tr>
<td>Clinical Investigation</td>
<td>Literature</td>
</tr>
<tr>
<td>------------------------</td>
<td>------------</td>
</tr>
<tr>
<td>Device</td>
<td>Equivalent</td>
</tr>
</tbody>
</table>
| No | No | No | YES: generic literature published in peer reviewed journals on endovascular procedure including reference to Guidewires, PTCA Balloons, Introducers, sheaths and Stents. | No | Yes:  
Technical:  
- Both families are PTFE coated or heparin coated.  
- Both families have a core wire manufactured with the same polymer family.  
Technical testing’s have been done to confirm the technical equivalences between the both families.  
Shape of both families are similar, confirmation has been done based on website and IFU of both families.  
Clinical: same intended purpose  
Biocompatibility: the product is compliant with ISO 10993 |
Device has been marketed for 15 years with no substantial changes.

Used on daily basis and is considered as a commodity device by medical societies.

The safety and performance of this medical device is related to the procedure and well positioning of catheters.

Curves and shapes of Guidewire are consistent in the European market.

PMCF has been exempted. The post market data are continuously collected through literature review and safety reporting (complaints/ vigilance database...).
Area of interest for this case

- Robustness of the equivalency
- Robustness of the literature compilation
- Claims
- The exemption of the PMCF