Improving Technical Documentation
Key pit falls to avoid in preparing technical documentation

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Overview

- Provide an understanding on the requirements for technical documentation
- Provide an understanding on how/what Notified Bodies assess in technical documentation reviews
- Address some key pitfalls when preparing technical documentation
Case 1: CE Marking

- The key to CE marking is passing the QMS audit

- Fact or Fiction?

- One of the common pitfalls...
  - Some deem technical documentation assessment not really as important as QMS audit!
  - ... an after thought?
CE Marking Process – Medical Devices

- Medical Device? Classification?
- Select Conformity Assessment Route
- Notified Body Conformity Assessment
- Sign Declaration Of Conformity, and Affix “CE Mark”
CE Marking Process – Medical Devices

Medical Device? Classification?

Select Conformity Assessment Route

Notified Body Conformity Assessment

Sign Declaration Of Conformity, and Affix “CE Mark”

QMS

ISO 13485

Technical Documentation

93/42/EEC (MDD)
90/385/EEC (AIMD)
CE Marking: Similar Requirements (MDD vs AIMD)

93/42/EEC (Medical Device Directive) ⇔ 90/385/EEC (Active Implantable Device Directive)
Requirements: Technical Documentation

93/42/EEC, Annex VII (section 2):

• “The manufacturer must prepare the technical documentation described in Section 3…”

93/42/EEC, Annex VII (section 3):

• “The technical documentation must allow assessment of the conformity of the product with the requirements of the Directive”

• Requirements in many other Annexes and 90/385/EEC
Technical Documentation

Requirements - the Basics
Technical Documentation – 93/42/EEC

Annex VII (section 2):
• “The manufacturer must prepare the technical documentation described in Section 3...”

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• “The technical documentation must allow assessment of the conformity of the product with the requirements of the Directive”
### Technical Documentation: NB Assessment

<table>
<thead>
<tr>
<th>Classification</th>
<th>Production</th>
<th>Design</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class I</td>
<td>Self-declaration</td>
<td>Self-declaration</td>
</tr>
<tr>
<td>Class IIa</td>
<td>Notified Body</td>
<td>Notified Body</td>
</tr>
<tr>
<td>Class IIb</td>
<td>Notified Body</td>
<td>Notified Body</td>
</tr>
<tr>
<td>Class III</td>
<td>Notified Body</td>
<td>Notified Body</td>
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</tbody>
</table>
Technical Documentation: NB Assessment

- NB scrutiny increases with risk classification
  - ...and novelty

![Risk Pyramid Diagram]

- Class III
- Class IIb
- Class IIa

- Manufacturing and design control
- Manufacturing control
Contents of Technical Documentation
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• The requirements technical documentation content stated in MDD:
  • Annex VII (explicitly)
  • Conformity assessment Annexes (Annex II, III, VI, V, VI)

• The requirements technical documentation content stated in AIMD:
  • Conformity assessment Annexes (Annex 2, 3, 4, 5)

• 93/42/EEC (MDD) ⇔ 90/385/EEC (AIMD)
Content of Technical Documentation (Annex VII)

- Product description, variants, intended use(s),
- Design drawings, manufacture process...
- Risk analysis, standards applied (full or part)
- Sterilisation method and validation reports
- Essential requirements (proof of compliance)
- Pre-clinical evaluation, design verification
- Solutions adopted...to conform to safety principles w.r.t. state of the art
- Clinical evaluation (Annex X, includes PMS/PMCF)
- Labels and instructions for use
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Annex II (MDD)  
Annex I (AIMD)

- Statement if device incorporates… “a medicinal substance or a human blood derivative” – NB assesses usefulness
- Statement on “utilisation of animal tissue”
Guidance to expand upon the Requirements
Key Guidance Documents

• NB-Med 2.5.1 Technical Documentation (2000)

• IMDRF/RPS WG/N9 (2014) - Non-In Vitro Diagnostic Device Market Authorization Table of Contents (nIVD MA ToC) Regulated Product Submissions ToC WG
  • GHTF SG1 Summary Technical Documentation (STED) N011R16 2008

• NBOG_BPG_2009_1 Design Dossier Examination and

• NB Guidance Document
Key Pitfalls ...

Audience Participation Exercises
Frequent Mistakes
What NB Reviewers look at
Case 2

- Mfr-A applies for CE marking for a Class III surface coated knee joint replacement implant
- US Manufacturer (with BSI), and supplies uncoated device to Mfr-A.
- Mfr-A further processes the implant to apply proprietary coating (+ sterilisation & packaging).
- Mfr-A submits “Partial” Dossier and states that the remainder is covered by submission of US Manufacturer of uncoated knee implant

Submission included:

- Description of coating, processing methods, coating characterisation
- Risk covers processing risks for the coating
- CER covers detailed biocompatibility testing of the coating
- No DoC
- IFU & labels of US MFR
Case 2: Outcome

- Submission was rejected

- No clear responsibility for the coated knee implant

- CER, Description, Risk documents all referred to ONLY the coating material and process

- Also the general content was inadequate
Exercise: Common Errors

In groups – discuss the common...

• Errors you make/encounter from your experience preparing technical documentation

• Push backs from your Notified Bodies on your technical documentation
Common Non-Conformities

For Reference
Areas with Frequent Findings: TF / DD Construction

• Not clear how documentation is controlled
  • TF / DD not a controlled document
  • TF contents not all controlled or signed/dated
  • DOC date precedes date of TF
  • Signed DOC provided in DD submission
  • Approval date, revision, signatory name / function not identified on documents
  • Documents approved by individuals w/ insufficient credentials (particularly for Biocompatibility and CER)

• No executive summary / reason for supplement not clear
• Insufficient detail in section summaries (to find or understand data)
Areas with Frequent Findings: DOC and Product Description

• Unambiguous descriptions not provided
• Product list in TF does not match DOC
• Description does not include all components
• Classification summary does not site all applicable rules and/or applicable content within rule
• No summary of design changes
• Some significant changes (design / process) not included or NB not notified in advance (class III only)
Areas with Frequent Findings: Specifications / Verification / Validation

- Design requirements not included in documentation
- Test reports included but deficient
  - Do not identify scope
  - Insufficient justification for sample size or test method selection or discussion of deviations / failures
  - Discussion not linked to requirements
  - Insufficient justification for representation of “worst case devices/testing”
- Accelerated stability testing used as basis for shelf-life but no real time testing initiated
- Product stability not considered in conjunction with package stability
- Transportation testing not conducted
- Biocompatibility assessment considers only raw materials and not manufacturing process
Areas with Frequent Findings: ERs / Standards

• Insufficient justification for ERs being N/A
• Lifetime (ER 4, life in use) confused with Shelf-life (ER 5 / 7.2, life prior to use) … lifetime not identified
• Standards not referenced for all pertinent ERs (e.g. performance standards not referenced for ER 13 even though there are specific labelling requirements)
• Relevant harmonized standards not referenced
  • Confusion between harmonized vs. other standards
  • Presumption of conformity / Z Annex
• Level of compliance to harmonized standard not identified (full or partial)
  • If full compliance to harmonized standard not claimed, no gap analysis provided relative to ability of solution to meet ERs
Areas with Frequent Findings: Manufacturing / Sub-Contractors

• No description of manufacturing flow (i.e. flowchart) w/subcontractor and inspection requirements
• Manufacturer cedes authority of purchased parts / services to OEM / sub-contractor when legally responsible
  • Insufficient understanding of processing aids / materials utilized during manufacturing
  • Does not determine safety / performance of entire device
Areas with Frequent Findings: Labels and IFUs

• Medical purpose not clear in IFU – Must meet Article 1
• Non-harmonized symbols used in labelling (including some in EN ISO 15223-1 per notes) not defined
• Labels do not adequately identify device / contents to non-English speaking users
• Claims on websites / promotional material not supported by data or imply use outside indications
Areas with Frequent Findings: Risk Management

• Normative elements of ISO 14971 (RMP, RA, RMR) not all included
• Deviations from EN ISO 14971:2012 not addressed
• All risks (i.e. design, process, application) not considered
  • Process risks frequently not included if subcontracted
  • Review of subcontracted risks not evaluated by manufacturer for completion or agreement
  • Clinical risks not included
• RMF not actively updated / PMS not integrated into RMF
Areas with Frequent Findings: CER / PMS / PMCF

- Clinical evaluation reports not provided
- Clinical Investigation not provided (for implants / class III) and not duly justified
- Clinical data not provided for all indications or justified based on representative data
- Clinical investigation not carried to full term or deviations justified
- Impact of design changes not addressed in CER

- CER attests “safety and efficacy” rather than “safety and performance as intended”
  - efficacy: ability of device to produce a desired effect
- CER does not cross-reference RMF
- No device / family-specific PMS Plan
- No PMCF when CER approved based on equivalence
- EU / WW sales history not provided with summary of complaints / vigilance over same period
Notified Body Review

What the NB Reviewer looks at
| Device descriptions, variants, intended use | Manufacturing process, device construction, subcontractors | General contents, ER checklists, CER, Risk, PMS/PMCF, |
| Standards (fully or partially applied), design verification & validation | Declaration of Conformity, legal manufacturer, EU rep? | A process for generating or controlling technical documentation |
Reviewer will Check: Changes

- Description of the changes
- Impact on ERs, safety and performance (as intended)
- What designs, sizes, indications are covered by the change? Worst case?
- Impact and update on Risk, Clinical, PMS, performance & validation studies
- (if applicable) Update and follow-up on sales, complaints, results from PMS activities
- Manufacturer’s assessment of the change/s, conclusions and acceptability
Reviewer will Check: Essential Requirements

Latest version of Directive?

- Reference to harmonised standards
  - Full or partial compliance?

Review of ER checklist
- Which ERs are applicable?
- If applicable, how is this met – standards, procedures, test reports – PROVE IT!

Is there a justification if not applicable?
- Is it an acceptable justification?
- Is it a complete justification?
Reviewer will Check: Clinical Evaluation

<p>| Clinical data required for ALL device classification – source of clinical data (clinical investigation, literature) |
| Clinical investigation conducted? If not – is justification provided – esp. for Class III &amp; Implantable devices |
| Has equivalence been demonstrated? Comparison of similarities and differences. Is the clinical data presented clearly from the equivalent device |
| Critical evaluation of the clinical data, quality of data sources. Does data support variants, indications? |
| Are conclusions sound and based on clinical data? Is CER written/reviewed by suitably qualified person? |
| Does clinical data/experience feedback to risk management and PMS |</p>
<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
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<tr>
<td>PMS plan? Does is have proactive elements?</td>
<td><em>Does PMS review include clinical data as well as complaints and incidents?</em></td>
</tr>
<tr>
<td></td>
<td><em>Does PMS feedback into risk assessment and clinical evaluation?</em></td>
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<tr>
<td>Does PMS/PMCF plan cover different design variants and indications?</td>
<td></td>
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<tr>
<td></td>
<td><em>The PMS plan (consistent with clinical evaluation, risk, and lifetime of device) &amp; implementation of that plan in renewals</em></td>
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<td></td>
<td><em>If PMCF is deemed unnecessary, an adequate rationale</em></td>
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Reviewer will Check: Labelling and IFU

- Check label against ER13.3
- Appropriate use of symbols – use of ISO 980/15223
- Check IFU against ER13.6

- Does intended use correspond with stated claims and clinical data presented?
- Have residual risks been warned against?
Summary
Manufacturer’s Role

- Manufacturer should have evidence and be able to summarise data which supports the conclusions drawn
- Meet ERs or has justifications why “N/A”
- Fit for purpose? i.e. not just “meets harmonised standards” (most innovative manufacturers usually ahead of the “state of the art”)
- Positive benefit/risk analysis?
- Conclusions are based on clinical data
- Reliance on data on other devices needs clear justifications & evidence
Technical Documentation Review: NB’s Role

• Ensure that the manufacturer’s conclusions are sound
  • ... and based on evidence
• Cannot draw conclusions based on data presented by the manufacturer
• Cannot tell manufacturer how to arrive at the answer
• NB may call in other specialist expertise ... as/if required
  • Clinician, biostatistician, animal tissue expert, medicinal expert, toxicologist etc...
Conclusions

• Do not assume prior knowledge of your product
  • The Notified Body cannot assume, interpret or conclude for the Manufacturer

• Know what is required... and expected... from your NB
  • If in doubt... ask

• Telling the story...
Thank You for your attention and participation
Contact

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