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**Assessment of technical documentation of  
medical devices for clinical investigation**

B. Roszek<sup>1</sup>, A.C.P. de Bruijn, A.W. van Drongelen, R.E. Geertsma

<sup>1</sup> Contact:  
Dr. B. Roszek  
Centre for Biological Medicines and Medical Technology, RIVM  
E-mail: [Boris.Roszek@rivm.nl](mailto:Boris.Roszek@rivm.nl)  
Telephone: +31 30 2743521

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## Abstract

### **Assessment of technical documentation of medical devices for clinical investigations**

The technical documentation on non-market approved medical devices intended for clinical investigation contains major shortcomings. This could imply increased risks which could affect patient safety. The investigation described here focused on the availability and quality of the technical documentation which is required in the Medical Devices Directive 93/42/EEC (MDD), complemented by items directly related to the use and safety of a device but which are not explicitly required in the current MDD. Even though the response of included manufacturers (n=19) was high, the timely availability of such documentation could be improved. For 95% of the manufacturers, the quality of a substantial part of the explicitly required technical documentation was inadequate. Major shortcomings were found in items concerning risk analysis, sterilisation, labelling, instructions for use and vigilance, which are vital for the quality and safety of medical devices. Likewise the quality of complementary items concerning medicinal substance and post market surveillance was inadequate. In order to safeguard the quality and safety of medical devices more extensively manufacturers could liaise more with their notified bodies before the start of a clinical investigation. Furthermore, European competent authorities and ethics committees could consider an increased surveillance on clinical investigations with medical devices. Proposed amendments during the revision of the MDD are addressing some of its shortcomings, e.g. medicinal substances and post market surveillance.

Key words: clinical investigation, medical device, Medical Devices Directive, patient safety, regulation



## Rapport in het kort

### **Beoordeling van technische documentatie van medische hulpmiddelen voor klinisch onderzoek**

De technische documentatie van medische hulpmiddelen, die nog niet zijn toegelaten tot de markt en bedoeld zijn voor klinisch onderzoek, bevat ernstige tekortkomingen. Dit zou een verhoogd risico kunnen betekenen en de patiëntveiligheid kunnen beïnvloeden. Het onderzoek richtte zich op de beschikbaarheid en kwaliteit van de technische documentatie zoals vereist in de Richtlijn medische hulpmiddelen 93/42/EEG (RMH), aangevuld met onderdelen die in direct verband staan met het gebruik en de veiligheid van een hulpmiddel, maar in de vigerende RMH niet explicet vereist zijn. Hoewel de respons van de geïncludeerde fabrikanten (n=19) hoog was, zou de tijdige beschikbaarheid van dergelijke documentatie verbeterd kunnen worden. Gebleken is dat bij 95% van de fabrikanten de kwaliteit van een aanzienlijk deel van de explicet vereiste technische documentatie ontoereikend was. Ernstige tekortkomingen werden gevonden in de onderdelen risicoanalyse, sterilisatie, etikettering, gebruiksaanwijzing en vigilantie. Deze onderdelen zijn essentieel voor de kwaliteit en veiligheid van medische hulpmiddelen. De kwaliteit van de aanvullende onderdelen betreffende eventuele geneesmiddelencomponenten en ‘post market surveillance’ was eveneens ontoereikend. Fabrikanten zouden voor het begin van een klinisch onderzoek nauwer kunnen gaan samenwerken met hun ‘notified bodies’ om de kwaliteit en veiligheid van medische hulpmiddelen beter te garanderen. Bovendien zouden Europese bevoegde autoriteiten en medisch ethische toetsingscommissies kunnen overwegen om het toezicht op klinisch onderzoek met medische hulpmiddelen te verhogen. Tijdens de lopende revisie van de RMH worden aan de onderdelen geneesmiddelencomponent en ‘post market surveillance’ al scherpere eisen gesteld.

Trefwoorden: klinisch onderzoek, medisch hulpmiddel, patiëntveiligheid, regelgeving, Richtlijn Medische Hulpmiddelen



## Preface

The authors acknowledge G.W.M. Peters-Volleberg (National Institute for Public Health and the Environment) for her contribution during the initial phase of the investigation and J. Moleveld (Dutch Health Care Inspectorate) for his contribution concerning the selection of manufacturers and the request for technical documentation of medical devices.



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## 1. Introduction

Medical device companies preparing, performing or sponsoring a clinical investigation of non-market approved medical devices have to comply with the requirements of the Medical Devices Directive 93/42 EEC (MDD) (1). The MDD covers all medical devices with the exception of active implantable medical devices and *in vitro* diagnostic medical devices which are regulated in separate directives (2, 3). Harmonised European standards (4, 5) and a guidance document (6) have been developed to aid a manufacturer in achieving compliance. A clinical investigation means any systematic study in human subjects undertaken to assess the feasibility, and verify the safety and performance of a medical device under normal conditions for use on a representative sample of a patient population.

Prior to the start of a clinical investigation with a non-market approved medical device, manufacturers should prepare all technical documentation items required by the MDD for a market-approved device. The minimal content of the technical documentation of non-market approved medical devices is specified in Annex VIII ('Statement concerning medical devices for special purposes'), and Annex X ('Clinical evaluation') of the MDD. Only those aspects of the medical device that are to be investigated clinically can be included in the technical documentation in a later phase. The technical documentation provides the evidence used in the conformity assessment procedure. Moreover, manufacturers must inform the national competent authority before commencing a clinical investigation and must be able to submit the prepared technical documentation to the competent authority if requested.

Recently, it has been shown that the technical documentation of medical devices with a Conformité Européenne (CE) mark<sup>1</sup> has major shortcomings (7, 8, 9). In general, risk analysis, labelling and instructions for use, post market surveillance and vigilance procedures were often insufficiently documented. These technical documentation items are crucial for the continuous iterative process of quality and risk management.

The Dutch Health Care Inspectorate is the national competent authority enforcing laws for health care, and regulations and decrees concerning medical devices. At their request, the Centre for Biological Medicines and Medical Technology of the National Institute for Public Health and the Environment (RIVM) has now investigated whether the technical documentation of non-market approved medical devices intended for clinical investigation fulfils the requirements of the MDD.

The specific aims of the investigation were:

- To evaluate the manufacturer's timely response to the request for technical documentation submission;
- To evaluate the availability of technical documentation items;
- To assess the quality of technical documentation items.

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<sup>1</sup> The CE marking certifies that the medical device conforms to all relevant essential requirements (i.e., Annex I of the MDD) in order to protect health and safety of patients, users, and third parties. A CE mark enables products to be traded freely within the European Economic Area.



## 2. Methods

### 2.1 Selection of manufacturers and medical devices

After a manufacturer<sup>2</sup> notified a clinical investigation of medical devices with participating human subjects to the Dutch Health Care Inspectorate, the notifications were evaluated. The enrolment of manufacturers started in June 2005 and closed August 2006.

Inclusion and exclusion criteria were used to select appropriate medical devices. These criteria were based on type of medical device, classification of medical device, starting date of clinical investigation, and other factors.

Inclusion criteria were:

- Medical devices intended for clinical investigation covered by the MDD;
- Medical devices classified as Class IIa, IIb, or III; or a device system containing at least one component classified as Class IIa, IIb, or III;
- Clinical investigations starting in April 2005 or later;
- One medical device but not more than two devices per manufacturer.

Exclusion criteria were:

- CE-marked medical devices where these device are to be used for a new indication;
- Medical devices used in a comparative study, where each device has obtained prior CE marking and each is used for their original indication;
- Medical devices used in a post CE marking clinical investigation;
- Manufacturers who did not respond to a reminder. In a later stage these manufacturers will be contacted by the Dutch Health Care Inspectorate.

### 2.2 Request for technical documentation

The Dutch Health Care Inspectorate requested manufacturers to submit technical documentation within four weeks to the RIVM. If a manufacturer did not respond to this initial request, a reminder was sent. Upon receiving documentation, a general availability check on the submitted technical documentation items was performed. If any part of the documentation was not submitted or if additional information was needed for a proper assessment in the view of the assessors, the manufacturer received a final request. The submission deadline of the final request was four weeks at the most. If the manufacturer did not respond to the request for additional information or submitted only part of it, no further reminder was sent. All documentation was regarded as confidential.

In addition to the minimal content of the technical documentation described explicitly in Annex VIII of the MDD, and the additional aspect on vigilance (Annex X), complementary technical documentation items were requested which are related to the use and safety of a medical device. Eventually, the complementary items will be part of the technical documentation when the medical device has obtained CE mark approval. In Annex VIII a manufacturer's statement is required that the medical device in question conforms to the

<sup>2</sup> In the context of this report the term manufacturer is meant to include also the EU-authorised representative or contract research organisation.

essential requirements (i.e., Annex I of the MDD) apart from those aspects covered by the clinical investigation and that, with regard to these aspects, every precaution has been taken to protect the health and safety of the patient. Thus, manufacturers have to comply with Annex I accordingly.

The following items were requested:

1. A general description of the medical device (Annex VIII);
2. A general description of any variants planned (complementary);
3. Design specifications (Annex VIII);
4. Results of the risk analysis (Annex VIII);
5. Standards which will be applied (Annex VIII);
6. A description of the solutions adopted to fulfil the essential requirements which apply to the products if the standards are not applied in full (Annex VIII);
7. Techniques used to control and verify the design, the processes and systematic measures which will be used when the products are being designed (Annex VIII);
8. If the device is to be connected to other device(s) in order to operate as intended, proof must be provided that it conforms to the essential requirements when connected to any such device(s) having the characteristics specified by the manufacturer (Annex I);
9. Statement whether or not the device incorporates, as an integral part, a substance or a human blood derivative which, if used separately, may be considered to be a medicinal product, and data on the tests conducted in this connection to assess the safety, quality and usefulness of that substance or human blood derivative, taking into account of the intended purpose of the device (complementary);
10. Processes and procedures which will be used for sterilisation (Annex VIII);
11. Draft label (Annex I);
12. Draft of instructions for use (Annex I);
13. Post market surveillance procedure (complementary);
14. Vigilance procedure (Annex X);
15. Conformity assessment procedure that will be followed (complementary).

## 2.3 Assessment of technical documentation

A form was developed for the assessment of technical documentation by modifying a previous form used for the assessment of technical documentation of Annex II medical devices (8) (see Appendix I). The dedicated form consisted of:

- A general information page with name of manufacturer, medical device, etc.
- An availability checklist concerning all 15 requested technical documentation items.
- An assessment checklist concerning the quality of 13 out of the 15 requested technical documentation items. With the exception of adopted solutions if standards are not applied in full and the conformity assessment procedure to be followed (item 6 and 15, respectively), all other technical documentation items were assessed.

Two assessors independently evaluated the technical documentation of each medical device. As assessors may subject the technical documentation to different interpretations, guidance was written facilitating objective and consistent assessments (see Appendix II). The two evaluations were compared, and inconsistencies were checked and resolved.

For the availability check, technical documentation items could be rated as 'absent', 'present – final' (i.e., after the final request), 'present – initial' (i.e., after the initial request), or 'not applicable'.

For the assessment, the content for each technical documentation item was listed. Based on these content elements, a set of criteria was drawn up concerning the assessment of technical documentation items (see Appendix II). For each technical documentation item the presence of a particular set of assessment criteria yielded an assessment score, viz 'insufficient', 'moderate', 'good', or 'not applicable'. A major shortcoming of a technical documentation item resulted from the 'insufficient' score. A minor shortcoming of an item resulted from the 'moderate' score. No shortcoming meant that a technical documentation item was rated as 'good' or 'not applicable'. For each item, additional textual remarks could be made on the form.



## 3. Results

### 3.1 Response of manufacturers

During the period of approximately one year, a total of 21 manufacturers out of 39 notifying manufacturers were identified who could be suitable for enrolment into the investigation (Figure 1). Eighteen medical devices could be excluded beforehand because the notifications concerned clinical investigations with either active implantable medical devices, CE-marked medical devices, or Class I medical devices (i.e., drug delivery device).

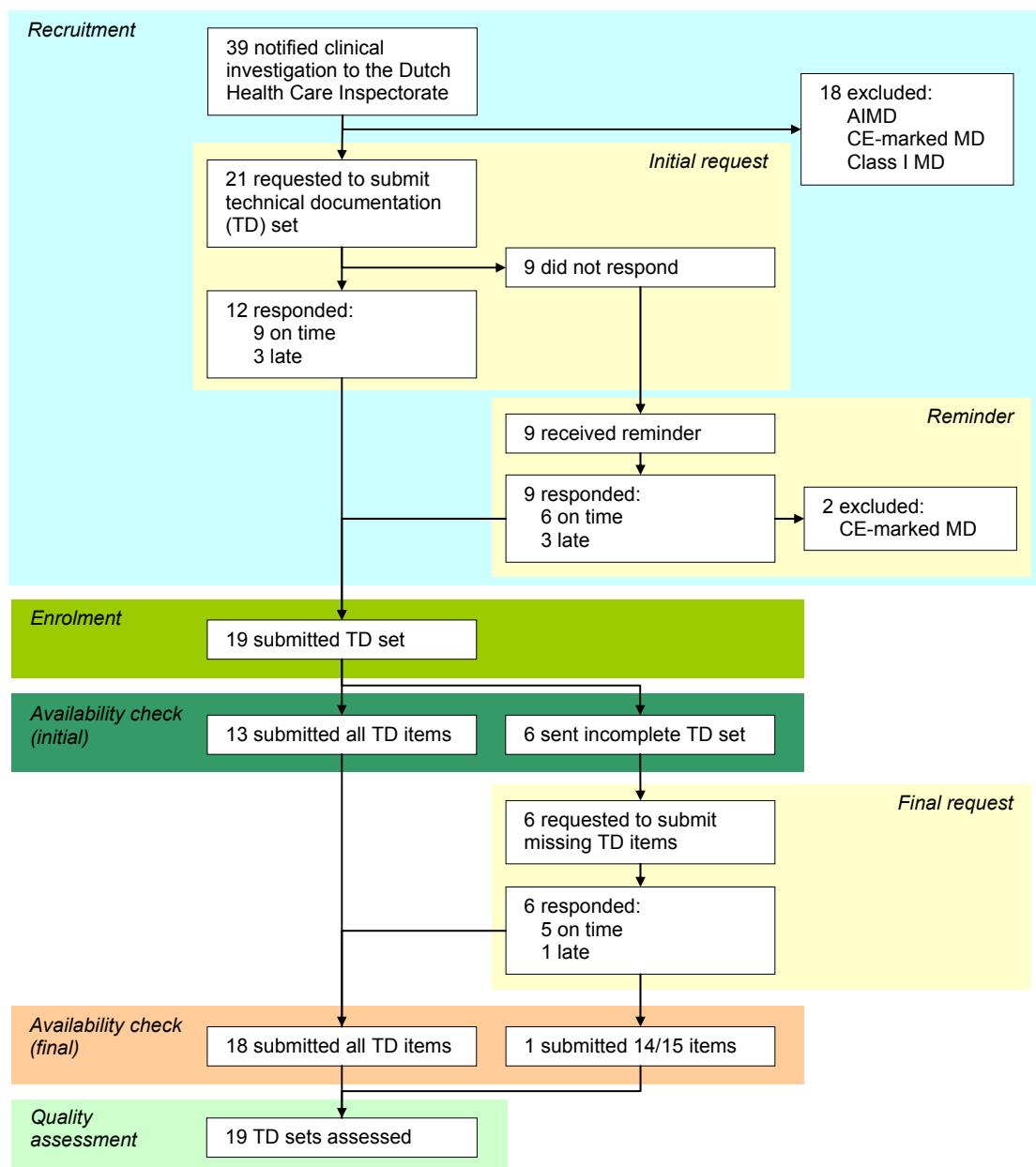


Figure 1. Flow diagram of manufacturers' responses submitting technical documentation of non-market approved medical devices intended for clinical investigation. One manufacturer did not submit a list of solutions when standards are not applied in full. AIMD denotes active implantable medical device.

However, in some cases the notifications provided hardly any information on whether the clinical investigation would be conducted using non-market approved medical devices in order to obtain data substantiating the technical documentation for CE mark approval or whether the clinical investigation involves medical devices which were already CE-marked. Consequently, the content of the technical documentation was checked first to determine if medical devices comply with the inclusion and exclusion criteria. This resulted in the exclusion of two more medical devices from the sample population after the initial request for technical documentation submission because these manufacturers stated that their ongoing clinical investigations were post CE marking studies.

Less than half of the manufacturers (9/21) initially submitted the requested technical documentation on time, i.e. within one week after the deadline of the request. Three manufacturers were late, i.e. one to three weeks. Initial non-responders (9/21) were reminded. Six of these manufacturers responded before the new deadline, whereas three manufacturers submitted the technical documentation 2, 6 and 11 weeks after this deadline.

Ultimately, 19 manufacturers and their medical devices were included. The initial availability check revealed 13 technical documentation sets with all 15 requested items submitted, and 6 incomplete sets. The majority of manufacturers who were requested to submit additional or missing documentation responded on time whereas one manufacturer exceeded the deadline for submission three weeks. One manufacturer submitted 14 of the 15 items. Since the missing item (i.e., adopted solutions) was not assessed, assessors decided not to exclude this manufacturer.

Starting dates of clinical investigations ranged from April 2005 to March 2006 and end dates from June 2005 to March 2011. Six notifications did not mention end dates of the clinical investigations.

## 3.2 Overview of included medical devices

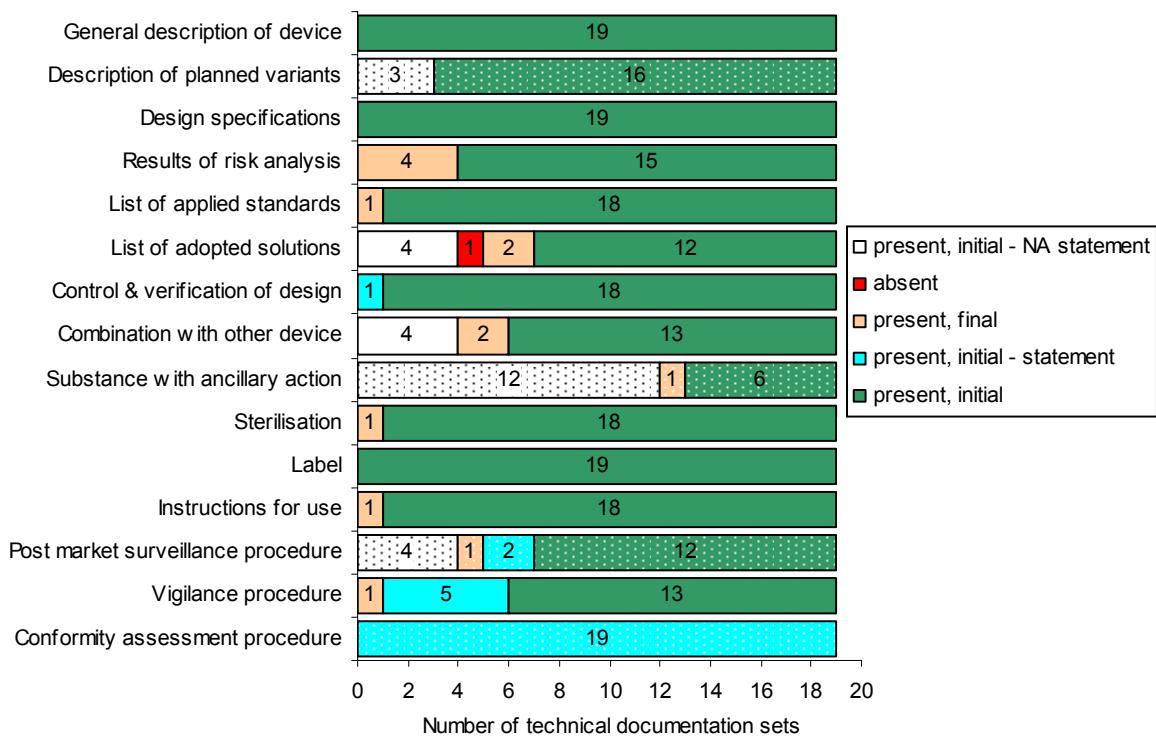
A brief general description of the included medical devices is shown in Appendix V – Table V.1. Medical devices were classified as Class IIb (n=3) and Class III (n=16). Devices were intended for long term implantation (n=15) or transient use, i.e. normally intended for continuous use for less than 60 minutes (n=4).

Conformity assessment procedures to be followed for CE marking as described in the MDD were Annex II (n=16) and Annex III+V (n=1). Two remaining manufacturers mentioned Annex III without indicating which of the mandatory additional Annex IV, V, or VI will be applied.

## 3.3 Availability of technical documentation items

Manufacturers provided actual technical documentation as well as statements (Figure 2A, see also Appendix V – Table V.2). Noticeably, the results of the risk analysis after the initial request were not present in a substantial number of cases (4/19). Often manufacturers submitted a summary of the risk analysis without elaboration on hazard identification, cause, potential harm or effect, risk estimation (unmitigated and mitigated), proposed control methods (e.g., design, verification, validation, labelling, and / or instructions for use), etc. (see Section 3.4.4). The technical documentation items concerning planned variants, adopted solutions, combinations with other devices, incorporation of substances with ancillary action,

A



B

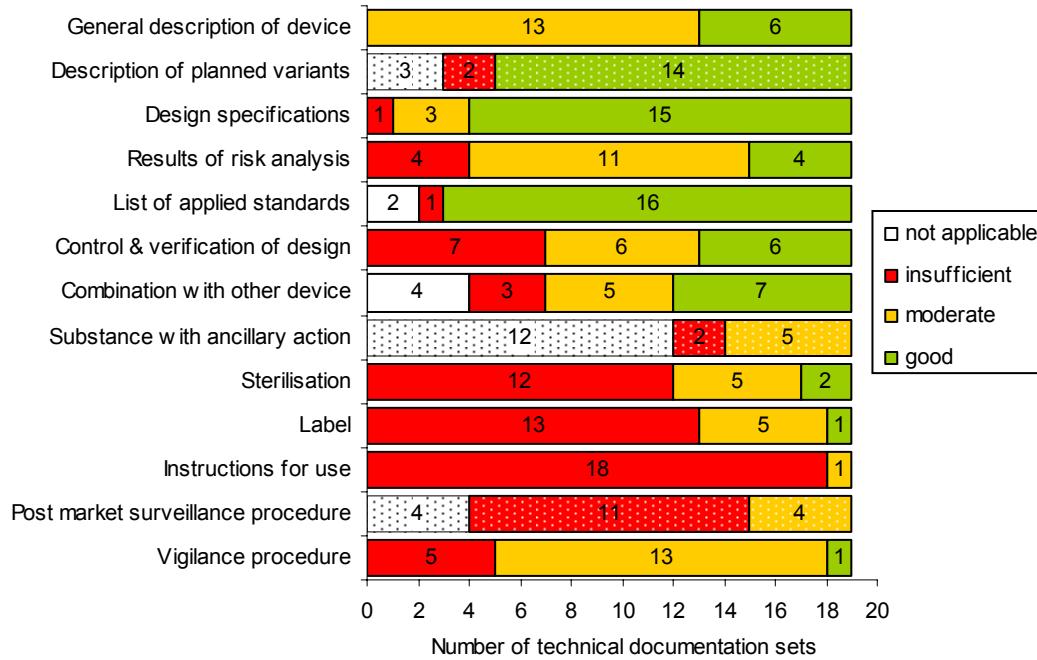


Figure 2. Technical documentation of non-market approved medical devices intended for clinical investigation. Availability (A) and quality (B) was assessed of submitted documents and statements. Solid and dotted bars indicate items which are explicitly required in the MDD or complementary, respectively. NA statement denotes a manufacturer's statement that an item was not applicable.

post market surveillance and vigilance procedures were often submitted as statements. If statements were contradicted by other information in the technical documentation in view of the assessors, the assessors' view took precedence over the manufacturer's statement.

Thus, the availability check revealed that all requested technical documentation items were either present as actual documents (81%) or statements (19%) (see also Section 3.5 and Appendix V – Table V.2). One technical documentation item, i.e. adopted solutions if standards are not applied in full, of a total of 285 submitted items was absent.

## 3.4 Quality assessment of technical documentation items

For the assessment of technical documentation items either the actual content of documentation items or the manufacturer's statement was used. A statement was assumed to be accurate. All 13 types of assessed technical documentation items showed shortcomings (Figure 2B, see also Appendix V – Table V.3 and Table V.4). In the following sections the results for each item are presented.

### 3.4.1 General description of the medical device

A good general description of the medical device contains the (generic) name of the medical device, classification of the medical device, physical description of the medical device, schematic drawing / diagram / photograph of the medical device, mode of action, short description of the intended use, and short description of the contraindications, warnings, precautions, and / or stop criteria.

The general descriptions of the medical devices showed no major shortcomings and were addressed well in 6/19 cases. The 'moderate' score for this item merely originated from the classification of the medical device which was often absent in the technical documentation (13/19). Contraindications were mentioned in all except one of the technical documentation sets.

Some criteria concerning the general description of the medical device were present in other technical documentation items such as mode of action in the risk analysis, contraindications / warnings / precautions in the instructions for use, and drawings of the medical device on the label. Overall, the structure of this item was not very consistent throughout the sample.

### 3.4.2 General description of any variants planned

A good description of any variants planned contains information concerning variant characteristics such as physical dimensions, colour, weight, etc. In addition, model numbers are mentioned (if applicable).

Variants planned were addressed adequately except for two technical documentation sets lacking a physical description of variants and model numbers. Information on variants was often present in technical documentation items such as the general description of the medical device, design specifications, risk analysis, checklist essential requirements, and / or instructions for use. Noticeably, three manufacturers stated that no variants were planned despite actual descriptions of variants found in the technical documentation:

- A manufacturer developed several 'lines' of stents taking into account the different blood vessel diameters.
- A manufacturer developed angioplasty catheters and mentioned a group of four catheter 'models' differing in balloon diameters.
- A manufacturer developed hyoid bone implants provided in two 'configurations', i.e. straight and angled, to accommodate anatomical variations.

Apparently, from the manufacturer's point of view terms like 'lines', 'models', and 'configurations' were not equivalent with 'variants'.

### 3.4.3 Design specifications

Good design specifications contain (design) drawing(s) (if relevant), specification of the materials used, biomaterials or components, product specification, and descriptions / explanations necessary for the understanding of the drawing(s) (if applicable).

Design specifications were often addressed adequately (15/19). Shortcomings were due to the absence of (design) drawings, specifications of materials used, and / or product specifications. One (design) drawing did not specify any essential device dimensions or even an indication of the physical size of the medical device.

Some design specifications were present in other technical documentation items, e.g. drawings on labelling, specifications of materials in risk analysis, and product specifications on labelling and in instructions for use. Drawings on labelling were often vague and small. Nevertheless, essential sizes of the medical device were indicated appropriately. Thus, (design) drawings were scored as present if drawings were printed on labelling.

### 3.4.4 Results of the risk analysis

In a good risk analysis all known or foreseeable hazards are identified, risks arising from the identified hazards are estimated, actions taken to reduce or eliminate the risks are adequate, i.e. control measures are consistently described in line with essential requirement 2 (eliminate or reduce risks as far as possible by inherently safe design and construction, take adequate protection measures including alarms if necessary, in relation to risks that can not be eliminated, and inform users of residual risks / hazards due to any shortcomings of any protection measures adopted), and residual risks / hazards are justified in relation to anticipated benefits.

The results of the risk analysis showed some major (4/19) and many minor shortcomings (11/19). In a major part of the risk analyses several known or foreseeable hazards were not identified (see Appendix III and V – Table V.5). In addition, though to a lesser extent, risks arising from the identified hazards were not estimated. Moreover, a substantial part of the analyses did not mention adequate actions to reduce or eliminate these estimated risks and did not conclude with a justification of residual risks / hazards in relation to anticipated benefits. The date of the risk analyses ranged from January 2005 up to June 2006 and two analyses were not dated. All risk analyses were according to the standard EN ISO 14971:2000 Medical devices – Application of risk management to medical devices.

For the assessment of the technical documentation, the coherence between the risk analysis and the information for users supplied by the manufacturer was also taken into consideration (Figure 3).

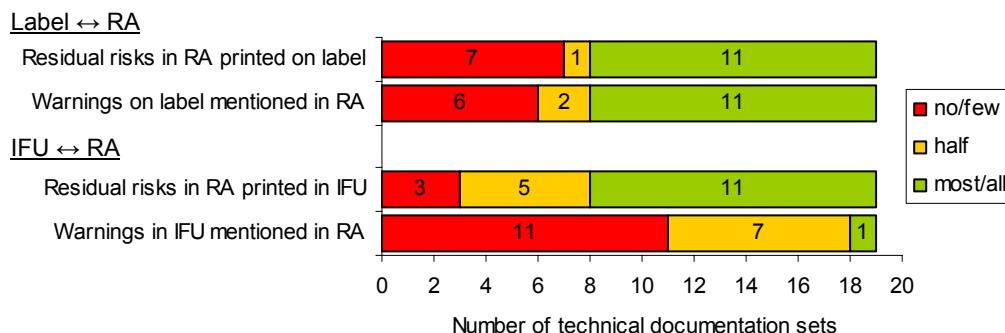


Figure 3. Coherence between information for users supplied by the manufacturer, i.e. label and instructions for use (IFU), and risk analysis (RA). Reciprocal relationships between residual risks/hazards addressed in RA and warnings/precautions mentioned on label or IFU are shown in the upper and lower part, respectively.

Sound risk management and quality assurance implies that all warnings and precautions on the label and in the instructions for use should be addressed in the risk analysis and vice versa, i.e. all residual risk-related hazards, which are relevant for the user to know and should be printed on the label as warnings and precautions, and ditto for all residual risk-related hazards relevant for instructions for use.

This reciprocal relationship showed major shortcomings for both labelling as well as instructions for use. In only 11/19 of the technical documentation sets all / most warnings and precautions on the label were addressed in the risk analysis and vice versa. Most remarkably, in just one case all / most warnings and precautions in the instructions for use were addressed as hazards in the risk analysis and vice versa this score was 11/19. Moreover, in 8/19 of the technical documentations only half or less of the residual risk-related hazards were mentioned in the instructions for use. Thus, users who will read the instructions for use and labelling will be unaware of many hazards.

### 3.4.5 List of applied standards

A list of applied standards shall contain products standards (if applicable) corresponding to the list drawn up the assessors.

In all technical documentation sets the applied standards were listed. The standards were either given in a checklist essential requirements (13/19) and / or a separate list (18/19). Only seven checklists essential requirements were dated, ranging from February 2005 up to April 2006. These findings suggest that most manufacturers do not update the checklist essential requirements on a regular basis.

For three medical devices the technical documentation did not include product-specific standards. Instead, only general standards were used to demonstrate conformity of the medical device to the essential requirements of the MDD, such as:

- EN ISO 13485:2003 Medical devices – Quality management systems – Requirements for regulatory purposes;
- EN ISO 14155-1:2003 Clinical investigations of medical devices for human subjects – Part 1: General requirements;
- EN ISO 14155-2:2003 Clinical investigations of medical devices for human subjects – Part 2: Clinical investigation plans;
- EN ISO 14971:2000 Medical devices – Application of risk management to medical devices.

Two medical devices were manufactured utilising tissues originating from equine and porcine pericardium. Manufacturers stated that compliance has been met with the relevant specific standard series 12442 on animal tissues and their derivatives. Viral contamination was covered by this standard series and was addressed adequately in the risk analysis.

### 3.4.6 List of adopted solutions

The list of adopted solutions if standards are not applied in full was not assessed. It should be noted that one technical documentation set did not include any solutions to fulfil particular essential requirements at all.

### 3.4.7 Control and verification of the design

For a good control and verification of the design, test results and procedures are present, and design verification techniques are mentioned.

Control and verification of the design showed several major (7/19) and minor (6/19) shortcomings and, thus, was not adequately addressed. Major shortcomings in the technical

documentation sets were due to the absence of tests results in combination with either design verification techniques or procedures. Minor shortcomings were always due to the absence of procedures. One manufacturer stated that a comprehensive quality management system was maintained without submitting any test results, design verification techniques, and / or procedures. This was regarded inadequate. Therefore, control and verification of the design of this particular sample scored 'insufficient'.

### 3.4.8 Proof of conformity if connected to other medical devices

A good proof of conformity if connected to other medical device(s) contains a description of possible practical combinations and extensive proof.

This technical documentation item showed some major (3/19) and several minor (5/19) shortcomings. Major shortcomings were due the absence of descriptions of possible combinations together with extensive proof. Thus, only a reference document was mentioned in essential requirement 9.1 or the combination was only addressed in the risk analysis without an elaboration or a description of the actual combination. Minor shortcomings were only due to the absence of extensive proof. Noticeably, nine manufacturers stated that their medical devices cannot be connected even though in five of these cases either device combinations were shortly addressed in the checklist essential requirements or in the risk analysis or more detailed descriptions of actual combinations were given in other technical documentation items.

### 3.4.9 Substance with ancillary action

Good documentation regarding a substance with ancillary action (medicinal substance or blood product) contains a description of the intended purpose within the context of the medical device, source and / or product license (if applicable), method by which the substance is incorporated into the device, tests performed on the substance (toxicological, pharmacological, stability, etc.), pharmacovigilance, notification duty for reporting of serious adverse drug reactions to competent authorities and / or European Medicines Agency, assessment of the substance by national authority or European Medicines Agency.

In seven medical devices a substance was incorporated having an ancillary medicinal action. Remarkably, in none of the technical documentation sets this item was addressed adequately. Present aspects were mainly the intended purpose within the context of the medical device, product source, method of incorporation, and tests performed on the substance. However, pharmacovigilance and notification duty for reporting serious adverse drug reactions to competent authorities and / or the European Medicines Agency were always absent. Information on the assessment of the medicinal substance by a national authority or European Medicines Agency was only present in one of the seven technical documentation sets.

### 3.4.10 Sterilisation

A good description of the sterilisation contains (detailed) information on the cleaning process prior to sterilisation (if applicable), method of sterilisation, parameters of the sterilisation process, a summary of sterilisation validation data, including the appropriateness of the sterilisation method, and packaging material used.

The method of sterilisation was always present and included e-beam irradiation, gamma irradiation, ethylene oxide sterilisation, steam sterilisation, and sterilisation by liquid chemicals. Overall, however, sterilisation was not addressed adequately in the major part of the technical documentation sets (12/19). Major and minor shortcomings were due to the absence of the information concerning the cleaning process, parameters of the sterilisation process, summary of sterilisation validation data, and packaging material used.

### 3.4.11 Label

Good information for the user contains a label in Dutch or otherwise in a foreign language accompanied by a grant exemption from the Dutch language requirement. Moreover, labelling complies with the essential requirements 13.3.a – 13.3.m. Labelling bears the wording ‘Exclusively for clinical investigations’, is without CE marking, mentions manufacturer’s and / or the EU-authorised representative’s name / address / city (country), and warnings / precautions printed on the label are addressed in the risk analysis and v.v.

For the assessment of this technical documentation item it is assumed that the labelling of a non-market approved medical device should also comply with the Dutch language requirement for a CE-marked medical device. Labelling showed many major (13/19) and several minor (5/19) shortcomings. Labels with major shortcomings were not in Dutch and grant exemptions from the national language requirement were absent. In eight of these cases labelling did not comply with the essential requirements concerning the information to be supplied by the manufacturer. Labels with minor shortcomings were in Dutch; however, they did not comply with the essential requirements. Only one label was in Dutch *and* complied fully with the essential requirements.

If the national language requirement for non-market approved medical devices would not be compulsory, fourteen labels would have minor shortcomings (assessment score ‘moderate’) and five labels no shortcomings at all (assessment score ‘good’).

The wording ‘Exclusively for clinical investigations’, as explicitly required in the essential requirement 13.3.h of the MDD, was often not printed on the label (10/19). In two of these cases alternative wordings were used instead. Other shortcomings were related to the presence of CE marking (5/19), which is not allowed on an investigational device. In four of these cases labels included a CE mark with the identification number of the notified body. Additional shortcomings were related to the manufacturer’s and / or EU-authorised representative’s name / address / city (8/19):

- Manufacturer was not printed (n=1);
- Manufacturer’s address was not complete (n=6);
- EU-authorised representative was not printed (n=3);
- EU-authorised representative’s address was not complete (n=4).

The criterion concerning warnings / precautions is addressed in Section 3.4.4. Overall, the requirements for labelling were not addressed adequately.

### 3.4.12 Instructions for use

Good information for the user contains instructions for use in Dutch or otherwise in a foreign language accompanied by a grant exemption from the Dutch language requirement. Moreover, instructions for use comply with the essential requirements 13.6.a – 13.6.p. Instructions for use bear the wording ‘Exclusively for clinical investigations’, are without CE marking, mention manufacturer’s and / or the EU-authorised representative’s name / address / city (country), and warnings / precautions mentioned in the instructions for use are addressed in the risk analysis and v.v.

For the assessment of this particular technical documentation item it is assumed that instructions for use of a non-market approved medical device should also comply with the Dutch language requirement for a CE-marked medical device. Except for one, all instructions for use showed major shortcomings. In these eighteen cases the instructions for use were printed in English and grant exemptions from the national language requirement were absent. Furthermore, in twelve of these eighteen cases the instructions for use did not comply with the essential requirements concerning the information to be supplied by the manufacturer. Dutch instructions for use were only present in one case, which however did not comply with the essential requirements.

If the national language requirement for non-market approved medical devices would not be compulsory, fourteen instructions for use would have minor shortcomings (assessment score 'moderate') and five no shortcomings at all (assessment score 'good').

The wording 'Exclusively for clinical investigations', as explicitly requested in essential requirement 13.6.a of the MDD, was often not mentioned in the instructions for use (10/19). In four of these cases alternative wordings were printed in the instructions for use instead. Other shortcomings were related to the presence of a CE mark (2/19), which is not allowed on an investigational device. In one of these two cases instructions for use included a CE mark with the identification number of the notified body. Additional shortcomings were related to the manufacturer's and / or EU-authorised representative's name / address / city (9/19):

- Manufacturer was not printed (n=1);
- Manufacturer's address was not complete (n=2);
- EU-authorised representative was not printed (n=6);
- EU-authorised representative's address was not complete (n=2).

The criterion concerning warnings / precautions is addressed in Section 3.4.4. Overall, the requirements for the instructions for use labelling were poorly addressed.

### **3.4.13 Post market surveillance procedure**

A good post market surveillance procedure contains a procedure for the active collection and review of experiences, a description of resources to collect experiences other than customer-reported complaints, and a procedure for the lessons to be learnt from experiences such as a procedure for corrective and preventive actions taken, including updating the results of the risk analysis.

The assessment of the post market surveillance procedure was based on actual documentation as well as manufacturers' statements. A post market surveillance procedure is not required for non-market approved medical devices intended for clinical investigation in the current MDD, yet most manufacturers (13/19) submitted documentation. One manufacturer even submitted a surveillance procedure for non-market approved and CE-marked medical devices. Noticeably, in none of these technical documentation sets, the post market surveillance procedure was adequately addressed, mainly due to the absence of a proactive procedure to collect and review experiences, and the absence of a procedure for corrective and preventive actions including updating the risk analysis as an action to be taken. In two out of eleven cases, manufacturers submitted an unsubstantiated statement implying that a post market surveillance procedure was either maintained and not actually submitted, or under development and will be in place by commercial release. Four manufacturers stated that a post market surveillance procedure was not required for non-market approved medical devices and their corresponding item was rated accordingly, i.e. 'not applicable'.

### **3.4.14 Vigilance procedure**

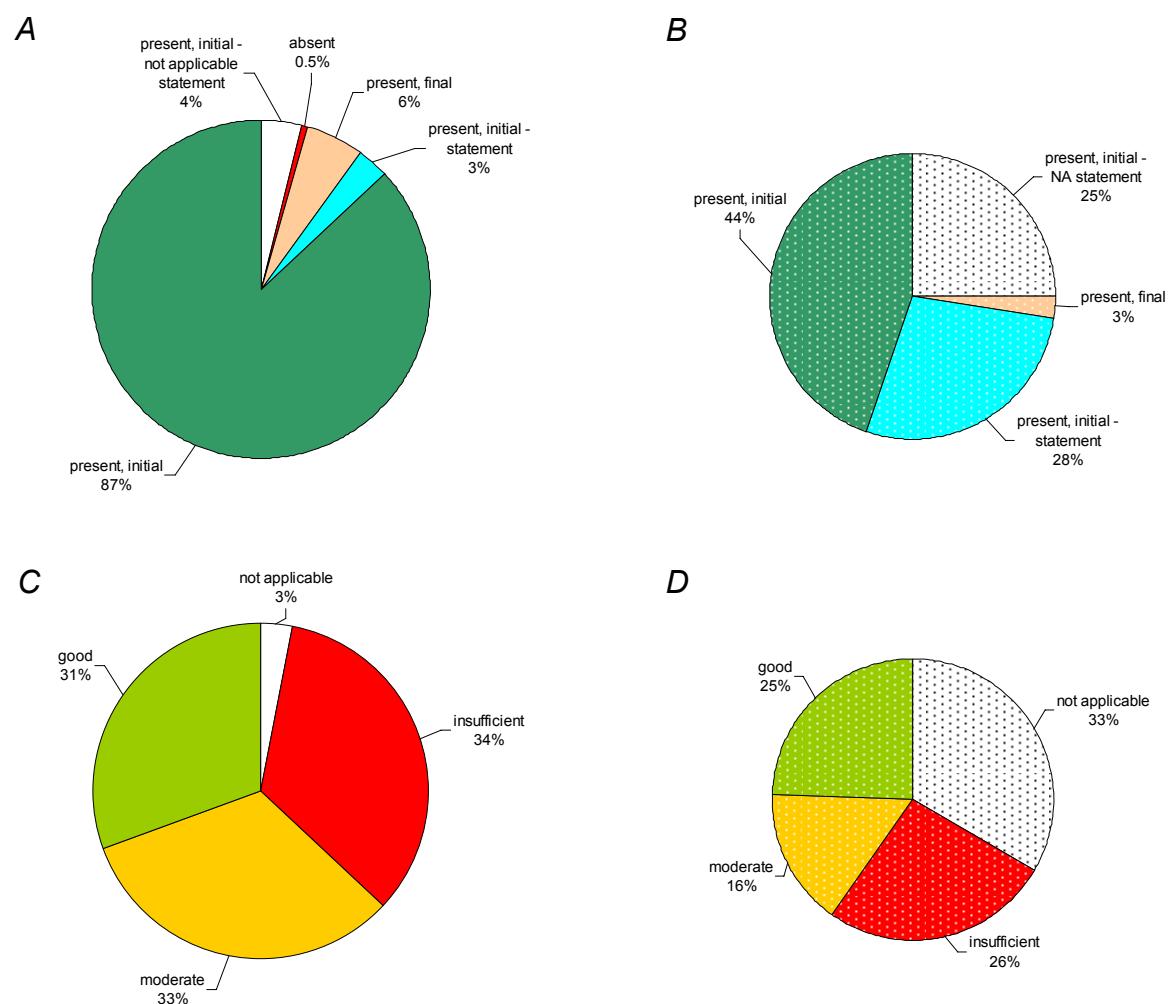
A good vigilance procedure contains a procedure for serious adverse event reporting mentioning the notification duty to competent authorities, and a procedure for the lessons to be learnt from serious adverse event reporting (changes in the product design, risk analysis, intended use, and labelling or instructions for use).

The principle of the vigilance procedure is to notify competent authorities of any malfunction or shortcoming that led to the death of a patient or user or led to a serious deterioration in the health of the subject that resulted in life threatening injury or illness. The vigilance procedure showed some major (5/19) and many minor shortcomings (13/19) due to the absence of a procedure for serious adverse event reporting (5/19), notification duty to competent authorities (5/19), and a procedure for corrective and preventive actions addressing the need to update the results of the risk analysis (17/19). Two manufacturers stated that the vigilance

procedure was not required for non-market approved medical devices. Three manufacturers submitted an unsubstantiated statement that the vigilance procedure was maintained but was not actually submitted. Thus, in most cases the vigilance procedure was not adequately addressed.

### 3.5 Overall availability and quality assessment of technical documentation items

After the initial request, approximately 87% of the explicitly in the MDD required technical documentation items were present as actual documents and 7% as statements, i.e. the sum of 4% 'not applicable' statements and 3% other statements, e.g. concerning the conformity assessment procedure to be followed or the vigilance procedure (Figure 4A, see also Appendix V – Table V.2).



*Figure 4. Technical documentation of non-market approved medical devices intended for clinical investigation. For explicitly in the MDD required items (solid pie areas), the availability (A) was based on a total sum of 209 items (19 medical device × 11 items) and the assessment (C) on 190 items (19×10). For complementary items (dotted pie areas), the availability (B) was based on 76 items (19×4) and the assessment (D) on 57 items (19×3).*

The remaining 6% of the items were submitted after a repeated request with the exception of one technical documentation item concerning adopted solutions which was absent. Thus, 94% of explicitly in the MDD required technical documentation items were readily supplied. A similar result was obtained if the complementary items (i.e. items concerning variants, medicinal substance, and post market surveillance) were taken into account (Figure 4B, see also Appendix V – Table V.2). 97% of these technical documentation items were readily supplied. However, the percentage of statements was considerably higher. The overall outcome of the quality assessment of the explicitly in the MDD required technical documentation items (based on a total sum of 190 items; 19 medical devices  $\times$  10 items) showed that 34% of these items had major shortcomings (assessment score ‘insufficient’), 33% had minor shortcomings (score ‘moderate’), and 33% had no shortcomings (i.e., sum of score ‘good’ and ‘not applicable’) (Figure 4C, see also Appendix V – Table V.3). The assessment of complementary items revealed that the quality of a substantial part of these items was inadequate (Figure 4D, see also Appendix V – Table V.3).

If all technical documentation items were taken into account, i.e. the explicitly in the MDD required technical documentation items plus complementary items, the quality assessment revealed that 32% of all these items scored ‘insufficient’, 29% scored ‘moderate’, 29% scored ‘good’, and 10% scored ‘not applicable’ (see Appendix V – Table V.3).

Altogether, the assessment showed that the quality of the technical documentation items of non-market approved medical devices intended for clinical investigation was mediocre.

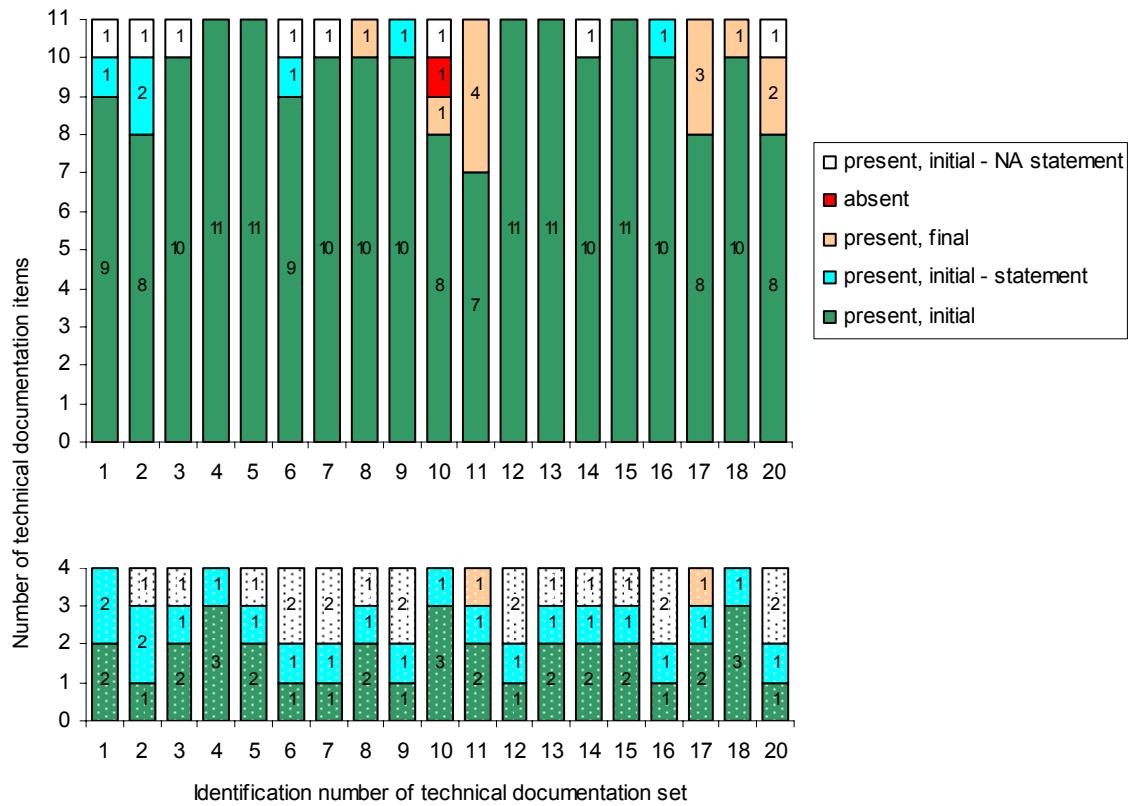
### **3.6 Availability and quality assessment of technical documentation sets**

The majority of manufacturers (13/19) promptly submitted all technical documentation items after the initial request (Figure 5A, and see also Appendix V – Table V.2). However, a substantial part (6/19) needed an additional request. In three technical documentation sets several items (i.e., two up to five) were initially not present, whereas in three sets only one item was initially absent. Note that in one of the technical documentation sets, the item concerning ‘adopted solutions’ was not submitted. The absence of this item did not interfere with the assessment, because it was checked on availability only.

When assessing solely the technical documentation items which are explicitly required in the relevant Annexes of the MDD, 18/19 of the manufacturers submitted technical documentation that was inadequate, i.e. at least two and maximally seven items (Figure 5B, see also Appendix V – Table V.3). In one of the technical documentation sets (id 18) seven items scored ‘insufficient’ and two items scored ‘moderate’. Thus, this set showed the highest number of total shortcomings. The set with the fewest shortcomings (id 13) five items scored ‘good’ and five ‘moderate’. All other technical documentation sets (17/19) showed mixed results with two up to seven major shortcomings, two up to six minor shortcomings, and one up to five items with no shortcomings. Note that for a specific device group, i.e. coronary stents, the assessment of the technical documentation varied considerably.

The assessment of the quality of the explicitly in the MDD required and complementary technical documentation items per set revealed similar outcomes (Figure 5B, see also Appendix V – Table V.3). 18/19 of the manufacturers submitted a substantial part of the technical documentation items which quality was inadequate, i.e. at least three and maximally seven items. Two extreme outcomes were shown for the same sets, i.e. technical documentation set with identification number 13 and 18.

A



B

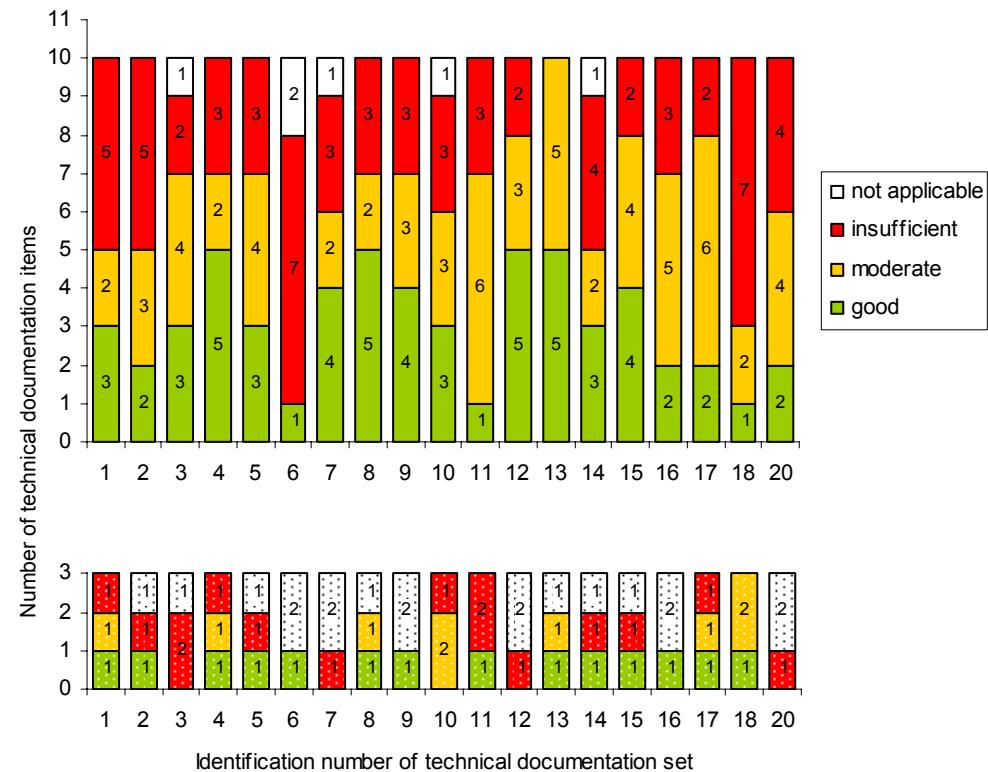


Figure 5. Availability (A) and quality assessment (B) per technical documentation set of non-market approved medical devices intended for clinical investigation. Solid and dotted bar areas indicate the number of technical documentation items which are explicitly required in the MDD or are complementary, respectively. NA statement denotes a manufacturer's statement that an item was not applicable.

## 4. Discussion and conclusions

### 4.1 Discussion

In this investigation manufacturers were requested to submit technical documentation of non-market approved medical devices intended for clinical investigation in human subjects. The timely response was evaluated, the availability of the technical documentation was checked, and the quality was assessed.

#### 4.1.1 Extrapolation of results

During almost one and a half year all manufacturers' notifications of clinical investigations to the Dutch Health Care Inspectorate were examined whether medical devices met the inclusion and exclusion criteria for this study. This yielded full coverage of non-market approved Class IIa, IIb, and III medical devices regulated by the MDD and submitted to clinical investigations in the Netherlands. This reflected the situation during a given period of time and for a given geographical region. Note the very large percentage of Class III medical devices included (84%) and that a large percentage of the devices (79%) was intended for percutaneous (cardio) vascular interventions, which provide less invasive surgical and more minimally invasive solutions in disease treatment. Extrapolation of the results of the current prospective investigation to other manufacturers, medical devices, time windows, and / or clinical investigations in other countries may be difficult. Therefore, generalisations based on the current results should be performed carefully.

#### 4.1.2 Structure of technical documentation

Technical documentation was received either in printed form or digitally by e-mail or on disc. In general, the structure of technical documentation sets was heterogeneous. Apparently, manufacturers derived the content of the submitted technical documentation from the total technical documentation which manufacturers are planning to prepare for market approval. For the arrangement of information manufacturers used a tabular format with requested items in sequential order. However, the arrangement was often sloppy and essential information was found in other documentation items instead of the identified part of the item. This dispersal hampered the search for relevant information only slightly and it was, therefore, not considered a major obstacle for the assessment. Nevertheless, a well-ordered structure enables technical documentation to be easily and readily used. The Global Harmonization Task Force recommended and proposed a basic format for technical documentation of medical devices to be submitted to either a regulatory authority or to a notified body for review, validation, or approval (10). This format could also be adapted to the technical documentation set requested for this investigation.

#### 4.1.3 Response and availability of technical documentation

After the initial request, 68% of the included manufacturers provided 95% of all requested technical documentation items on time (either as documents or statements). After the final request the manufacturer's response was 100%. Thus, although some manufacturers refrained from a timely response, they were cooperative and all requested technical documentation

items were supplied. The willingness and initial availability of documentation were improved considerably compared with the results of previous investigations of CE-marked medical devices (7, 8, 9). The explanation could be that the outcome of the current study was mainly based on technical documentation of Class III medical devices. In contrast, in our previous study manufacturers of Class IIa and Class IIb CE-marked medical devices were often reluctant: 83% of the manufacturers responded and only 17% of the manufacturers provided technical documentation after the initial request (8).

Following the conformity assessment procedure laid down in Annex II of the MDD, a manufacturer of Class IIa or IIb medical devices who followed the Annex II procedure was in the past not obliged to actually submit technical documentation because the notified body audited the quality system of the manufacturer and not the technical documentation of each medical device. Note that in the future, notified bodies will assess the technical documentation of a representative sample of the product line of CE-marked medical devices (see also Section 4.1.5). On the other hand, a manufacturer of Class III medical devices always has to submit a design dossier, which contains much of the technical documentation requested in the current investigation, to a notified body before CE mark approval. This could be a reason why manufacturers of Class III medical devices will have their technical documentation more readily available.

#### **4.1.4 Assessment of technical documentation**

The results indicate that manufacturers often interpreted the content of the required technical documentation items in different ways. For instance, some manufacturers did mention the classification of the medical device, whereas others did not. Most likely, manufacturers do not consider the classification as part of the general description of the medical device. However, manufacturers will have to classify the medical device in order to establish the conformity assessment procedure to be followed. In our opinion the classification should be regarded as an integral part of the general description of the medical device and should be mentioned accordingly in the technical documentation.

Furthermore, there was a discrepancy regarding the interpretation of variants. Most manufacturers of coronary stents defined stents with different diameters as variants, whereas one manufacturer stated no variants were planned, despite the presence of information indicating the existence of variants with different diameters. In our opinion, medical devices such as coronary stents with different diameters are actually variants.

Many manufacturers submitted statements concerning the content of specific technical documentation items. If no further information was present, these statements were regarded as being accurate for technical documentation items such as the incorporation of a medicinal substance or sterilisation.

##### *Risk analysis*

Definitely in need for improvement is the assessed risk analysis. Drawing on past medical device experiences, manufacturers should be able to identify and evaluate all reasonably foreseeable and recognized hazards that may result in patient risk. Although all manufacturers applied the current risk management standard (11), many manufacturers struggled with the implementation of risk management principles. Specifically, manufacturers failed to identify hazards that may occur due to characteristics or properties of the medical device during normal use or misuse. This is one of the first activities in sound risk management. Some manufacturers recognised that long-term outcomes are unknown at present. Risks associated with long-term outcomes and potential benefits should be clarified after the accumulation of clinical investigation experience. Once the clinical investigation

results are available the risk assessment should be updated to address any additional risks based on actual data. Risk evaluation and risk control showed fewer shortcomings compared to risk analysis.

The observed lack of the mutual exchangeability between residual risks / hazards in the risk analysis and warnings and precautions in the instructions for use and on labelling can be corrected promptly by manufacturers. This correction is definitely needed and should be relatively easy to implement. Users who will read the instructions for use and labelling will be unaware of many hazards identified in the risk analysis. On the other hand, we had the impression that many precautions and warnings mentioned in the instructions for use and on the labelling were just added without any systematic preceding analysis in the risk assessment procedure opposing sound risk management principles.

#### *Label and instructions for use*

The label and the instructions for use were often not in Dutch, which was scored as a major shortcoming. Although there is no national language requirement in case of non-market approved medical devices for clinical investigation, we have used the same language requirement as for CE-marked medical devices. Physicians are assumed to have good command of the English language, but not all other users involved in handling medical devices can be expected to have sufficient command of the English language to understand subtleties in the instructions, and therefore user information in Dutch is necessary. It is recognized that this language requirement might be an extra burden for the manufacturer because it is likely that after a clinical investigation, user information has to be revised.

#### *Post market surveillance*

Post market surveillance is a broad term covering all monitoring activities of medical devices in use. The principle of the post market surveillance procedure is to collect and review experiences with medical devices in a proactive manner. Although a post market surveillance procedure is not (yet) required for non-market approved medical device intended for clinical investigation in the current MDD, we included the assessment on post market surveillance because post market clinical follow-up is a proposed amendment in the official review of the MDD (see Section 4.1.5).

For non-market approved medical devices, manufacturers could state that a post market surveillance procedure is not necessary as these medical devices are not on the market yet. Indeed, some established medical device companies in the current report submitted such a statement without referring to any maintenance of a procedure for CE-marked medical devices and the corresponding item was scored accordingly, i.e. not applicable. However, we feel that submission of such a statement is not sufficient. Established medical device companies must have a post market surveillance procedure in place. Most of the established companies actually stated that a procedure is maintained, whereas start-up companies could state that a procedure is being developed and will be in place by time of commercial release of the medical device.

Apparently, some manufacturers became confused by the term 'post market' in relation to non-market approved medical devices intended for clinical investigation. However, manufacturers involved in a clinical investigation actually do collect and review experiences in a proactive *and* systematic manner. Therefore, it could be argued that such gathering of experiences with a non-market approved medical device is a surveillance procedure 'pur sang' though not post market but pre market. Thus, manufacturers should be able to supply information on how they practically implemented this issue because it is very vital in the life cycle of a medical device.

The gathered experiences during the clinical investigation should be used for corrective and preventive actions. In addition, the risk analysis documents should be reviewed to determine if the failure modes and their level of severity have previously been identified, and if current methods for mitigation (i.e., risk analysis tools) are effective. The results of this review could support whether immediate action is required and if additional mitigation steps are needed to improve the quality and safety of the medical device, the accompanying information for the user, or training of user. However, a procedure for corrective and preventive actions was often missing in the submitted technical documentation. Furthermore, in submitted procedures the integration of the risk management process into the corrective and preventive action process was poorly or not at all described. Thus, these findings imply that the continuous iterative cycle ensuring the quality and safety of medical devices is insufficiently guaranteed.

#### *Vigilance*

A number of manufacturers failed to fulfil the requirements of the MDD with respect to vigilance. The necessity of vigilance has been embedded throughout the entire MDD; see for instance provision 3.1 in Annex II and 2.3.5 in Annex X. Every manufacturer is required to have a vigilance procedure in place for medical devices, whether CE-marked or non-market approved and under clinical investigation. The rationale behind the requirement of a vigilance procedure in place is to be prepared, in case of a serious adverse event (and serious adverse device effect) or an (near) incident, to quickly warn other users of the medical device and competent authorities and to evaluate the experiences gained from devices. It is important to know why serious adverse events occur and how they might be prevented in the future. One could argue that for devices intended for clinical investigation it is even more important to have a vigilance procedure in place. The probability of an unexpected serious adverse event could be higher with a non-market approved device intended for clinical investigation than with a similar device that is already on the market for some time. When the procedure for corrective and preventive actions is considered, similar findings were obtained for vigilance as for post market surveillance.

Manufacturers should take due notice of the obligation and importance to have a vigilance procedure in place, even for non-market approved medical devices intended for clinical investigation. It is recommended that the manufacturer's notification of a clinical investigation to the national competent authority should include a declaration stating that a vigilance system is in place.

#### **4.1.5 European medical devices regulation**

For manufacturers placing Class IIa, IIb, or III medical devices on the market, a notified body is involved in establishing whether manufacturers meet the legal requirements. Notified bodies are seen as a critical element in the implementation of the MDD. Currently, manufacturers are only obliged to contract a notified body for CE mark approval, i.e. at some point in time before the market release of the medical device. In our opinion, manufacturers should seek the view of their notified body in a relatively early stage. It would be valuable for the quality and safety of the medical device which is used in a clinical investigation, if the related technical documentation would be discussed with the notified body before embarking on a clinical investigation. This would also facilitate the actual CE mark approval process, and thus would not mean an additional burden on the manufacturer, especially for manufacturers of Class III medical devices. In particular the review of the risk analysis by the notified body could provide valuable feedback to the manufacturer and it might even lead to a modified set-up of the investigation.

The European Commission published a draft proposal to amend the MDD through regulatory clarifications to ensure consistency of interpretation and implementation (12). Some of the proposed changes aim to clarify the requirements for a clinical investigation (Annex VIII and X), clinical evaluation (Annex X), and the role of the notified body in auditing the quality management system of manufacturers (Annex II). In Annex II, the draft requires a notified body to sample technical documentation across the range of CE-marked medical devices evaluating the design documentation for a representative sample of the product line. Furthermore, the required clinical evaluation referred to in Annex X determines whether a critical evaluation of relevant scientific literature will suffice, or a critical evaluation of the results of all clinical investigations has to be made, or a combination of both to demonstrate conformity with the essential requirements. However, the role of the notified body is not explicitly mentioned in the proposed amendments of Annex VIII and X. Nevertheless, the proposed amendments of Annex VIII and X are addressing some of the complementary technical documentation items having major shortcomings. These amendments of Annex VIII concern additional statements on the incorporation of medicinal substances / human blood derivatives and the utilisation of tissues of animal origin. Moreover, tests on the medicinal substance / human blood derivative to assess the safety, quality, and usefulness of that substance or derivative are required, and the risk analysis must address appropriate measures to reduce the risk of infection if tissues of animal origin are used for the manufacturing of medical devices. In Annex X a post market clinical follow-up will be required as part of the clinical evaluation or if not deemed necessary, it must be duly substantiated.

#### **4.1.6 Implications**

Altogether, the assessments showed that the available technical documentation of non-market approved medical devices intended for clinical investigation in human subjects contains major shortcomings. Although these shortcomings in the documentation do not necessarily mean that the quality and safety of the actual medical devices are also inadequate, there is definitely a reason for concern. If the risk analysis and the description of the sterilisation process or procedures regarding the added medicinal substance are inadequate, then the product safety may not be sufficiently guaranteed. Furthermore, if the instructions for use and the labelling are lacking warnings and precautions, then this means that a safe application of the medical devices could be in jeopardy, implying increased risks which could seriously affect patient safety during a clinical investigation. These results give rise to the question whether European competent authorities and ethics committees should increase surveillance on medical devices intended for use in clinical investigations. During the approval process for conducting a clinical investigation with medical devices, ethics committees could use the method described in this report for their assessments of research dossiers of applicants to check whether essential aspects concerning the quality and safety of medical devices are submitted completely and addressed adequately.

## 4.2 Conclusions

- Improvement of the quality of the technical documentation of non-market approved medical devices intended for clinical investigation is necessary.
  - For 95% of the manufacturers, the quality of a substantial part of the technical documentation explicitly required in the MDD was inadequate.
  - The assessment revealed that 34% of the total number of all explicitly in the MDD required technical documentation items from all manufacturers had major shortcomings, 33% had minor shortcomings, and 34% had no shortcomings.
  - Distributed over manufacturers, major shortcomings were found in nine out of ten types of assessed technical documentation items. Only the general description of the medical device showed merely minor shortcomings.
  - Most major shortcomings were observed for the items concerning risk analysis, control and verification of the design, sterilisation, labelling, instructions for use, and vigilance.
  - In addition, the quality of technical documentation was inadequate for complementary items concerning medical devices incorporating a medicinal substance and post market surveillance.
  - Although a post market surveillance procedure is not required for non-market approved medical devices in the current MDD, it is advisable that manufacturers indicate on how they practically implemented this issue. Actually, a clinical investigation is one of the first opportunities for manufacturers to collect and review experiences with medical devices in a proactive and systematic manner.
  - Submitted technical documentation was often not well-structured.
- Vital aspects in the life cycle of medical devices were underexposed. This could affect the continuous iterative process ensuring the quality and safety of medical devices, and thus, it could affect patient safety during clinical investigations.
  - For manufacturers, this could be a reason to consult their notified bodies more extensively at an earlier stage, i.e. before the start of the clinical investigation.
  - For European competent authorities and ethics committees, this could be a reason to consider the need for increased surveillance on medical devices intended for clinical investigation.
  - Proposed amendments concerning the revision of the current MDD are addressing some of the shortcomings.
- The method described in this report provides a practical guide for manufacturers, notified bodies, competent authorities, and ethics committees to check whether technical documentation of medical devices contains the necessary aspects.

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## Appendix I: Assessment form

### ***Assessment form for technical documentation of medical devices***

#### **General information on manufacturer**

Name of manufacturer

Address

PO Box

Zip code

City

Country

Name of contact person

Telephone

Fax

#### **General information on medical device (MD)**

Name of MD

General description of MD

Classification rule(s)

Classification of MD (e.g. Class III)

Conformity assessment procedure (e.g. Annex II)

#### **General description on clinical investigation (CI)**

Acronym of CI

Date of start of CI (mmm yyyy)

Date of end of CI (mmm yyyy)

#### **Date of correspondence**

Request 1	(dd.mm.yyyy)	Request 2	(dd.mm.yyyy)	Request 3	(dd.mm.yyyy)
-----------	--------------	-----------	--------------	-----------	--------------

Deadline 1	(dd.mm.yyyy)	Deadline 2	(dd.mm.yyyy)	Deadline 3	(dd.mm.yyyy)
------------	--------------	------------	--------------	------------	--------------

Received 1	(dd.mm.yyyy)	Received 2	(dd.mm.yyyy)	Received 3	(dd.mm.yyyy)
------------	--------------	------------	--------------	------------	--------------

Note 1:

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Identification number (1, 2, 3 ...)

Assessors' initials

Date of assessment (dd.mm.yyyy)

Status technical documentation (included, excluded, not yet received)

Status assessment (first version, final version, not assessed)

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<b><u>Availability check</u></b>	<i>Absent</i>	<i>Present, final</i>	<i>Present, initial</i>	<i>NA</i>
1. General description of the MD	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
2. General description of any variants planned	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. Design specifications	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
4. Results of the risk analysis	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
5. List of applied standards	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. List of adopted solutions	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7. Control and verification of the design	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
8. Proof of conformity when connected to other MD	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9. Substance with ancillary action	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
10. Sterilisation	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
11. Label	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
12. Instructions for use	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
13. Post market surveillance procedure	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
14. Vigilance procedure	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
15. Statement of conformity assessment procedure	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	

*Note 2:*

	Absent	Present
1.1. Name of the MD	<input type="checkbox"/>	<input type="checkbox"/>
1.2. Classification of the MD	<input type="checkbox"/>	<input type="checkbox"/>
1.3. Physical description	<input type="checkbox"/>	<input type="checkbox"/>
1.4. Drawing, diagram, and / or photograph	<input type="checkbox"/>	<input type="checkbox"/>
1.5. Mode of action	<input type="checkbox"/>	<input type="checkbox"/>
1.6. Intended use	<input type="checkbox"/>	<input type="checkbox"/>
1.7. Contraindications, warnings, precautions	<input type="checkbox"/>	<input type="checkbox"/>

<u>Assessment</u>	Insufficient	Moderate	Good
1. General description of the MD	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Remark 1

2. General description of any variants planned	Absent	Present	NA
2.1. Variants mentioned without physical description	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2.2. Physical description of variants	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2.3. Model numbers	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2.4. Manufacturer's statement: no variants are planned	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

<u>Assessment</u>	Insufficient	Good	NA
2. General description of any variants planned	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Remark 2

3. Design specifications	Absent	Present	NA
3.1. (Design) drawings (if relevant)	<input type="checkbox"/>	<input type="checkbox"/>	
3.2. Specifications of materials used	<input type="checkbox"/>	<input type="checkbox"/>	
3.3. Product specifications	<input type="checkbox"/>	<input type="checkbox"/>	
3.4. Explanation for understanding drawings (if applicable)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

<u>Assessment</u>	Insufficient	Moderate	Good
3. Design specifications	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Remark 3

4. Results of the risk analysis (RA)	No	Yes	NA
4.1. Not all foreseeable or known hazards are identified (see 4.A.)	<input type="checkbox"/>	<input type="checkbox"/>	
4.2. All foreseeable or known hazards are identified	<input type="checkbox"/>	<input type="checkbox"/>	
4.4. Risks arising from identified hazards are estimated	<input type="checkbox"/>	<input type="checkbox"/>	
4.5. Actions taken to reduce / eliminate risks are poor	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4.6. Actions taken to reduce / eliminate risks are adequate	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4.7. Residual risks are justified in relation to anticipated benefits	<input type="checkbox"/>	<input type="checkbox"/>	

<b>4.A. Possible hazards and contributing factors</b>	<b>No</b>	<b>Yes</b>	<b>NA</b>
<i>Energy hazards</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<i>Biological and chemical hazards</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<i>Mechanical hazards</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<i>Hazards related to environment and property</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<i>Hazards related to information</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<i>Design</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<i>Manufacturing process</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<i>Transport and storage</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<i>Environmental effects</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<i>Installation, maintenance, and service</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<i>Cleaning, disinfection, and sterilisation</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<i>Disposal and scrapping</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<i>Normal operation</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<i>Use errors</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<i>Clinical hazards associated with use</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<i>Other</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<i>Remark 4A</i>			

<b>4.B. Residual risks / hazards in RA</b>	<b>No/few</b>	<b>Half</b>	<b>Most/all</b>
<i>Residual risks / hazards are printed on label</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<i>Residual risks / hazards are printed in instructions for use (IFU)</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<i>Warnings / precautions on label are mentioned in RA</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<i>Warnings / precautions in IFU are mentioned in RA</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<i>Remark 4B</i>			

<b>4.C. MD is manufactured utilising tissues of animal origin</b>	<b>No</b>	<b>Yes</b>	<b>NA</b>
<i>Risk analysis addresses animal-derived material</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

*Remark 4C***4.D. Additional information***RA according to* (e.g. ISO 14971)*Date of RA* (mmm yyyy)*Remark 4D*

<b><u>Assessment</u></b>	<b>Insufficient</b>	<b>Moderate</b>	<b>Good</b>
<b>4. Results of the risk analysis</b>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

*Remark 4*

<b>5. List of applied standards</b>	<b>No</b>	<b>Yes</b>	<b>NA</b>
<i>5.1. List of product standards corresponds hardly</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<i>5.2. List of product standards corresponds considerably</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<i>5.3. List of product standards corresponds fully</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<i>5.4. Manufacturer's statement is present: standards NA</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<i>5.5. Product standards are NA</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

<b>5.A. Additional information</b>	<b>Absent</b>	<b>Present</b>	<b>NA</b>
<i>Checklist essential requirements including standards</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<i>Separate list including standards</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<i>Date of checklist essential requirements</i> (mmm yyyy)			

<u>Assessment</u>	Insufficient	Moderate	Good	NA
<b>5. List of applied standards</b>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<i>Remark 5</i>				

<b>6. List of adopted solutions if standards are not applied</b>	Absent	Present	NA
Checklist essential requirements including solutions	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Separate list including solutions	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Manufacturer's statement: only standards are applied	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

<u>Assessment</u>
<b>6. List of adopted solutions (not assessed)</b>
<i>Remark 6</i>

<b>7. Control and verification of the design</b>	Absent	Present
7.1. Test results	<input type="checkbox"/>	<input type="checkbox"/>
7.2. Design verification techniques	<input type="checkbox"/>	<input type="checkbox"/>
7.3. Procedures	<input type="checkbox"/>	<input type="checkbox"/>
7.4. Manufacturer's statement: QMS is maintained	<input type="checkbox"/>	<input type="checkbox"/>

<u>Assessment</u>	Insufficient	Moderate	Good
<b>7. Control and verification of the design</b>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<i>Remark 7</i>			

<b>8. Proof of conformity if connected to other device</b>	Absent	Present	NA
8.1. Reference documentation in ER 9.1 or combination addressed in RA	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8.2. Description of actual combination	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8.3. Extensive proof of conformity	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8.4. Manufacturer's statement: MD cannot be connected	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

<u>Assessment</u>	Insufficient	Moderate	Good	NA
<b>8. Proof of conformity (combination)</b>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<i>Remark 8</i>				

<b>9. Substance with ancillary action</b>	Absent	Present	NA
9.1. Intended purpose within the context of MD	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9.2. Source and / or product licence	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9.3. Method of incorporation of substance into MD	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9.4. Tests performed on substance	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9.5. Procedure for pharmacovigilance	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9.6. Notification duty for reporting serious adverse reaction to competent authority	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9.7. Assessment of substance by national auth. / European Medicines Agency	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9.8. Manufacturer's statement: no substance with ancillary action used	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

<u>Assessment</u>	Insufficient	Moderate	Good	NA
<b>9. Substance with ancillary action</b>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<i>Remark 9</i>				

	Absent	Present	NA
10.1. Cleaning process (if applicable)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
10.2. Method of sterilisation	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
10.3. Parameters of sterilisation process	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
10.4. Summary of sterilisation validation data	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
10.5. Packaging material used	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
10.6. Manufacturer's statement: MD is non-sterile	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

<b>Assessment</b>	<i>Insufficient</i>	<i>Moderate</i>	<i>Good</i>	<i>NA</i>
<b>10. Sterilisation</b>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<i>Remark 10</i>				

	No	Yes	NA
11.1. Label only in foreign language	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
11.2. Label in Dutch	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
11.3. Grant exemption from Dutch language requirement included	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
11.4. Label complies partially with essential requirements (see 11.A.)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
11.5. Label complies fully with essential requirements	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<b>11.A. Additional information</b>	<b>No</b>	<b>Yes</b>	
Label bears wording 'Exclusively for clinical investigations'	<input type="checkbox"/>	<input type="checkbox"/>	
Label is without CE mark	<input type="checkbox"/>	<input type="checkbox"/>	
Manufacturer's / EU-authorised representative's name / address / city is printed fully	<input type="checkbox"/>	<input type="checkbox"/>	
Warnings / precautions on label are mentioned in RA	<input type="checkbox"/>	<input type="checkbox"/>	

<b>Assessment</b>	<i>Insufficient</i>	<i>Moderate</i>	<i>Good</i>	
<b>11. Label</b>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
<i>Remark 11</i>				

	No	Yes	NA
12.1. IFU in foreign language	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
12.2. IFU in Dutch	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
12.3. Grant exemption from Dutch language requirement included	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
12.4. IFU complies partially with essential requirements (see 12.A.)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
12.5. IFU complies fully with essential requirements	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
12.6. Manufacturer's statement: MD does not contain IFU	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<b>12.A. Additional information</b>	<b>No</b>	<b>Yes</b>	
IFU bears wording 'Exclusively for clinical investigations'	<input type="checkbox"/>	<input type="checkbox"/>	
IFU is without CE mark	<input type="checkbox"/>	<input type="checkbox"/>	
Manufacturer's / EU-authorised representative's name / address / city is printed fully	<input type="checkbox"/>	<input type="checkbox"/>	
Warnings / precautions in IFU are mentioned in RA	<input type="checkbox"/>	<input type="checkbox"/>	

<b>Assessment</b>	<i>Insufficient</i>	<i>Moderate</i>	<i>Good</i>	<i>NA</i>
<b>12. Instructions for use</b>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<i>Remark 12</i>				

	Absent	Present	NA
13.1. Manufacturer's statement: PMS is maintained	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
13.2. Complaint procedure for users	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
13.3. Non-proactive approach to collect experiences	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
13.4. Procedure for active collection / review of experiences	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
13.5. Resource description	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
13.6. CAPA procedure including RA update	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
13.7. Manufacturer's statement: PMS is not required	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

<u>Assessment</u>	Insufficient	Moderate	Good	NA
13. Post market surveillance procedure	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Remark 13				

	Absent	Present	NA
14.1. Manufacturer's statement: vigilance is not required	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
14.2. Manufacturer's statement: vigilance is maintained	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
14.3. Procedure for serious adverse event (SAE) reporting	<input type="checkbox"/>	<input type="checkbox"/>	
14.4. Notification duty for reporting SAE to competent authority	<input type="checkbox"/>	<input type="checkbox"/>	
14.5. Procedure for lessons to be learnt, e.g. CAPA	<input type="checkbox"/>	<input type="checkbox"/>	

<u>Assessment</u>	Insufficient	Moderate	Good
14. Vigilance procedure	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Remark 14			

<u>15. Conformity assessment procedure</u>	Absent	Present
Manufacturer's statement	<input type="checkbox"/>	<input type="checkbox"/>
Conformity assessment procedure to be followed (e.g. Annex II)		

<u>Assessment</u>
15. Statement conformity assessment procedure (not assessed)
Remark 15

<b><u>Assessment summary</u></b>	<i>Insufficient</i>	<i>Moderate</i>	<i>Good</i>	<i>NA</i>
1. <i>General description of the MD</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
2. <i>General description of any variants planned</i>	<input type="checkbox"/>		<input type="checkbox"/>	<input type="checkbox"/>
3. <i>Design specifications</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
4. <i>Results of the risk analysis</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
5. <i>List of applied standards</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. <i>List of adopted solutions (not assessed)</i>				
7. <i>Control and verification of the design</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
8. <i>Proof of conformity when connected to other MD</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9. <i>Substance with ancillary action</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
10. <i>Sterilisation</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
11. <i>Label</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
12. <i>Instructions for use</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
13. <i>Post market surveillance procedure</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
14. <i>Vigilance procedure</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
15. <i>Statement of conformity ass. procedure (not assessed)</i>				

Note 3:

## Appendix II: Guideline for the assessment

The guideline gives information for the availability check and quality assessment of technical documentation items of non-market approved medical devices intended for clinical investigation.

### 1. GENERAL DESCRIPTION OF THE MEDICAL DEVICE

#### Availability options:

Absent: the technical documentation does not contain a general description of the medical device.

Present: a general description can be given as a separate document or in other technical documentation items, e.g. risk analysis or instructions for use.

#### Contents:

1. (generic) name of the medical device,
2. classification of the medical device,
3. physical description of the medical device,
4. schematic drawing, diagram or photograph of the medical device,
5. mode of action (mode of action is the means by which a product achieves its intended therapeutic effect or action, for example drug-eluting stents have two modes of action: one action is to provide a mechanical scaffold to be implanted in an artery to improve the resultant arterial luminal diameter following angioplasty and the second action of the product is the drug action, with the intended effect of reducing the incidence of restenosis and the need of target lesion revascularisation),
6. short description of the intended use, e.g. patient population, medical condition of the patient, and / or intended professional use,
7. short description of the contraindications, warnings, precautions, and / or stop criteria.

#### **Assessment score concerning general description of the medical device**

Insufficient: 1+3 **or** 1+6 **or** 1+5 **or** 1+3+5 **or** 1+3+6

Moderate: 1+3+5+6 **or** 1+3+4+5+6 **or** 1+3+4+5+7 **or** 1+3+4+5+6+7

Good: 1+2+3+4+5+6+7

### 2. GENERAL DESCRIPTION OF ANY VARIANTS PLANNED

#### Availability options:

Not applicable: manufacturer states that no variants are planned (and items 1, 2, and / or 3 below are absent).

Absent: any information on variants (including statement) is absent.

Present: technical documentation mentions variants.

#### Contents:

1. variants are implicitly mentioned in other technical documentation items, e.g. design specifications, risk analysis, or instructions for use,
2. description of variants including information about size, colour, weight, etc.,
3. model number(s) is (are) mentioned (if applicable),
4. manufacturer's statement: no variants are planned.

#### **Assessment score concerning general description of any variants planned**

Insufficient: 1 **or** 1+4

Good: 2+(3) **or** 2+(3)+4

NA: 4

Remark: make a note if the manufacturer's statement is present despite an indication of variants in other technical documentation items, i.e. if assessment score is based on '1+4' or '2+(3)+4'.

### 3. DESIGN SPECIFICATIONS

#### Availability options:

Absent: the technical documentation does not contain information concerning design specifications.

Present: the technical design is univocally laid down, e.g. in drawing, description, or list of parts.

#### Contents:

1. (design) drawing(s) (essential device sizes must be specified; design drawing only if relevant),
2. specification of the materials used, biomaterials or components,
3. product specification,
4. descriptions / explanations necessary for the understanding of the drawing(s) (if applicable).

#### **Assessment score concerning design specifications**

Insufficient:	<b>1 or 2 or 3</b>
Moderate:	<b>1+2 or 1+3 or 2+3</b>
Good:	<b>1+2+3+(4)</b>

### 4. RESULTS OF THE RISK ANALYSIS

#### Availability options:

Absent: the technical documentation does not contain the results of the risk analysis.

Present: a document containing the results of the risk analysis is present. Check and note date and type (FMEA, ISO 14791, EN 1441) of the risk analysis.

#### Contents:

1. not all known or foreseeable hazards are identified (see Appendix III),
2. all known or foreseeable hazards are identified,
3. risks arising from the identified hazards are estimated,
4. actions taken to reduce or eliminate the risks are not mentioned or poor,
5. actions taken to reduce or eliminate the risks are adequate, i.e. control measures are consistently described in line with essential requirement 2:
  - a. eliminate or reduce risks as far as possible (inherently safe design and construction),
  - b. take adequate protection measures including alarms if necessary, in relation to risks that can not be eliminated,
  - c. inform users of residual risks / hazards due to any shortcomings of any protection measures adopted,
6. residual risks / hazards are justified in relation to anticipated benefits.

#### **Assessment score concerning results of the risk analysis**

Insufficient:	<b>1+4 or 1+3+4 or 1+3+4+6</b>
Moderate:	<b>1+3+5 or 1+5+6 or 1+3+5+6 or 2+4 or 2+5 or 2+3+4 or 2+3+5</b>
Good:	<b>2+3+5+6</b>

#### 'Spotlight' options:

1. residual risks / hazards in risk analysis specific to labelling are mentioned on label (no / few, approximately half, most / all),
2. residual risks / hazards in risk analysis specific to instructions for use are mentioned in instructions for use (no / few, approximately half, most / all),
3. warnings / precautions on label are mentioned in risk analysis as residual risks / hazards (no / few, approximately half, most / all) (see also 11. Labelling, 'spotlight' options),
4. warnings / precautions in instructions for use are mentioned in risk analysis as residual risks / hazards (no / few, approximately half, most / all) (see also 12. Instructions for use, 'spotlight' options).

### 5. LIST OF APPLIED STANDARDS

#### Availability options:

Not applicable: manufacturer states that (harmonised product) standards are not applicable.

Absent: the technical documentation does not contain a document with (harmonised product) standards.

Present: a separate list of applied standards or a checklist essential requirements with applied standards is present. Check and note the date of the document.

Make a list of *product* standards for the medical device, if applicable. Only harmonised standards are relevant. Compare manufacturer's vs. assessor's list.

Contents:

1. list corresponds hardly,
2. a considerable part of the list corresponds,
3. list corresponds fully,
4. manufacturer's statement: harmonised standards are not applicable,
5. product standards are not applicable.

**Assessment score concerning list of applied standards**

Insufficient:	1
Moderate:	2
Good:	3
NA:	4 or 5

**6. LIST OF ADOPTED SOLUTIONS**

These solutions have to be adopted if standards are not applied in full.

Availability options:

Not applicable: manufacturer states that only standards are applied.

Absent: the technical documentation does not contain a document or a checklist essential requirements with adopted solutions.

Present: a document with references or a checklist essential requirements containing adopted solutions is present.

**Assessment score concerning list of adopted solutions**

No assessment of the adopted solutions is performed.

**7. TECHNIQUES USED TO CONTROL AND VERIFY THE DESIGN AND THE PROCESSES AND SYSTEMATIC MEASURES THAT WILL BE USED WHEN THE PRODUCTS ARE BEING DESIGNED**

Availability options:

Absent: the technical documentation does not contain relevant documents.

Present: manufacturer's statement (see item 4 below) or a document containing information on test results, techniques, and procedures is present.

Contents:

1. test results are present,
2. design verification techniques are mentioned,
3. procedures are present,
4. manufacturer's statement: a (comprehensive) quality management system is maintained.

**Assessment score concerning control and verification of the design**

Insufficient:	1 or 2 or 3 or 4 or 2+4
Moderate:	1+2 or 1+3 or 2+3
Good:	1+2+3

**8. PROOF OF CONFORMITY TO THE ESSENTIAL REQUIREMENTS WHEN CONNECTED TO OTHER MEDICAL DEVICE**

Availability options:

Not applicable: manufacturer states that the medical device cannot be connected to other medical device(s) (and items 1 – 3 below are absent).

Absent: the technical documentation does not contain information concerning the proof of conformity.

Present: the proof of conformity is present.

**Contents:**

1. proof of conformity is given in essential requirement 9.1 (MDD 93/42/EEC, Annex I) as reference document (actual document is not present) or combination is addressed in risk analysis,
2. description of the actual combination,
3. extensive proof of conformity,
4. manufacturer's statement: medical device cannot be connected to another medical device.

**Assessment score concerning proof of conformity (combination)**

Insufficient:	<b>1 or 1+4</b>
Moderate:	<b>(1)+2 or (1)+2+4</b>
Good:	<b>(1)+2+3 or (1)+2+3+4</b>
NA:	<b>4</b>

Remark: make a note if the manufacturer's statement is present despite indication of actual combination in the technical documentation, i.e. if assessment score is based on '1+4', '(1)+2+4', or '(1)+2+3+4'.

## **9. MEDICAL DEVICES INCORPORATING A SUBSTANCE HAVING AN ANCILLARY ACTION (MEDICINAL SUBSTANCE / HUMAN BLOOD DERIVATIVE)**

**Availability options:**

Not applicable: manufacturer states that the medical device does not incorporate a substance with ancillary action (and items 1 – 7 below are absent).

Absent: the technical documentation does not contain information concerning incorporation of a substance with ancillary action.

Present: a document containing information with regard to the incorporation of a substance with ancillary action is present.

**Contents:**

1. intended purpose within the context of the medical device,
2. source and / or product licence (if applicable),
3. method by which the substance is incorporated into the device,
4. tests performed on the substance (toxicological, pharmacological, stability, etc.),
5. procedure for pharmacovigilance,
6. notification duty of reporting serious adverse drug reaction to competent authority and / or the European Medicines Agency,
7. assessment of the substance by national authority or European Medicines Agency,
8. manufacturer's statement: medical device does not incorporate a substance with ancillary action.

**Assessment score concerning substance with ancillary action**

Insufficient:	<b>1 or 2 or 3 or 4 or 1+2 or 1+3 or 2+3 or 1+2+3</b>
Moderate:	<b>1+2+3+4 or 1+2+3+4+7</b>
Good:	<b>1+2+3+4+5+6+7</b>
NA:	<b>8</b>

## **10. STERILISATION**

**Availability options:**

Not applicable: manufacturer states that the medical device is a non-sterile product.

Absent: the technical documentation does not contain information with regard to the sterilisation.

Present: a document containing information on sterilisation is present.

**Contents:**

1. (details of any) cleaning process prior to sterilisation (if applicable),
2. method of sterilisation, e.g. steam, ethylene oxide, radiation,
3. parameters of the sterilisation process,
4. a summary of sterilisation validation data, including the appropriateness of the sterilisation method,
5. packaging material used,
6. manufacturer's statement: medical device is a non-sterile product.

**Assessment score concerning sterilisation**

Insufficient:	<b>1 or 2 or 3 or 4 or 5 or (1)+2+3 or (1)+2+4 or (1)+2+5 or (1)+3+4</b>
Moderate:	<b>(1)+2+3+4 or (1)+2+3+5 or (1)+2+4+5</b>
Good:	<b>(1)+2+3+4+5</b>
NA:	<b>6</b>

**11. LABEL**Availability options:

Absent: the technical documentation does not contain a label.

Present: an original label or a copy thereof has been submitted.

Note: if label of other medical device is submitted, mark / tick present box (for instance in case of a stent, manufacturer states that only the coating of the actual medical device differs).

Contents:

1. label in foreign language,
2. label in Dutch,
3. a grant exemption from Dutch language requirement is included,
4. label complies partially with the essential requirements concerning information supplied by the manufacturer, i.e. 13.3.a – 13.3.m in Annex I of the MDD 93/42/EEC (see also ‘spotlight’ options below),
5. label complies fully with the essential requirements 13.3.a – 13.3.m.

**Assessment score concerning label**

Insufficient:	<b>1+4 or 1+5</b>
Moderate:	<b>2+4 or 1+3+4</b>
Good:	<b>2+5 or 1+3+5</b>

‘Spotlight’ options:

1. label bears the wording ‘Exclusively for clinical investigations’ (no / yes), if ‘Caution – Investigational device. Limited by (federal) law to investigational use’ or ‘For investigational use only’ are mentioned only then label wording is not correct,
2. label is without CE mark (no / yes),
3. manufacturer’s / EU-authorised representative’s name, address, and city (country) are printed completely on label (no / yes),
4. warnings / precautions on label are mentioned in risk analysis (no / yes) (see also 4. Results of the risk analysis, ‘spotlight’ options).

**12. INSTRUCTIONS FOR USE**Availability options:

Not applicable: manufacturer states that medical device does not contain separate instructions for use and essential aspects of instructions for use are indicated on label, e.g. by means of symbols.

Absent: the technical documentation does not contain instructions for use.

Present: original instructions for use or a copy thereof has been submitted.

Note: if instructions for use of other medical device is submitted, mark / tick present box (see also 11. Label, availability option ‘Present – Note’).

Contents:

1. instructions for use in foreign language,
2. complete instructions for use in Dutch,
3. a grant exemption from Dutch language requirement is included,
4. instructions for use complies partially with the essential requirements concerning information supplied by the manufacturer, i.e. 13.6.a – 13.6.p in Annex I of the MDD 93/42/EEC (see also ‘spotlight’ options below),
5. instructions for use complies fully with the essential requirements 13.6.a – 13.6.p,
6. manufacturer’s statement: medical device is not supplied with instructions for use.

**Assessment score concerning instructions for use**

Insufficient:	1+4 <b>or</b> 1+5
Moderate:	2+4 <b>or</b> 1+3+4
Good:	(1)+2+5 <b>or</b> 1+3+5
NA:	6

**'Spotlight' options:**

1. instructions for use bears the wording 'Exclusively for clinical investigations' (no / yes), if 'Caution – Investigational device. Limited by (federal) law to investigational use' or 'For investigational use only' are mentioned only then instructions for use wording is not correct,
2. instructions for use is without CE mark (no / yes),
3. manufacturer's / EU-authorised representative's name, address, and city (country) are printed completely in instructions for use (no / yes),
4. warnings / precautions in instructions for use are mentioned in risk analysis (no / yes) (see also 4. Results of the risk analysis, 'spotlight' options).

**13. POST MARKET SURVEILLANCE PROCEDURE****Availability options:**

Not applicable: manufacturer states that a post market surveillance procedure is not required for non-market approved medical devices intended for clinical investigations (and items 2 – 6 below are absent).

Absent: the technical documentation does not contain information with regard to a post market surveillance procedure or non-systematic approach.

Present: manufacturer's statement (see item 1 below), procedure or non-systematic approach with regard to collect and review experiences gained from devices during the clinical investigation or after market release is present.

**Contents:**

1. manufacturer's statement: a post market surveillance procedure is maintained, however the actual procedure is not submitted,
2. a complaint procedure for users,
3. a procedure to collect and review experiences in a non-*proactive* or an ad hoc manner, or a non-systematic approach (i.e., no procedure),
4. a procedure for the *proactive* collection and review of experiences,
5. a description of resources (used in procedure(s)) to collect experiences other than customer-reported complaints (see Appendix IV),
6. a procedure for the lessons to be learnt from experiences: corrective and preventive actions will be taken and results of risk analysis will be updated,
7. manufacturer's statement: a post market surveillance procedure is not required for non-market approved medical devices intended for clinical investigation.

**Assessment score concerning post market surveillance procedure**

Insufficient:	1 <b>or</b> 2 <b>or</b> 3 <b>or</b> (1)+(2)+3+5
Moderate:	4 <b>or</b> (2)+4+5 <b>or</b> (2)+3+5+6
Good:	4+5+6
NA:	7

**14. VIGILANCE PROCEDURE****Availability options:**

Absent: the technical documentation does not contain information with regard to vigilance.

Present: manufacturer's statement (see items 1 or 2 below) or procedure with regard to notify competent authorities of any malfunction or shortcoming of a medical device that might lead or might have led to the death of a patient or user or to a serious deterioration in his state of health.

**Contents:**

1. manufacturer's statement: a vigilance procedure is not required for non-market approved medical devices intended for clinical investigation,

2. manufacturer's statement: a vigilance procedure is maintained, however the actual procedure is not submitted,
3. procedure for serious adverse event reporting,
4. notification duty to competent authority of any malfunction or shortcoming of the medical device is mentioned in a procedure,
5. a procedure for the lessons to be learnt from serious adverse event reporting: corrective and preventive actions, changes in the product design, risk analysis, intended use, labelling and / or instructions for use.

**Assessment score concerning vigilance procedure**

Insufficient: **1 or 2 or 3 or 4**

Moderate: **3+4**

Good: **3+4+5**

**15. CONFORMITY ASSESSMENT PROCEDURE**Availability options:

Absent: the documentation does not contain information related to the conformity assessment procedure, e.g. Annex II or Annex III in combination with Annex V of the MDD 93/42/EEC.

Present: manufacturer's statement concerning the conformity assessment procedure which the manufacturer plans to follow is present.

**Assessment score concerning conformity assessment procedure**

No assessment of the information concerning the conformity assessment procedure is performed.



## Appendix III: Hazards and contributing factors

This appendix provides a non-exhaustive list of possible hazards together with contributing factors that can initiate foreseeable sequences of events that can result in hazardous situations (according to EN ISO 14971:2000 Medical devices – Application of risk management to medical devices).

### **Possible hazards**

#### Energy hazards

##### Electromagnetic energy

- Line voltage
- Leakage current
  - o Enclosure leakage current
  - o Earth leakage current
  - o Patient leakage current
- Electric fields
- Magnetic fields
- Electric shock
- Component drift
- Dielectric strength

##### Radiation energy

- Ionizing radiation
- Non-ionizing radiation
- Visible light
- UV light
- Infrared light
- Microwaves

##### Thermal energy

- High temperature
- Low temperature

##### Mechanical energy

- Gravity
  - o Falling
  - o Suspended masses
- Vibration
  - o Resonance
- Release of stored energy
- Inertia
- Moving parts
  - o Squeezing
  - o Crushing
  - o Shearing
  - o Cutting or severing
  - o Entanglement
  - o Trapping
  - o Stabbing or puncturing
  - o Friction or abrasion
  - o Expelled parts
  - o Instability
  - o Impact
  - o Moving and positioning of patient
- Acoustic energy
  - o Ultrasonic energy
  - o Infrasound energy
  - o Sound
- High pressure fluid injection due to leakage

**Biological and chemical hazards**

- Bio-contamination
  - o By bacteria or
  - o By viruses or
  - o Inability to maintain hygienic safety
- Contact with organic material skin/airway
- Contact with organic material invasive
- Contact with non-organic material (skin/airway/invasive)
- Bio-incompatibility
  - o Toxicity
  - o Allergenicity
  - o Mutagenicity
  - o Oncogenicity
  - o Teratogenicity
  - o Carcinogenicity
  - o Re- and/or cross-infection
  - o Pyrogenicity
  - o Substances that produce adverse physiological effects
- Animal tissue
- Chemical hazards
  - o Contacts to acids or alkalis
  - o Leakage of gases or liquids
  - o Gas, liquid, dirt resistance
  - o Impurity

**Mechanical hazards**

- Faulty dimensioning
- Tolerances
- Strength
- Breakage
- Fatigue
- Ageing
- Tensional cracks
- Loose connections
- Sealing

**Hazards related to environment and property**

- Medical gases
- Anaesthetic agents
- Emission of electromagnetic fields
- Substances that produces adverse physiological effects

**Hazards related to the information**

- Inadequate labelling
- Inadequate operating instructions
  - o Inadequate specifications of accessories to be used with medical device
  - o Inadequate specifications of pre-use checks
  - o Overcomplicated operating instructions
- Inadequate specification of service and maintenance
- Insufficient warnings of side effects
- Inadequate warning of hazards likely with re-use of single use devices
- Incorrect measurements and other metrological aspects

**Contributing factors that can result in hazardous situations****Design**

- Material degradation
- Incompatibility with other devices with which the device is intended to be used

**Manufacturing processes**

- Change in manufacturing process
- Insufficient material compatibility information
- Insufficient control of manufacturing processes
- Insufficient control of subcontractors

**Transport and storage**

- Inadequate packaging

**Environmental effects**

- Corrosion
- Degradation
- Biodegradation
- Electromagnetic fields
- Susceptibility to electromagnetic interference

**Installation, maintenance and service****Cleaning, disinfection and sterilisation****Disposal and scrapping****Normal operation**

- Ageing
- Inadequate supply of power
- Inadequate supply of coolant

**Use errors**

- Use by unskilled/untrained personnel
- Reasonable foreseeable misuse
- Potential for intentional misuse
- Confusing or missing instructions for use
- Insufficient warning of side effects
- Inadequate warnings of hazards associated with re-use of single-use medical devices
- Incorrect measurement and other metrological aspects
- Incompatibility with consumables/accessories/other medical devices
- Incorrect formulation
- Inability to maintain hygienic safety
- Operation outside prescribed environmental conditions
- Human factors
  - o Mistakes and judgment errors
  - o Lapses and cognitive recall errors
  - o Slips and blunders
  - o Violation or abbreviation of instructions, procedures, etc.
  - o Complex or confusing control system
  - o Ambiguous or unclear device state
  - o Ambiguous or unclear presentation of settings, measurements, or other information
  - o Misrepresentation of results
  - o Insufficient visibility, audibility or tactility
  - o Poor mapping of controls to action, or of displayed information to actual state
  - o Controversial modes or mappings as compared to existing equipment
- Failure modes
  - o Erroneous data transfer
  - o Lack of, or inadequate specification for, maintenance including inadequate specification of post-maintenance functional checks
  - o Inadequate maintenance
  - o Lack of adequate determination of the end of life of the medical device
  - o Loss of electrical/mechanical integrity
  - o Deterioration in function as a result of repeated use
  - o Failure to perform to essential performance requirements

**Clinical hazards associated with use of the device**

Acute myocardial infarction  
Angina  
Arrhythmias  
Dissection  
Drug reaction  
Emboli  
Emergent coronary artery bypass surgery  
Haemorrhage  
Hypotension  
Hypertension  
Myocardial ischemia  
Perforation  
Pseudoaneurysm  
Restonosis of stented segment

## Appendix IV: Resources for post market surveillance

Resources of information for post market surveillance are (proactive / reactive):

- expert users groups
- customer surveys
- customer complaints and warranty claims
- post CE market clinical investigations
- literature reviews
- user feedback other than complaints: surveys, customer satisfaction
- device tracking / implant registries
- user reactions during training programs
- competent authorities
- the media, including internet and email
- experience with similar devices made by the same or different manufacturer
- maintenance / service reports
- retrieval studies on explants
- in-house testing
- failure analysis (analysis of complaints)
- fieldworkers
- retailers
- buyers satisfaction forms
- panel sessions
- meeting with users
- feedback from marketing data



## Appendix V: Tables

*Table V.1. Medical devices included in the investigation*

Medical specialty	Medical device description	Class	Id of TD set <sup>a</sup>
<i>Ear, nose &amp; throat</i>			
	Hyoid myotomy & lateral suspension device	IIb	3
	Pharyngeal wall implant <sup>†</sup>	IIb	6
<i>Vascular</i>			
	Peripheral vascular prosthesis	IIb	20
<i>Cardiovascular<sup>‡</sup></i>			
	Aortic heart valve bioprosthesis, delivery system & crimper <sup>§</sup>	III	8,16
	Atrial fibrillation ablation catheters & RF generator unit <sup>¶</sup>	III	14
	Catheter for temporary blood flow occlusion <sup>†</sup>	III	12
	Coronary catheter with measuring function	III	15
	Coronary laser catheter	III	7
	Coronary stent & delivery system	III	13
	Drug-eluting coronary stent & delivery system	III	1,4,5,11,18
	Drug-eluting bioabsorbable coronary stent & delivery system	III	17
	Mitral valve regurgitation implant & delivery system	III	9
<i>Vascular<sup>‡</sup></i>			
	Non-coronary absorbable metal stent	III	2
<i>Wound care</i>			
	Silver-based wound dressing	III	10

<sup>a</sup> Identification number of technical documentation set

<sup>†</sup> Implant used for treatment of obstructive sleep apnoea syndrome

<sup>‡</sup> Medical devices used for percutaneous interventions

<sup>§</sup> Crimper classified as Class I medical device

<sup>¶</sup> Radio frequency generator unit classified as Class IIb medical device

<sup>†</sup> Medical device used for interventional procedures in coronary arteries and saphenous vein grafts

Table V.2. Availability of technical documentation (TD)

TD item	Identification number of TD set															Score per TD item									
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	na	a	f	i-s	i
1. General description of device <sup>‡</sup>	i	i	i	i	i	i	i	i	i	i	i	i	i	i	i	i	i	i	i	-	-	-	-	19	
2. Description of planned variants	i	i	i	i	i	i	i	na	i	i	na	i	i	i	i	i	na	3	-	-	-	-	-	16	
3. Design specifications <sup>‡</sup>	i	i	i	i	i	i	i	i	i	i	i	i	i	i	i	i	-	-	-	-	-	-	-	19	
4. Results of risk analysis <sup>‡</sup>	i	i	i	i	i	i	i	i	f	i	i	i	i	i	f	i	f	-	-	-	-	4	-	15	
5. List of applied standards <sup>‡</sup>	i	i	i	i	i	i	i	i	f	i	i	i	i	i	i	i	i	-	1	-	1	-	-	18	
6. List of adopted solutions <sup>‡</sup>	na	na	i	i	i	na	i	i	a	f	i	i	i	i	i	f	na	4	1	2	-	-	-	12	
7. Control & verification of design <sup>‡</sup>	i	i-s	i	i	i	i	i	i	i	i	i	i	i	i	i	i	i	-	-	-	-	-	-	18	
8. Combination with other device <sup>‡</sup>	i	i	na	i	i	na	i	i	i	na	i	i	i	i	f	i	f	4	-	2	-	-	-	13	
9. Substance with ancillary action	i	na	na	i	i	na	na	na	i	f	na	na	na	na	na	i	na	12	-	1	-	-	-	6	
10. Sterilisation <sup>‡</sup>	i	i	i	i	i	i	i	i	i	f	i	i	i	i	i	i	i	-	1	-	-	-	-	18	
11. Label <sup>‡</sup>	i	i	i	i	i	i	i	i	i	i	i	i	i	i	i	i	i	-	-	-	-	-	-	19	
12. Instructions for use <sup>‡</sup>	i	i	i	i	i	i	i	i	i	f	i	i	i	i	i	i	i	-	-	-	-	-	-	18	
13. Post market surveillance procedure	i-s	i-s	i	i	i	na	i	i	na	i	i	i	i	i	na	f	i	i	4	-	-	-	-	2	12
14. Vigilance procedure <sup>‡</sup>	i-s	i-s	i	i	i	i-s	i	i	i-s	i	i	i	i	i	i-s	f	i	i	-	-	-	-	-	5	13
15. Conformity assessment procedure	i-s	i-s	i-s	i-s	i-s	i-s	i-s	i-s	i-s	i-s	i-s	i-s	i-s	i-s	i-s	i-s	i-s	-	-	-	-	-	-	-	-
Not applicable – statement (na)																				27					
<b>Absent (a)</b>																				1					
Present, final (f)																				14					
Present, initial – statement (i-s)																				27					
Present, initial (i)																				216					
Score per TD set																				Overall					
8 <sup>†</sup>																				182 <sup>†</sup>					
19 <sup>†</sup>																				34 <sup>†</sup>					

<sup>‡</sup> Explicitly required in the MDD; <sup>†</sup> Sum of all explicitly in the MDD required TD items; <sup>\*</sup> Sum of all complementary TD items

Table V.3. Assessment of technical documentation (TD)

<sup>a</sup> Required in the MDD; <sup>b</sup> Not assessed; <sup>c</sup> Sum of all explicitly required TD items; <sup>d</sup> Sum of all complementary TD items

Table V.4. Technical documentation (TD) of medical devices

TD items and contents	Number of TD sets
<b>1. General description of the medical device</b>	
1.1. Name of the medical device	0 <sup>‡</sup>
1.2. Classification of the medical device	13 <sup>‡</sup>
1.3. Physical description	0 <sup>‡</sup>
1.4. Drawing, diagram, and / or photograph	0 <sup>‡</sup>
1.5. Mode of action	0 <sup>‡</sup>
1.6. Intended use	0 <sup>‡</sup>
1.7. Contraindications, warnings, precautions, and / or stop criteria	1 <sup>†</sup>
<b>2. General description of variants planned</b>	
2.2. Physical description including information about size, colour, etc.	1 <sup>‡</sup>
2.3. Model numbers	2 <sup>‡</sup>
2.4. Manufacturer's statement: no variants are planned	6 <sup>¶</sup>
<b>3. Design specifications</b>	
3.1. (Design) drawings	1 <sup>‡</sup>
3.2. Specifications of materials used	2 <sup>‡</sup>
3.3. Product specifications	2 <sup>‡</sup>
3.4. Explanation for understanding drawing	1 <sup>‡</sup>
<b>4. Results of the risk analysis (RA)</b>	
4.2. All known or foreseeable hazards identified	14 <sup>†</sup>
4.3. Risks arising from hazards estimated	3 <sup>†</sup>
4.5. Adequate actions taken to reduce or eliminate risks	5 <sup>†</sup>
4.6. Residual risks justified in relation to anticipated benefits	6 <sup>¶</sup>
<b>5. Standards applied</b>	
Standards applied (general & product-specific)	0 <sup>‡</sup>
<b>6. Solutions adopted if standards are not applied in full</b>	
Solutions adopted	1 <sup>‡</sup>
<b>7. Control and verification of the design</b>	
7.1. Test results	8 <sup>‡</sup>
7.2. Verification techniques of the design	4 <sup>‡</sup>
7.3. Procedures	9 <sup>‡</sup>
7.4. Manufacturer's statement: quality management system is maintained	2 <sup>¶</sup>
<b>8. Proof of conformity when connected to other medical device</b>	
8.1. Reference document mentioned in ER 9.1 or combination addressed in RA	3 <sup>‡</sup>
8.2. Description of actual combination	3 <sup>‡</sup>
8.3. Extensive proof of conformity	8 <sup>‡</sup>
8.4. Manufacturer's statement: medical device cannot be connected	9 <sup>¶</sup>
<b>9. Medical devices incorporating a substance having an ancillary action</b>	
9.1. Intended purpose within the context of the medical device	0 <sup>‡</sup>
9.2. Source and / or product license of the substance	2 <sup>‡</sup>
9.3. Method of incorporation	0 <sup>‡</sup>
9.4. Tests performed on substance	1 <sup>‡</sup>
9.5. Procedure for pharmacovigilance	7 <sup>‡</sup>
9.6. Notification duty for reporting serious adverse reaction to competent authority	7 <sup>‡</sup>
9.7. Assessment of the substance by national authority or European Medicines Agency	6 <sup>‡</sup>
9.8. Manufacturer's statement: no substance used	10 <sup>¶</sup>
<b>10. Sterilisation</b>	
10.1. Cleaning process prior to sterilisation	5 <sup>‡</sup>
10.2. Method of sterilisation	0 <sup>‡</sup>
10.3. Parameters of the sterilisation process	8 <sup>‡</sup>
10.4. Summary of sterilisation validation data	12 <sup>‡</sup>
10.5. Packaging material used	12 <sup>‡</sup>
10.6. Manufacturer's statement: medical device is non-sterile	0 <sup>¶</sup>

<sup>‡</sup> Absent; <sup>†</sup> Present<sup>¶</sup> No; <sup>§</sup> Yes

Table V.4 (continued). Technical documentation (TD) of medical devices

TD items and contents	Number of TD sets
<b>11. Label</b>	
11.1. Label in foreign language	13 <sup>§</sup>
11.2. Label in Dutch	6 <sup>§</sup>
11.3. Grant exemption of national language requirement is present	13 <sup>†</sup>
11.5. Full compliance with essential requirements	13 <sup>†</sup>
Label bears wording 'Exclusively for clinical investigation'	10 <sup>†</sup>
Label is without CE mark	5 <sup>†</sup>
Manufacturer's / EU-auth. representative's name / address / city printed completely	8 <sup>†</sup>
Warnings / precautions on label are mentioned in RA	4 <sup>†</sup>
<b>12. Instructions for use</b>	
12.1. Instructions for use in foreign language	19 <sup>§</sup>
12.2. Instructions for use in Dutch	1 <sup>§</sup>
12.3. Grant exemption of national language requirement is present	18 <sup>†</sup>
12.5. Full compliance with essential requirements	14 <sup>†</sup>
Instructions for use bears wording 'Exclusively for clinical investigation'	10 <sup>†</sup>
Instructions for use is without CE mark	2 <sup>†</sup>
Manufacturer's / EU-auth. representative's name / address / city printed completely	9 <sup>†</sup>
Warnings / precautions in instructions for use are mentioned in RA	5 <sup>†</sup>
12.6. Manufacturer's statement: medical device is not supplied with instructions for use	0 <sup>¶</sup>
<b>13. Post market surveillance (PMS) procedure</b>	
13.1. Manufacturer's statement: PMS is maintained (actual procedure not submitted)	2 <sup>¶</sup>
13.2. Complaint procedure for users	11 <sup>¶</sup>
13.3. Non-proactive approach to collect experiences	6 <sup>¶</sup>
13.4. Procedure for active collection and review of experiences	12 <sup>‡</sup>
13.5. Description of resources to collect experiences	5 <sup>‡</sup>
13.6. Procedure for lessons to be learnt from experiences, updating RA	14 <sup>‡</sup>
13.7. Manufacturer's statement: PMS is not required	4 <sup>¶</sup>
<b>14. Vigilance procedure</b>	
14.1. Manufacturer's statement: vigilance not required	2 <sup>¶</sup>
14.2. Manufacturer's statement: vigilance is maintained (actual procedure not submitted)	3 <sup>¶</sup>
14.3. Procedure for serious adverse event (SAE) reporting	5 <sup>‡</sup>
14.4. Notification duty for reporting SAE to competent authority	5 <sup>‡</sup>
14.5. Procedure for lessons to be learnt from SAE reporting, updating RA	18 <sup>‡</sup>
<b>15. Conformity assessment procedure</b>	
Manufacturer's statement: procedure to be followed	19 <sup>¶</sup>

<sup>‡</sup> Absent; <sup>¶</sup> Present<sup>†</sup> No; <sup>§</sup> Yes

*Table V.5. Hazards and contributing factors not addressed in risk analysis*

Hazards and contributing factors	Number of TD sets
<i>Hazards</i>	
Energy hazards	1
Biological and chemical hazards	1
Mechanical hazards	1
Hazards related to environment and property	1
Hazards related to information	2
<i>Contributing factors</i>	
Design	1
Manufacturing process	5
Transport and storage	3
Environmental factors	3
Installation, maintenance and service	-
Cleaning, disinfection, sterilisation	3
Disposal and scrapping	13
Normal operation	5
Use errors	1
Clinical hazards associated with use	1
Other	-