MDR Changes and Impact on Industry: A Notified Body Perspective

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What we will cover

• The Change
• The Notified Body
• The Industry
• The Future
Background

The road to new EU Medical Device regulations

• Patient safety issues were key driver
  • PIP
  • MoM
  • Pelvic floor mesh

• Advances in technology
  • Nanomaterials
  • 3D Printing (custom made devices)

• Demographic shifts
  • Long term implantable devices are being implanted for a longer term
  • Patients have greater access to information, becoming more litigious
General Safety and Performance Requirements – Annex I

• There are 23 GSPRs in the MDR – 13 (Essential Requirements) in the MDD

• 3 sections –
  • Chapter 1: General requirements
  • Chapter 2: Requirements regarding design and manufacture
  • Chapter 3: Requirements regarding the information supplied with the device
General Safety and Performance Requirements – Annex I

• The GSPRs act as a “how to” guide when developing a device or making a significant change
• They are the rules which a Notified Body will hold a manufacturer to when reviewing technical documentation

• Example: GSPR 5:
  • In eliminating or reducing risks related to use error, the manufacturer shall:
    • reduce as far as possible the risks related to the ergonomic features of the device and the environment in which the device is intended to be used (design for patient safety),
Technical Documentation – Annex II & III

• There are 2 annexes for technical documentation – one on general technical documentation and one on post market surveillance

• Similar to GSPR, you should familiarise yourself early on

• Annex II is broken into 6 sections- matches the STED layout as discussed previously

• Use the headings to generate a skeleton tech file as early as you can
Technical Documentation – Annex II & III

- Device description and specification, including variants and accessories
- Information to be supplied by the manufacturer
- Design and manufacturing information
- General safety and performance requirements
- Benefit-risk analysis and risk management
- Product verification and validation

1: Device description
2: Information to be supplied by the manufacturer
3: Design and manufacturing information
4: General safety and performance requirements
5: Benefit-risk analysis and risk management
6: Product verification and validation
Technical Documentation – Annex II & III

• Annex II is very prescriptive for what is required in each section

• Similar to the GSPOs the Notified Body will expect to see each element addressed

• If available use Notified Bodies application documents to supplement your development of a tech file
**Technical Documentation – Annex II & III**

• Annex II section 3:

3. **DESIGN AND MANUFACTURING INFORMATION**

(a) information to allow the design stages applied to the device to be understood;

(b) complete information and specifications, including the manufacturing processes and their validation, their adjuvants, the continuous monitoring and the final product testing. Data shall be fully included in the technical documentation;

(c) identification of all sites, including suppliers and sub-contractors, where design and manufacturing activities are performed.

• **NSAI Application Doc: GRF 25-44a**

**Section 12: DEVICE TESTING**

12.1 – Device Design Testing

1. Please supply a Design Traceability Matrix or Design input/ Output document and verify that the following have been included:
   - Design Input / User Need
   - Specification for each Input
   - Source of each specification
   - Justification of the source (via use of a standard: Harmonised, Non-Harmonised ASTM, AAMI), predicate device testing, internally validated specification with clinical feedback, etc.
   - Design Output/ Documented Evidence
   - Comment on whether D/I was met or not
Technical Documentation – Annex II & III

- Even for new devices a Notified Body must review the PMS plan
- Chapter VII – Article 83 Post-market surveillance system
  - Manufacturer must plan, implement and update a PMS system
  - The data it generates must be used to:
    - Update benefit-risk determination and improve risk management
    - Update the clinical evaluation
    - Identify the need for preventative, corrective or field safety corrective action
    - Identify the option to improve the usability, performance and safety of the device
Periodic Safety Update Report – Chapter VII

- Article 86 – PSUR required for all devices class IIa, IIb and III

- This is an output of the post-market surveillance plan – which is detailed in annex III

- The PSUR must:
  - Draw conclusions of the benefit-risk determination
  - Outline the main findings of the PMCF
  - State the volume of sales, size of population using the device and if possible the frequency of use

- Interval:
  - Class IIb and III: At least annually
  - Class IIa: When necessary and at least every two years

- Class III and implantable devices must have PSUR approved by NB
Clinical Evaluation & PMCF – Annex XIV

• Clinical evaluation ≠ clinical investigation

• All devices require a clinical evaluation no matter the class
  • The level of data required will depend on the class

• MEDDEV 2.7/1 Rev.4 very useful guidance doc
Clinical Evaluation & PMCF – Annex XIV

- Annex XIV – Part A sets out requirements for a CEP
  - Identify available clinical data relevant to the device and its intended purpose and any gaps in clinical evidence through a systematic scientific literature review
  - Appraise all relevant clinical data by evaluating their suitability for establishing the safety and performance of the device
  - Generate, through properly designed clinical investigations in accordance with the clinical development plan, any new or additional clinical data necessary to address outstanding issues
  - Analyse all relevant clinical data in order to reach conclusions about the safety and clinical performance of the device including its clinical benefits.
Clinical Evaluation & PMCF – Annex XIV

• Annex XIV – Part B sets out requirements for PMCF

• Continuous process that updates the clinical evaluation
  • For class III and implantable devices must be updated at least annually

• Links back in with annex III – TD on PMS

• Its purpose is to:
  • Confirming the safety and performance of the device throughout its expected lifetime
  • Identifying previously unknown side-effects
  • Identifying and analysing emergent risks on the basis of factual evidence
  • Ensuring the continued acceptability of the benefit-risk ratio
  • Identifying possible systematic misuse or off-label use
Clinical Evaluation & PMCF – Annex XIV

Clinical evaluation based on equivalence

• This process is more difficult under the MDR
  • **Technical**: similar design; is used under similar conditions of use
  • **Biological**: device uses the same materials or substances in contact with the same human tissues
  • **Clinical**: device is used for the same clinical condition or purpose, including similar severity
  • Must be equivalent to one single predicate for all 3 categories

• Key element is that a difference can't result in a clinically significant difference in safety or clinical performance

• Manufacturer must have sufficient access to data of predicate
Clinical Evaluation & PMCF – Annex XIV

Clinical evaluation of legacy devices

- MDR does not have grandfathering clause
- All devices will be treated as new when reviewed
- How well does your clinical data currently look?
Clinical Evaluation & PMCF – Annex XIV

Clinical evaluation of legacy devices

• What clinical data can you gather to include in CER?
  • Post market data:
    • PMCF
    • User experience survey
    • Registry
    • Complaints data
    • Vigilance reporting
    • Expert user group

• Bench testing
• Screening of scientific literature
The Notified Body

Current Notified Body numbers

- Currently ~58 across all codes
- Not all the same!

- NANDO code MD0105: Ophthalmological Devices: 40 available Notified Bodies
- Some Notified Bodies may be listed separate but are a regional office of a larger one
The Notified Body

Future Notified Body numbers

• Prediction that the number could drop to 35-40
• Might see consolidation
• Might see “specialist” Notified Bodies emerging

• Reason:
  • Designation requirements – competence, in-house vs contract
  • Financial liability
• Impact on capacity
The Industry

Resource issues

- Everyone's hiring!
  - EU commission
  - Competent Authorities
  - Notified Bodies
  - Manufacturers

- Actual workload
  - Initially meeting new requirements/getting certified first time
  - Maintaining the increased level of regulatory work
The Industry

Market access

• Potentially longer route to market for new devices
  • Capital requirements

• Product registration disruption
  • All devices must be initially certified under MDR – time factor
  • CE mark accepted in many jurisdictions

• Supply disruption

Number of Notified Bodies likely to decrease
Amount of regulatory approval work

EU Regulatory System

NSAI
The Industry

Portfolio adjustment

- Withdrawal of products
  - Cost of remediation vs revenue from product

- Temporary withdrawal while data generated
  - Not planning in time!

- Price pressure
  - Cost of remediation may price your device out of market
The Industry

Clinical data – EU vs US – Regulatory vs Reimbursement

• Perception
  • EU regulatory requirements becoming too difficult
  • The US is now a softer target for market entry

• Reality
  • EU regulatory requirements are increasing but not dramatically
  • There are increased clinical data requirements in EU
  • A greater number of clinical trials will need to be carried out
  • The FDA is actively trying to reduce approval times
  • FDA clearance **does not** equate to total US market entry
The Industry

Clinical data – EU vs US – Regulatory vs Reimbursement

• US reimbursement
  • The goal is to demonstrate your device as being “Reasonable and Necessary”
  • Can be difficult to prove the above without empirical clinical data
The Industry

Clinical data – EU vs US – Regulatory vs Reimbursement

• Ideal World – clinical trial which will
  • Deliver the safety, efficacy and performance data needed for regulatory approval (FDA & CE Mark)
  • Demonstrate that your device is “Reasonable and Necessary” and can deliver some economic benefit - ease reimbursement pathway
  • Deliver the endpoints which are being claimed in your IFU
  • Present a clear and marketable message of your devices performance

• You will need clinical data at some point – do it once, do it right
The Future

Opportunities created

• Previously met needs becoming unmet needs
  • Removal of existing products

• Proactive regulatory strategy can give edge in race to market
  • Early adoption of MDR aspects in product development
The Future

Opportunities created

• New regulation acting as barrier to entry form “outside” players
  • Tech industry
  • Who better to navigate tougher MD regs than the MD industry!?

• Increased acquisition potential for devices which comply early
  • Large companies buying similar devices in order to use them for predicate route
THANK YOU!

Questions welcome

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