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B. Roszek | A.C.P. de Bruijn | J.W.G.A. Pot | A.W. van Drongelen

# Assessment of technical documentation of Class III medical devices

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B. Roszek  
A.C.P. de Bruijn  
J.W.G.A. Pot  
A.W. van Drongelen

Contact:  
Arjan van Drongelen  
Centre for Biological Medicines and Medical Technology  
Arjan.van.Drongelen@rivm.nl

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## Abstract

### Assessment of technical documentation of Class III medical devices

European legislation requires that manufacturers of medical devices compile a file containing data demonstrating the safety and performance of the specified device. The quality of the files on medical devices falling into the highest risk class (Class III) needs to be improved. This is the conclusion of an investigation performed by the Dutch National Institute for Public Health and the Environment (RIVM) by order of the Netherlands Health Care Inspectorate.

The investigation was based on technical documentation submitted by manufacturers of medical devices. The medical devices themselves were not examined. In total, 25 dossiers on medical devices from three categories of Class III devices were assessed, namely, coronary stents, hip implants and silver-containing wound dressings.

In more than 90% of the files, major shortcomings were found in one or more items in the documentation. This was particularly evident for the risk analysis and the clinical evaluation of the device. In addition, in many cases the coherence between identified residual risks in the risk analysis and warnings and precautions reported in the manufacturer's instructions for use of the device was insufficient.

A manufacturer ought to provide an adequate description of the device, minimize the risks associated with using the device and substantiate the safety and performance of the device through adequate testing. The manufacturer should also provide detailed user instructions that include explicit information on the risks related to the use of the medical device.

Key words:

Class III, medical devices, technical documentation, instructions for use, coronary stent, hip implant, silver-containing wound dressing



## Rapport in het kort

### Beoordeling van technische documentatie van klasse III medische hulpmiddelen

Europese regelgeving vereist dat fabrikanten van medische hulpmiddelen een dossier opstellen waaruit blijkt dat het hulpmiddel veilig en functioneel is. De kwaliteit van dossiers van de hoogste risicoklasse medische hulpmiddelen, klasse III, laat evenwel te wensen over. Dit blijkt uit onderzoek van het RIVM in opdracht van de Inspectie voor de Gezondheidszorg.

Het onderzoek is uitgevoerd op basis van opgevraagde technische documentatie. De hulpmiddelen zelf zijn niet onderzocht. Voor het onderzoek zijn 25 dossiers van drie groepen medische hulpmiddelen uit klasse III beoordeeld. Het betreft coronaire stents (kleine, gaasachtige buisjes die bloedvaten openhouden), heupimplantaten en wondverbandmiddelen met antimicrobieel zilver.

In meer dan 90 procent van de dossiers zijn in een of meer onderdelen van de documentatie aanzienlijke tekortkomingen gevonden, in het bijzonder de risicoanalyse en de klinische evaluatie van het product. Daarnaast bleek er in veel gevallen onvoldoende samenhang te zijn tussen de risico's die in de risicoanalyse zijn geïdentificeerd en de waarschuwingen in de gebruiksaanwijzing.

Een fabrikant dient een goede beschrijving van het product te geven, de risico's van het gebruik tot een minimum te beperken en de functionaliteit en veiligheid via onderzoeken te onderbouwen. Verder dient de fabrikant een duidelijke gebruiksaanwijzing op te stellen, waarin hij de gebruiker ook waarschuwt voor risico's die aan het gebruik van het hulpmiddel zijn verbonden.

Trefwoorden:

klasse III, medische hulpmiddelen, technische documentatie, gebruiksaanwijzing, coronaire stent, heupimplantaat, zilverhoudend wondverband



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## **List of abbreviations**

BMT	Centre for Biological Medicines and Medical Technology of the RIVM
CE	Conformité Européenne
EEA	European Economic Area
GHTF	Global Harmonization Task Force
IFU	Instructions for use
IGZ	The Netherlands Health Care Inspectorate
MDD	Medical Devices Directive 93/42/EC
RIVM	National Institute for Public Health and the Environment
STED	Summary Technical Documentation



# 1 Introduction

## 1.1 Background information

In 1993, the Council of European Communities issued the Medical Devices Directive (MDD) [1], which has been transposed into national legislation throughout the European Economic Area (EEA). The purpose of the EEA's adoption of the MDD was to allow the medical device industry to benefit from the advantages of a single European market.

Medical devices have to comply with the MDD, and especially with the essential (product) requirements described in Annex I of the MDD. A specified conformity assessment procedure has to be followed to demonstrate compliance of a certain medical device with these requirements. After successful completion of this procedure, the CE (Conformité Européenne) mark can be affixed to the product. Once a medical device has been granted a CE mark in one Member State, it can be freely marketed within the entire EEA.

Medical devices are assessed and categorized according to the levels of risk involved in their application. For low risk medical devices (Class I) the manufacturer can follow the procedure given in Annex VII of the MDD. After completing this procedure, he can affix the CE mark without interference of a third party. The manufacturer shall register himself with their national competent authority. Manufacturers of medium risk (Class IIa/IIb) and high risk medical devices (Class III) have to follow different procedures, all involving a third party. This third party is a so-called notified body, an independent organisation accredited by national competent authorities.

For Class III medical devices, the MDD requires that a 'design dossier' of the medical device concerned has to be assessed by the notified body. However, the requirements for the design dossier are not specified in the MDD. The Global Harmonization Task Force (GHTF) developed the format of the 'summary technical documentation' (STED) [2]. The aim of the STED is to enable manufacturers to supply, if requested, a standardized set of documentary evidence that their medical device conforms to regulatory requirements, which is adequate for the purposes of all regulatory authorities or conformity assessment bodies.

## 1.2 Previous assessments of technical documentation

By the order of the Dutch competent authority, the Health Care Inspectorate (IGZ), the Centre for Biological Medicines and Medical Technology (BMT) of the National Institute for Public Health and the Environment (RIVM) has previously assessed technical documentation of medical devices to verify compliance with the requirements given in the MDD, including:

- specific device categories such as infusion pumps [3, 4], ventilators [5], dialysis systems [6], infrared thermometers and wound care products [7];
- broadly defined device categories such as Class I medical devices [8], 'Annex II' medical devices [9], and non-CE-marked medical devices used in clinical investigations [4, 10].

The specific focus on Class III medical devices for this investigation was chosen as the compulsory examination of the design of the device by a notified body is not applicable to the medical devices and device categories previously investigated.

### 1.3 Scope of the study

The aim of the present study is to investigate the availability and quality of the technical documentation of three device categories of Class III medical devices. A secondary aim of this investigation is to evaluate the suitability of the STED as the basis for file assessment.

The quality of the medical devices, for which files are received, will not be assessed.

## 2 Methods

### 2.1 Selection of devices and manufacturers

Class III medical devices cover a wide range of products. Three categories of Class III medical devices were selected for this investigation. In January 2009, an inventory was made using the internet to identify eligible manufacturers in the field of interventional cardiology, orthopaedics, and wound care, and their marketed devices:

- bare metal cobalt-chromium coronary stents: 29 manufacturers and 34 devices;
- cemented total hip implants: 35 manufacturers and more than 50 devices;
- silver-containing wound dressings: 23 manufacturers and 42 devices.

The total hip implants are devices already marketed for many years as Class IIb devices, but they have recently been reclassified to Class III. Coronary stents are a relatively new type of device. Silver-containing wound dressings are a new variant of products already marketed for many years.

RIVM decided, in consultation with IGZ, which manufacturers and devices were to be included in the study. The selection had to contain both major market players and other manufacturers for each category. For each device category, European medical device companies as well as companies with headquarters outside Europe were selected. For each device category, eight manufacturers were initially selected. If a manufacturer was excluded or did not respond to the request and subsequent reminders, another manufacturer of the same device category was selected, fulfilling the same set of selection criteria as the manufacturer it was to replace.

### 2.2 Requesting technical documentation

For requesting technical documentation, it was decided to use the STED developed by the GHTF (see section 1.1). The STED was adjusted to make it suitable for the purpose of this investigation. A major change was the request of the full risk analysis instead of a summary. Post-market surveillance procedure(s), vigilance procedure(s) and directly-related procedures were also requested. Moreover, applicable EC design-examination or type-examination certificates were requested. For wound dressings, the scientific opinion of the national competent authority or the European Medicines Agency had to be submitted, as silver is considered to be a medicinal substance. The letter for requesting information included an annex specifying the documents to be submitted (Appendix I).

Between March and July 2009, IGZ sent a letter requesting the manufacturers to supply the technical documentation within four weeks. Moreover, the manufacturers had to supply the contact details (including name, e-mail address and telephone number) of the person who was in charge of handling the request within one week after receipt of the letter. A reminder was sent to non-responding manufacturers. If elements of the documentation were missing, RIVM contacted the contact person of the manufacturer.

### 2.3 Exclusion

A manufacturer or medical device was excluded if at least one of the following issues was applicable:

- Manufacturer did not respond to the request and reminders<sup>1</sup>
- Manufacturer refused to submit documentation
- Medical device for which documentation was requested was not a Class III device according to the manufacturer
- Manufacturer could only provide technical documentation in a language unfamiliar to assessors

## 2.4 Assessment of technical documentation

A form was developed for the assessment of the availability and quality technical documentation using Microsoft Access 2002.

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

For each technical documentation item, the different aspects it should contain were listed. Based on these aspects, a set of criteria was drawn up concerning the content 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, '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 the analysis of the data, PASW Statistics 18 (SPSS Inc., Chicago, USA) was used.

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<sup>1</sup> In a later stage, these manufacturers will be contacted by the IGZ.

### 3 Results

#### 3.1 Manufacturers' response

Figure 1 shows a schematic overview of the manufacturers' responses. Besides the 24 manufacturers initially selected and contacted, 12 additional manufacturers (3 coronary stents, 7 hip implants, 2 wound dressings) were selected and requested to submit their documentation, replacing excluded manufacturers.

Seven selected manufacturers were based outside Europe, without information on their authorised representatives from the internet search. Two of these manufacturers were excluded due to not responding to the requests. The responding manufacturers based outside Europe, indicated in their response that they had a European authorised representative.

Finally, 25 documentation sets were available for further assessment.

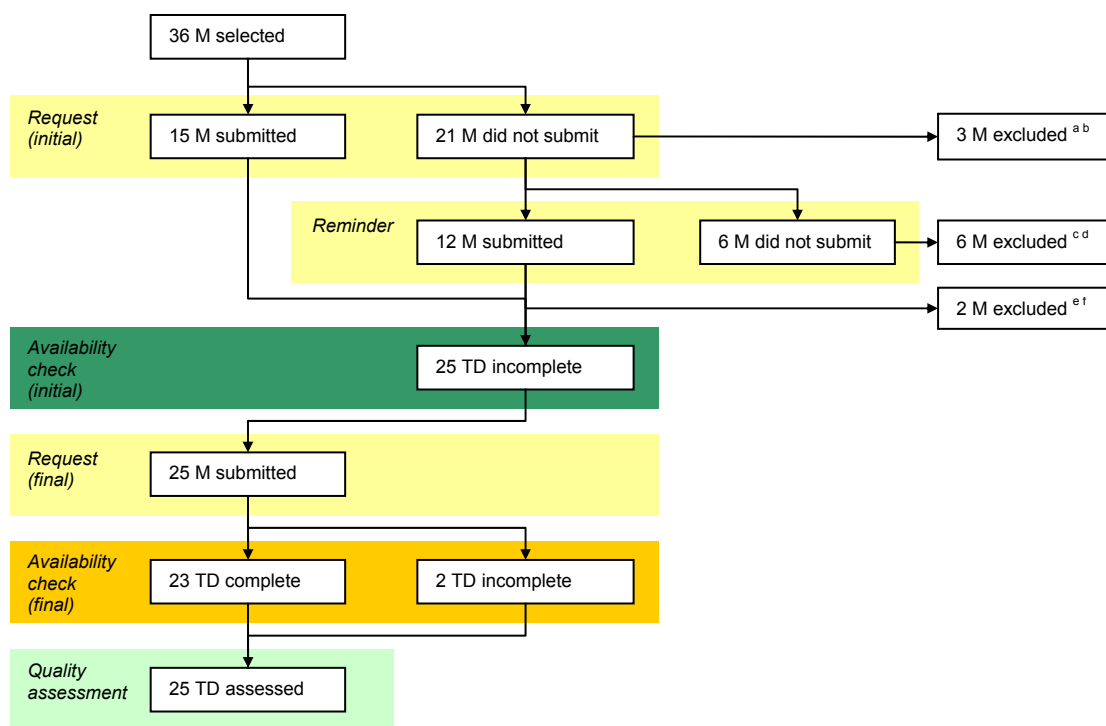


Figure 1. Schematic overview of the manufacturers' response. <sup>a</sup> Manufacturer stated that the technical documentation was not in a language familiar to the assessors (n=2). <sup>b</sup> Manufacturer refused to submit technical documentation (n=1). <sup>c</sup> Manufacturer did not respond (n=4). <sup>d</sup> Total hip implants classified as Class IIb, according to the original classification rule (n=2). <sup>e</sup> Submitted technical documentation in Portuguese (n=1). <sup>f</sup> Wound dressing classified Class IIb by the manufacturer, as it was claimed not to act upon the human body (n=1) (M – manufacturer, TD – technical documentation set).



## 3.2 Presentation of technical documentation

Manufacturers submitted the information on paper (n=6), electronically (n=17) or both (n=2). Manufacturers used either the STED format (n=10) or a different format (n=15). For the 10 files following the STED format, most files seemed to be specially prepared for this investigation. When using a different format, manufacturers often provided a table indicating where the information of each requested item could be found (n=8). Remaining manufacturers (n=7) provided information without any cross-reference.

The extent of the information ranged from approximately 300 pages for a wound dressing and coronary stent up to approximately 9900 pages for a total hip implant. For the latter hip implant, approximately half of the submitted information consisted of copies of literature. In general, the files submitted by manufacturers of wound dressings were less extensive than for the other two types of devices. Nearly all manufacturers submitted technical documentation in English (n=24). From these, a part of the technical documentation (e.g. test reports, procedures) was also provided in a non-English language (French, German, Italian; n=6). One file was completely in German, which was understood by the assessors.

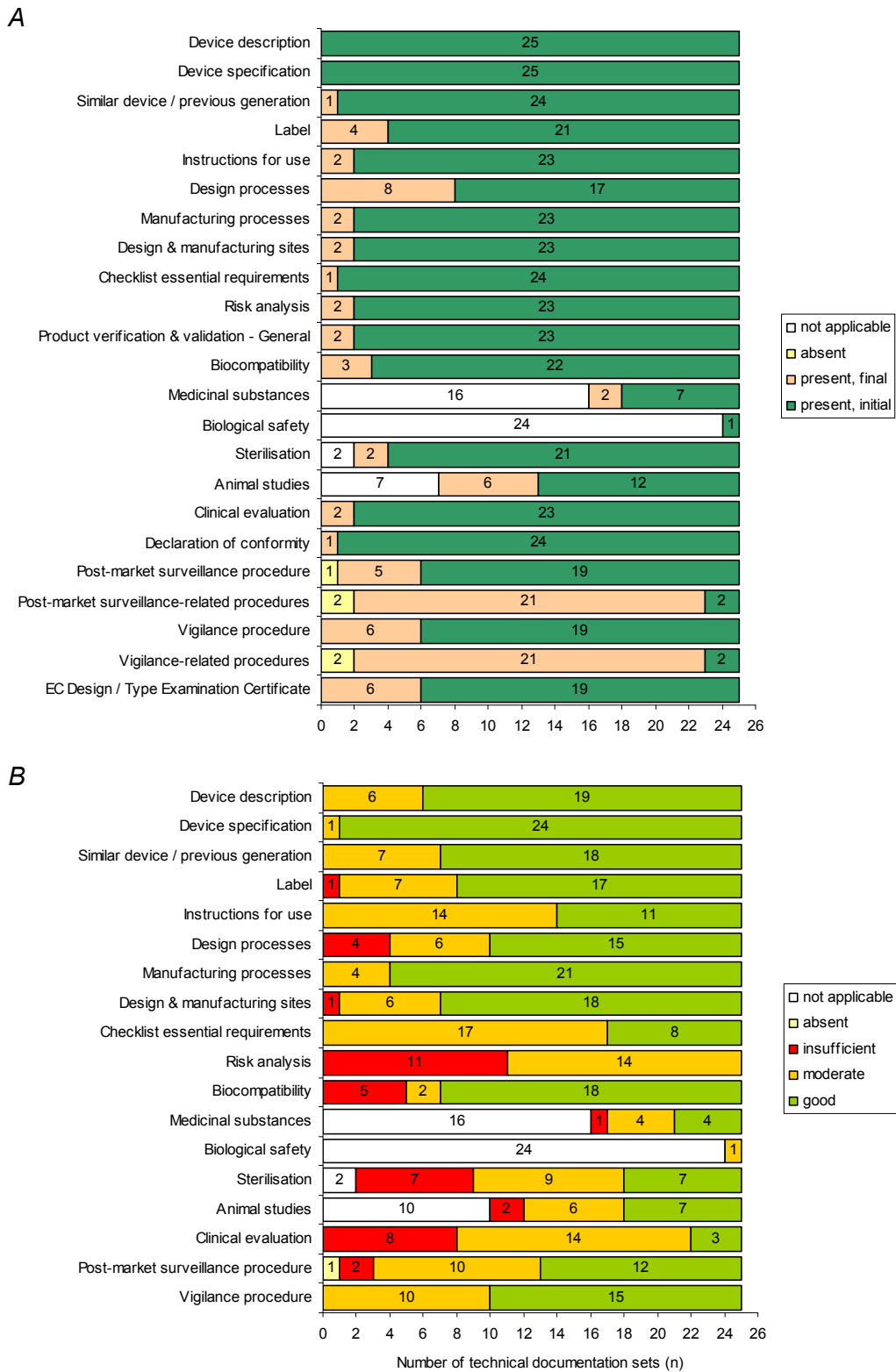
## 3.3 Availability of technical documentation

Following the initial request, 73% of all requested documentation items was provided (Figure 2A). Manufacturers always submitted device description, device specification, and biological safety, related to the presence of materials of human or animal origin (only applicable in one case). For all other items, an additional request was necessary. Post-market surveillance-related procedures and vigilance-related procedures (e.g. procedures for risk management and quality management) were submitted only twice upon the initial request.

## 3.4 Quality of technical documentation

All technical documentation items had minor and/or major shortcomings (Figure 2B). Major shortcomings were found for ten items. A substantial part of the major shortcomings were found in the risk analyses (11/25), followed by clinical evaluation (8/25) and sterilisation (7/25). It is striking that the risk analysis was never without shortcomings. Excluding the coherence between labels/instructions for use and risk analysis from the assessment of the risk analysis, the percentage of files scoring insufficient for the risk analysis decrease from approximately 40% to 20% (5/25).

For clinical evaluation, the items safety and performance analysis, a statement whether proposed medical device literature and instructions for use are consistent with clinical data, and intended therapeutic indications were most frequently absent.



**Figure 2. Availability (A) and quality of technical documentation (B) of Class III medical devices**  
 'Present, initial' means present after initial request and 'present final' means present after the final request.

Figure 3 presents the results of the quality assessment for the separate files. The results for the different files varied considerably. There were two files showing no major shortcomings. Two files received the score ‘insufficient’ for four items, which was the highest number of insufficient scores found. Two other files received the score ‘good’ for twelve items out of the eighteen items and four files received the score ‘good’ for eleven items, whereas one file scored ‘good’ in only four items.

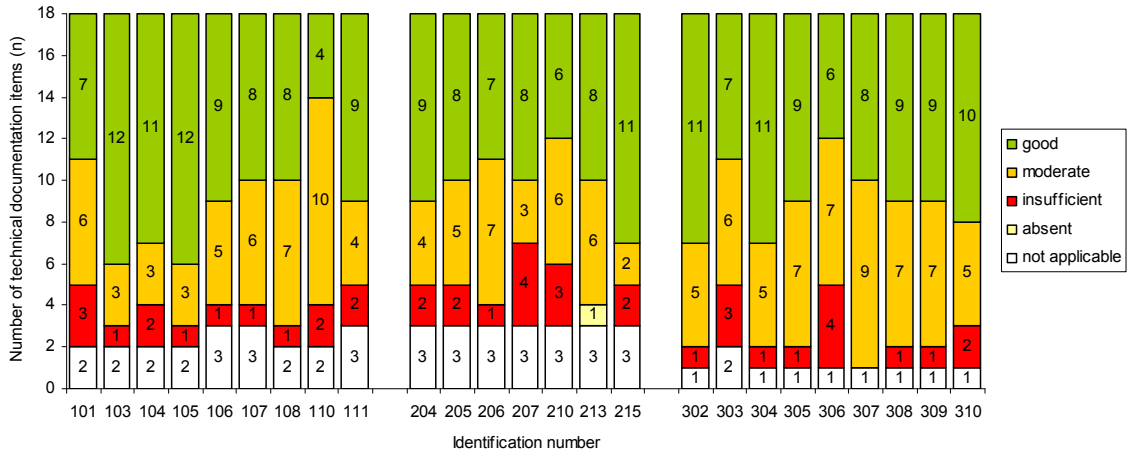


Figure 3. Quality assessment of technical documentation of Class III medical devices (100-series: coronary stents, 200-series: total hip implants, 300-series silver-containing wound dressings).

### 3.5 Coherence

A risk, remaining after risk control measures have been taken, is called a residual risk [11]. Information on residual risks should be present in the instructions for use (IFU) or label of the medical device. Vice versa, the risks related to warnings, precautions, contraindications and side effects mentioned in the IFU or on the label should be addressed in the risk analysis. In approximately half of the files, 80% or more of the residual risks in the risk analysis were mentioned in user information (Figure 4). Eighty percent or more of the warnings, precautions, contraindications and side effects mentioned on the label and in the IFU were addressed in the risk analysis in only three files and one file, respectively.

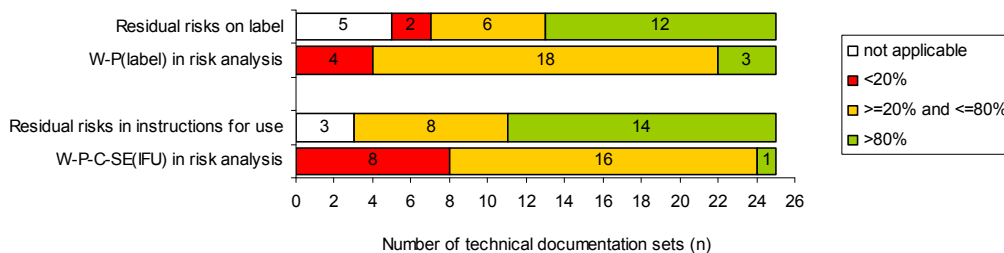
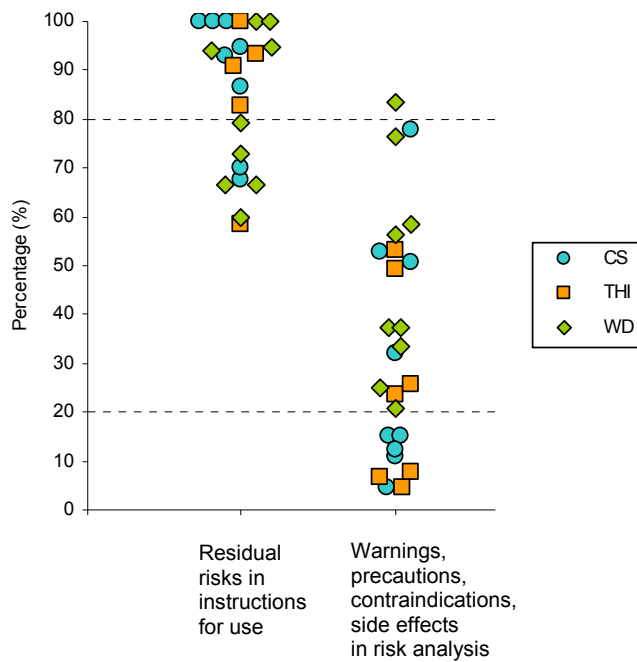


Figure 4. Coherence between risk analysis and user information of Class III medical devices. Upper pair of bars: the number of files for which the residual risks identified in the risk analysis specific for the label are mentioned on the label (upper bar), and vice versa warnings and precautions depicted on the label (W-P(label)) are addressed in the risk analysis (lower bar). Lower pair of bars: residual risks identified in the risk analysis specific for the instructions for use mentioned in the instructions for use (upper bar), and vice versa warnings, precautions, contraindications, and side effects mentioned in the instructions for use (W-P-C-SE(IFU)) and addressed in the risk analysis.

Figure 5 depicts details on the coherence between the risk analysis and the IFU for use for the three device categories. For incorporating remarks in the instructions for use concerning residual risks identified in the risk analysis, approximately half of the files scored  $\geq 90\%$ , whereas all files scored over 55%. No clear distinction can be seen between the different device categories. The check to see if the warning, precautions, contraindications and side effect, mentioned in the IFU are incorporated in the risk analysis showed that for wound dressings, no insufficient scores (i.e.  $<20\%$ ) were obtained, as is the case for the other medical devices. Moreover, the only good score was also for a wound dressing. It is remarkable that more than 2/3 of all files scored less than 50%.



**Figure 5. Coherence between the risk analysis and the instructions for use for coronary stents (CS), total hip implants (THI) and wound dressings (WD). Residual risks identified in the risk analysis to be mentioned in the instructions for use are shown on the left. Warnings, precautions, contraindications, and side effects mentioned in the instructions for use and addressed in the risk analysis are shown on the right.**



## 4 Discussion and conclusions

### 4.1 Discussion

#### 4.1.1 Response

The request to submit files was sent to manufacturers across the world. 19% of the manufacturers (7/36) contacted were based outside Europe. The EC-authorized representatives were unknown at the time of sending the initial letter to the manufacturers based outside Europe. From these manufacturers, two were excluded because they did not respond. One Brazilian manufacturer was excluded from this investigation due to submitting technical documentation in Portuguese.

Although a small number of the contacted companies were based outside Europe, they accounted for 50% of the non-responders in this investigation. This could be due to a wrong address or the unwillingness of these companies to follow up on the request of a foreign competent authority. The fact that non-European manufacturers did not respond to a request from a European competent authority is worrisome, as they might also not respond in other circumstances where action is needed (e.g. for a vigilance case). This underlines the importance of the EC-authorized representative, which can be contacted by the competent authority, as a representative of a manufacturer based outside Europe. All responding manufacturers based outside the EU indicated the existence of an authorized representative in their file.

#### 4.1.2 Presentation of technical documentation

Using the STED, a list of file items including explanations on what to submit was used for requesting documentation. As only a limited number of manufacturers supplied a file, fully compliant with the STED format, it can be concluded that the STED format is not yet widely used. Not following the STED format could be caused by the recent introduction of the STED, leading to unfamiliarity of the manufacturers with the STED, and the fact that it is a voluntary format, not legally required in any country or region. As the STED format was developed to present competent authorities with a limited set of documentation, supplying nearly 10,000 pages contradicts with this intention.

The STED format was modified to suit the purposes of our investigation. The main differences were:

- a checklist essential requirements instead of the Essential Principles of Safety and Performance of Medical Devices;
- the instructions for use associated with the device as marketed in the Netherlands [12];
- the full risk analysis was requested instead of a summary as given in the STED.

The last modification was considered crucial, as only a summary of the risk analysis gives very limited information and the risk analysis is considered a crucial part in the development and continuous cycle of improvement of medical devices [4]. In future revisions of the STED, we recommend the incorporation of a full risk analysis, as this is considered to be a crucial document in showing the activities of the manufacturer to design a safe device. Apart from the STED items, also the post-market surveillance and vigilance procedures were requested, as they provide information on the way the manufacturer has implemented the continuous cycle of product improvement. The requested items of the modified STED did not differ significantly from the items specified in several annexes of the MDD, apart from the product verification and validation. For product verification and validation, six specific file items were requested and one general item was incorporated. It was not always clear to the

manufacturers what information was to be included for the general product verification and validation. This is a point to be considered during a future revision of the STED.

### **4.1.3 Availability of technical documentation**

A considerable part of the information requested was received with the initial submission. So, most of the information was directly available. Also in other RIVM file assessment investigations, most information was received upon the initial request.

Post-market surveillance and vigilance related procedures were not readily submitted, due to companies having policies not to share internal procedures with external parties and therefore being hesitant to submit other procedures than the ones explicitly requested. Moreover, the request for post-market surveillance-related and vigilance-related procedures was worded generally (i.e. 'and any directly related procedures'). Some manufacturers might have considered their field safety corrective action (recall), corrective and preventive action, and risk management procedures to be separate procedures and not directly related to post-market surveillance and vigilance, as are procedures for entering complaints in the complaints database.

### **4.1.4 Quality of technical documentation**

Considering the quality of the documentation submitted, the most remarkable result is that in approximately 40% of the files (11/25), the risk analysis was scored insufficient. This could be caused by the fact that for devices being on the market longer, some risks are no longer addressed in the risk analysis for the current device. Risks, although still applicable, might be considered well known by the professionals involved and are therefore no longer considered during the latest risk management process. Probably, new instructions for use are produced by revising the previous one, incorporating the warnings and precautions, whereas for the risk analysis, a new document is drawn up.

Both the coherence between the labelling and the risk analysis and the absence of generally applicable risks in the risk analysis contributed to the insufficient scores for the risk analysis. In our opinion, there is a need to improve both the coherence between user information and risk analysis, and the deficiencies in the risk analysis such as the identification of known or foreseeable hazards.

Another finding is that the clinical evaluation scored insufficient in approximately one third of the files. This is striking as a clinical evaluation, based on clinical data, has been explicitly required for Class III medical devices since the MDD came into force. As a general rule, confirmation of conformity with the requirements concerning the characteristics and performances under the normal conditions of use of the device and the evaluation of the undesirable side effects must be based on clinical data in particular in the case of implantable devices and devices in Class III.

Design evaluation by the notified body is always required for Class III medical devices. The fact that the risk analysis and the clinical evaluation were often scored insufficient is striking, as one would expect that these items of the technical documentation are crucial in the assessment by the notified body.

Although the previous investigations of files on lower class medical devices were performed in a slightly different manner (see section 1.2), it can be concluded that technical documentation sets in general show similar major shortcomings. Comparison of the numbers of shortcomings is not possible due to the methodological differences. Further investigation into the reasons for the shortcomings could elucidate regulatory requirements which need to be strengthened for Class III medical devices and devices of lower classes as well.

Considering the number of shortcomings observed and the fact that critical items risk analysis and clinical evaluation most frequently showed shortcomings, improvement of the technical documentation of Class III medical devices should be pursued.

#### **4.1.5 Coherence**

One of the problems assessing the coherence between the instructions for use and label and the risk analysis is that in a number of risk analyses, no clear distinction was made between residual risks to be incorporated in the instructions for use or depicted on the label. In several risk analyses, the term labelling was used, which covered both the label and the instructions for use. As a practical approach, the term labelling was interpreted as label and/or instructions for use. However, some warnings, e.g. the storage conditions, need to be visible on the label. Addressing this in the instructions for use, included in the package, has only limited value. A clear distinction in the risk analysis between items to be mentioned on the label or in the instructions for use should be made in the risk analysis.

For devices that have been on the market for a long time (i.e. hip implants), the coherence between the instructions for use and the risk analysis was frequently insufficient. Apparently, previously identified risks are no longer considered risks during the risk management process for new devices, as was already discussed in the previous paragraph.

The coherence between the label and the risk analysis was qualified as 'good' in only 3 out of 25 files. This is probably caused by the fact that many manufacturers apparently do not consider items like lot number or storage conditions to be warnings or precautions (only legal labelling requirements), while some others do. These aspects are not considered risks by the manufacturer, but only as legal requirements.

In our opinion, sound risk management implies that all warnings, precautions, contraindications, and side effects communicated to the user via the instructions for use should originate from an evaluation of possible risks in the risk analysis. Only one manufacturer nearly came up to this principle.

#### **4.1.6 Method**

Except for one item (see section 4.1.2), the STED format provided clear directions on what to submit. If these directions were adhered to, the file was accessible for the assessors. The STED was therefore considered to be an adequate basis for file assessment. To assure consistent assessments, instructions for the assessment were written. Moreover, each file was assessed by two assessors and one assessor assessed all files.

As some very extensive files were submitted, the assessment took considerably more time to complete than assessing summary technical documentation should take.

#### **4.1.7 Extrapolation of results**

Three different groups of Class III medical devices were assessed, differing in time on the market, field of application and features. Although some differences in the results were observed, the general outcome is relatively consistent. We expect that the results for other types of Class III medical devices will not be significantly different from the results of this investigation. However, only 12% of the files (3/25) received were from manufacturers located outside Europe and the United States (US). This could have a positive influence on the results. One could argue that European and US manufacturers are used to extensive regulatory control and assessments by third parties. Assessments of files from manufacturers from other regions might lead to different results.

Although shortcomings in the submitted documentation do not necessarily mean that the quality and safety of the devices is insufficient, it is a cause for concern.



## 4.2 Conclusions

- The quality of the files submitted varied considerably. Only 8% of the files assessed did not show one or more major shortcomings.
- The risk analysis and clinical evaluation were the items most frequently showing major shortcomings.
- Device-related technical documentation was in most cases supplied following the initial request.
- The coherence between the risk analysis and the label and instructions for use was insufficient in 40% of the files.
- The STED format, as modified for this investigation, is a suitable format for file assessment according to the European legislation.
- The STED format is not yet widely used by manufacturers.
- After a comparison with previous assessments of files of lower risk class medical devices, it can be concluded that technical documentation sets in general show similar major shortcomings
- Further investigation into the reasons for the major shortcomings in the technical documentation, both for Class III devices and lower risk class devices is recommended.

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## Appendix I Requested technical documentation

The following annex was attached to the letter requesting the information (see section 2.2).

### Information to be submitted

The European Medical Devices Directive 93/42/EEC (MDD) requires the manufacturer of Class III medical devices to compile a design dossier for examination by the notified body. As the contents of the design dossier are not specified and a review of the complete design dossier is not within the scope of our investigation, the format of the 'summary technical documentation' (STED) was chosen as the basis for the submission. The STED was drawn up by the Global Harmonization Task Force<sup>2</sup>. We adapted this format using the specific wording and requirements of the MDD. You are requested to use the adapted format for the submission of the documentation.

The technical documentation items are given in this annex, including the specification for that item. An asterisk (\*) indicates that requested information differs substantially from the format of the STED. In addition, the submission of your technical documentation has to be supplemented by a declaration of conformity and surveillance procedures for gathering and reviewing device experiences in the post-production phase.

### Device description

The descriptive information for the device should include:

- a. a general description including its intended use/purpose;
- b. the intended patient population and medical condition to be diagnosed and/or treated and other considerations such as patient selection criteria;
- c. principles of operation;
- d. risk class and the applicable classification rule according to Annex IX of the European MDD (classification of medical devices for hip joint replacement should comply with the European Commission Directive 2005/50/EC [13])\*;
- e. an explanation of any novel features;
- f. a description of the accessories, other medical devices and other products that are not medical devices, which are intended to be used in combination with it;
- g. a description or complete list of the various configurations/variants of the device that will be made available;
- h. a general description of the key functional elements, e.g.
  - its parts/components (including software if appropriate),
  - its formulation,
  - its composition,
  - its functionality.

Where appropriate, this will include:

- labelled pictorial representations (e.g. diagrams, photographs, and drawings), clearly indicating key parts/components, including sufficient explanation to understand the drawings and diagrams;
- i. a description of the materials incorporated into key functional elements and those making either direct contact with a human body or indirect contact with the body, e.g. during extracorporeal circulation of body fluids.

### Device specification

The specification is a list of:

- a. features of the medical device;

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<sup>2</sup> See <http://www.ghtf.org/documents/sg1/sg1final-n11.pdf>.

- b. dimensions of the medical device;
- c. performance attributes of the medical device;
- d. variants of the medical device;
- e. accessories of the medical device.

This information would typically appear in the device specification made available to the end user, e.g. in brochures, catalogues and the like.

### **Reference to similar and previous generations of the device**

Where relevant to demonstrating conformity to the essential requirements, and to the provision of general background information, the documentation should contain an overview of:

- a. the manufacturer's previous generation(s) of the device, if such exist; and/or
- b. similar devices available on the local and international markets.

### **Labelling and instructions for use**

The documentation should contain:

- a. the label(s) and instructions for use of the device as described in essential requirement 13, including requirements 7.5, 8.7 and 9.1 of the European MDD\*;
- b. a list of language variants for the countries where the device will be marketed; and
- c. the promotion material for the device.

For the purpose of this investigation, the labels on the device and its packaging and the instructions for use should be the ones associated with the medical device as marketed in the Netherlands. Moreover, the labels on the device and its packaging and the instructions for use should also be supplied in English.

### **Design processes**

The documentation should contain information to allow a reviewer to obtain a general understanding of the design stages applied to the device. It is not intended to take the place of the more detailed information required for a quality management system audit or other conformity assessment activity.

The information may take the form of a flow chart.

### **Manufacturing processes**

The documentation should contain information to allow a reviewer to obtain a general understanding of the manufacturing processes. It is not intended to take the place of the more detailed information required for a quality management system audit or other conformity assessment activity. The information may take the form of a process flow chart showing, for example, an overview of production, assembly, any final product testing, and packaging of the finished medical device.

### **Design and manufacturing sites**

For the activities in section 5 and 6, the documentation should identify the sites where these activities are performed. If quality management system certificates, or the equivalent, exist for these sites, they should be annexed to the documentation.

### **Checklist essential requirements**

The documentation should contain a checklist essential requirements\* that identifies:

- a. the essential requirements;
- b. whether each essential requirement applies to the device and if not, why not;
- c. the method(s) used to demonstrate conformity with each essential requirement that applies;
- d. a reference for the method(s) employed (e.g., standard), and
- e. the precise identity of the controlled document(s) that offers evidence of conformity with each method used.

Methods used to demonstrate conformity may include one or more of the following:

- f. conformity with recognised or other standards;
- g. conformity with a commonly accepted industry test method(s);
- h. conformity with an in-house test method(s);
- i. evaluation of pre-clinical and clinical evidence;
- j. comparison to a similar device already available on the market.

The checklist essential requirements should incorporate a cross-reference to the location of such evidence within the full technical documentation held by the manufacturer.

### **Risk analysis**

This documentation should contain a full report\* (NOT a summary) of the risks identified during the risk analysis process and how these risks have been controlled to an acceptable level. Preferably, this risk analysis should be based on recognised standards, be part of the manufacturer's risk management plan, and be in English.

### **Product verification and validation – General**

The documentation should contain product verification and validation documentation. The level of detail will vary. As a general rule, the documentation should summarise the results of verification and validation studies undertaken to demonstrate conformity of the device with the essential requirements that apply to it. Such information would typically cover:

- o engineering tests;
- o laboratory tests;
- o simulated use testing;
- o any animal tests for demonstrating feasibility or proof of concept of the finished device;
- o any published literature regarding the device or substantially similar devices.

Such summary information may include:

- o declaration/certificate of conformity to a recognised standard(s) and summary of the data if no acceptance criteria are specified in the standard;
- o declaration/certificate of conformity to a published standard(s) that has not been recognised, supported by a rationale for its use, and summary of the data if no acceptance criteria are specified in the standard;
- o declaration/certificate of conformity to a professional guideline(s), industry method(s), or in-house test method(s), supported by a rationale for its use, a description of the method used, and summary of the data in sufficient detail to allow assessment of its adequacy;
- o a review of published literature regarding the device or substantially similar devices.

In addition, where applicable to the device, the documentation should contain detailed information on:

- biocompatibility (see Product verification and validation – Biocompatibility);
- medicinal substance(s) incorporated into the device, including compatibility of the device with the medicinal substance(s) (see Product verification and validation – Medical substances);
- biological safety of devices incorporating animal or human cells, tissues or their derivatives (see Product verification and validation – Biological safety);
- sterilisation (see Product verification and validation – Sterilisation);
- software verification and validation (see Product verification and validation – Software verification and validation);
- animal studies that provide direct evidence of safety and performance of the device, especially when no clinical investigation of the device was conducted (see Product verification and validation – Animal studies);
- clinical evidence (see Product verification and validation – Clinical evaluation).

Detailed information will describe:

- test design;
- complete test or study protocols;
- methods of data analysis, in addition to data summaries and test conclusions.

Where no new testing has been undertaken, the documentation should incorporate a rationale for that decision, e.g. biocompatibility testing on the identical materials was conducted when these were incorporated in a previous, legally marketed version of the device. The rationale may be incorporated into the checklist essential requirements.

### **Product verification and validation – Biocompatibility**

The documentation should contain a list of all materials in direct or indirect contact with the patient or user.

Where biocompatibility testing has been undertaken to characterize the physical, chemical, toxicological and biological response of a material, detailed information should be included on:

- a. the tests conducted;
- b. standards applied;
- c. test protocols;
- d. analysis of data; and
- e. summary of results.

At a minimum, tests should be conducted on samples from the finished, sterilised (when supplied sterile) device.

### **Product verification and validation – Medicinal substances**

Where the medical device incorporates a medicinal substance(s), the documentation should provide detailed information concerning:

- a. the identity and source of the medical substance;
- b. intended reason for its presence; and
- c. safety and performance of the medical substance in the intended application.

For the purpose of this investigation, the following documentation should be submitted\*:

- d. the scientific opinion of the national competent authority or the European Medicines Agency.

The scientific opinion concerns the quality and safety of the medicinal substance including the clinical benefit/risk profile of the incorporation of the substance into the device.

### **Product verification and validation – Biological safety**

The documentation should include:

- a. a list of all materials of animal or human origin used in the device;
- b. detailed information concerning the selection of sources/donors, the harvesting, processing, preservation, testing and handling of tissues, cells and substances of animal or human origin;
- c. process validation results to substantiate that manufacturing procedures are in place to minimize biological risks, in particular, with regard to viruses and other transmissible agents; and
- d. description of the system for record-keeping to allow traceability from sources to the finished device.

### **Product verification and validation – Sterilisation**

Where the device is supplied sterile, the documentation should contain:

- a. detailed information of the initial sterilisation validation including bioburden testing, pyrogen testing, testing for sterilant residues (if applicable); and
- b. packaging validation.

Typically, the detailed validation information should include:

- c. the method used;
- d. sterility assurance level attained;
- e. standards applied;
- f. sterilisation protocol developed in accordance with those standards; and
- g. summary of results.

Evidence of the ongoing revalidation of the process should also be provided. Typically this would consist of arrangements for or evidence of:

- h. revalidation of the packaging; and
- i. revalidation of the sterilisation processes.

### **Product verification and validation – Software verification and validation**

The documentation should contain information on:

- a. the software design;
- b. software development process; and
- c. evidence of the validation of the software, as used in the finished device.

This information should typically include:

- d. the summary results of all verification, validation and testing performed both in-house and in a simulated or actual user environment prior to final release; and
- e. all of the different hardware configurations and, where applicable, operating systems identified in the labelling.

### **Product verification and validation – Animal studies**

Where studies in an animal model have been undertaken to provide evidence of conformity with the essential requirements related to functional safety and performance, detailed information should be contained in the documentation.

The documentation should include:

- a. the study objectives;
- b. description of the methodology and analysis;
- c. results;
- d. conclusions;
- e. document conformity with Good Laboratory Practices; and
- f. a discussion on the rationale (and limitations) of selecting the particular animal model.

### **Product verification and validation – Clinical evaluation**

The documentation should contain the clinical evidence that demonstrates conformity of the device with the essential requirements that apply to it. The clinical evaluation report contains the following elements:

- a. the proprietary name of the medical device and any code names assigned during device development;
- b. identification of the manufacturer of the medical device;
- c. description of the medical device and its intended application;
- d. intended therapeutic and/or diagnostic indications
- e. safety and performance claims made for the medical device;
- f. context of the evaluation;
- g. choice of clinical data types;
- h. summary of the clinical data and appraisal;
- i. performance analysis of the medical device;
- j. safety analysis of the medical device;
- k. consistency of medical device literature and instructions for use with clinical data;
- l. conclusions.



More information on the contents of the clinical evaluation report can be found on the website of the Global Harmonization Task Force (<http://www.ghtf.org/sg5/sg5-final.html>).

## **Additional documentation items**

### **Declaration of conformity**

The documentation should contain a declaration of conformity, as required by the European MDD.

### **Post-market surveillance procedure**

The submitted documentation should contain the post-market surveillance procedure, as laid down in the European MDD, plus any directly related procedures, preferably in English.

The Medical Devices Directive 93/42/EEC (e.g. Annex II, 3.1) requires the manufacturers to institute 'an undertaking by the manufacturer to institute and keep up to date a systematic procedure to review experience gained from devices in the post-production phase and to implement appropriate means to apply any necessary corrective action'. This undertaking is known as post-market surveillance.

### **Vigilance procedure**

The submitted documentation should contain the vigilance procedure, as laid down in the European MDD, plus any directly related procedures, preferably in English.

The Medical Devices Directive 93/42/EEC (e.g. Annex II, 3.1) requires the manufacturer to institute 'an undertaking by the manufacturer to institute and keep up to date a systematic procedure to review experience gained from devices in the post-production phase and to implement appropriate means to apply any necessary corrective action. This undertaking must include an obligation for the manufacturer to notify the competent authorities of the following incidents immediately on learning of them:

- (i) any malfunction or deterioration in the characteristics and/or performance of a device, as well as any inadequacy in the instructions for use which might lead to or might have led to the death of a patient or user or to a serious deterioration in his state of health;
- (ii) any technical or medical reason connected with the characteristics or performance of a device leading for the reasons referred to in subparagraph (i) to systematic recall of devices of the same type by the manufacturer'. Practical guidance on vigilance is given in the European document MEDDEV 2.12-1 rev5 April 2007.

## Appendix II Instructions for quality assessment

### 1. Device description

#### Availability options:

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

Present: (parts of) a device description (e.g. principles of operation (1c)) can be given as a separate document or in other technical documentation items, e.g. risk analysis or instructions for use.

#### Contents:

- a. a general description including its intended use/purpose;
- b. the intended patient population and medical condition to be diagnosed and/or treated and other considerations such as patient selection criteria;
- c. principles of operation;
- d. risk class and the applicable classification rule according to Annex IX of the Council Directive 93/42/EEC on medical devices (classification of medical devices for hip joint replacement should comply with the European Directive 2005/50/EC);
- e. an explanation of any novel features, if applicable;
- f. a description of the accessories, other medical devices and other products that are not medical devices, which are intended to be used in combination with it, if applicable;
- g. a description or complete list of the various configurations/variants of the device that will be made available, if applicable;
- h. a general description of the key functional elements, e.g.
  - o its parts/components (including software if appropriate),
  - o its formulation,
  - o its composition,
  - o its functionality.

Where appropriate, this will include:

- o labelled pictorial representations (e.g. diagrams, photographs, and drawings), clearly indicating key parts/components, including sufficient explanation to understand the drawings and diagrams;
- i. a description of the materials incorporated into key functional elements (=1h) and those making either direct contact with a human body or indirect contact with the body, e.g. during extracorporeal circulation of body fluids.

<b>Assessment score concerning the device description</b>	
Good:	a+b+c+d+[e]+[f]+[g]+h+i
Moderate:	good minus 1-2 item(s)
Insufficient:	good minus $\geq 3$ items

### 2. Device specification

#### Availability options:

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

Present: (parts of) a device specification can be given as a separate document or in other technical documentation items. This information would typically appear in the device specification made available to the end user, e.g. in brochures, catalogues and the like.

#### Contents:

- a. features of the medical device;
- b. dimensions of the medical device;
- c. performance attributes of the medical device;
- d. variants of the medical device, if applicable;

- e. accessories of the medical device, if applicable.

<b>Assessment score concerning the device specification</b>	
Good:	a+b+c+[d]+[e]
Moderate:	good minus 1 item
Insufficient:	good minus $\geq 2$ items

### 3. Reference to similar and previous generations of the device

#### Availability options:

Absent: the technical documentation does not contain a reference to previous generation(s) of the device and/or to similar devices.

Present: the technical documentation contains a reference to previous generation(s) of the device and/or to similar devices. Or a statement is made that there is no previous generation of the device and/or similar device.

#### Contents:

- a. a reference to the manufacturer's previous generation(s) of the device;
- b. similar devices available on the local and international markets;
- c. manufacturer's statement: no previous generation(s) of the device;
- d. manufacturer's statement: no similar device.

<b>Assessment score concerning references to similar and previous generations of the device</b>	
Good:	(a+b) <b>or</b> (b+c)
Moderate:	a <b>or</b> b <b>or</b> c
Insufficient:	d <b>or</b> (c+d)

### 4. Label

#### Availability options:

Absent: the technical documentation does not contain a label.

Present: the label(s), a copy, or a text file ('master text') is present.

#### Contents:

- a. label complies fully with the essential requirements 9.1 and 13.3.a – 13.3.m. Note: complete name, address, and city (country) of manufacturer and, if applicable, EC-authorized representative are printed on label;
- b. a list of languages variants for the countries where the device will be marketed;
- c. label is in Dutch; or label is not in Dutch but information on label does not hamper the understanding for the user (i.e., information other than device name/description/identification, symbols, and for coronary stents compliance chart); or label is not in Dutch and the device is not placed on the Dutch market;
- d. label-related residual risks/hazards identified in risk analysis are mentioned on label (visualized as symbols or text, where appropriate):
  - 1. no/few, i.e. <20%;
  - 2. considerable, i.e. between 20% and 80%;
  - 3. most/all, i.e. >80%;
  - 9. not applicable.

<b>Assessment sub-score1 concerning the label</b>	
Good-1:	a+c
Moderate-1:	c
Insufficient-1:	a <b>or</b> (neither a nor c)

<b>Assessment <i>sub-score2</i> concerning the coherence between label and risk analysis</b>	
Good-2:	d3 or d9
Moderate-2:	d2
Insufficient-2:	d1

<b>Assessment score concerning the label (combination of <i>subscore1</i> and <i>subscore2</i>)</b>	
Good:	good-1+good-2
Moderate:	(good-1+moderate-2) or (moderate-1+good-2) or (moderate-1+moderate-2)
Insufficient:	other combinations of sub-scores

## 5. Instructions for use

### Availability options:

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

Present: the instructions for use, a copy, or a text file ('master text') is present.

### Contents:

- a. instruction for use complies fully with the essential requirements 7.5, 9.1, and 13.6.a – 13.6.o. Note: complete name, address, and city (country) of manufacturer and, if applicable, EC-authorized representative are mentioned in instructions for use;
- b. a list of languages variants for the countries where the device will be marketed;
- c. instructions for use are either in Dutch; or instructions for use are not in Dutch and device is not placed on Dutch market;
- d. instructions for use-related residual risks/hazards identified in risk analysis are mentioned in instructions for use, for examples as warnings, precautions, contraindications, side effects, etc.:
  1. no/few, i.e. <20%;
  2. considerable, i.e. between 20% and 80%;
  3. most/all, i.e. >80%;
  9. not applicable.

<b>Assessment <i>sub-score1</i> concerning the instructions for use</b>	
Good-1:	a+c
Moderate-1:	c
Insufficient-1:	a or (neither a nor c)

<b>Assessment <i>sub-score2</i> concerning the coherence between instructions for use and risk analysis</b>	
Good-2:	d3 or d9
Moderate-2:	d2
Insufficient-2:	d1

<b>Assessment score concerning the instructions for use (combination of <i>subscore1</i> and <i>subscore2</i>)</b>	
Good:	good-1+good-2
Moderate:	(good-1+moderate-2) or (moderate-1+good-2) or (moderate-1+moderate-2)
Insufficient:	other combinations of sub-scores

## 6. Design processes

### Availability options:

Absent: the technical documentation does not contain information on the design processes.

Present: the technical documentation contains information to allow a reviewer to obtain a general understanding of the design stages applied to the device. The information may take the form of a flow

chart or a procedure. It is not intended to take the place of the more detailed information required for a quality management system audit or other conformity assessment activity.

Contents:

A general understanding is obtained if the following stages are mentioned:

- a. key processes (e.g. design requirements, design verification, design validation)/responsible persons;
- b. risk management items (e.g. risk analysis, risk reduction);
- c. decision points/milestones.

**Assessment score concerning the design processes**

Good:	a+b+c
Moderate:	good minus 1 item
Insufficient:	good minus $\geq 2$ items

**7. Manufacturing processes**

Availability options:

Absent: the technical documentation does not contain information on the manufacturing processes.

Present: the technical documentation contains information to allow a reviewer to obtain a general understanding of the manufacturing stages. The information may take the form of a flow chart. It is not intended to take the place of the more detailed information required for a quality management system audit or other conformity assessment activity.

Contents:

A general understanding is obtained if the following stages are mentioned:

- a. production/assembly;
- b. final product testing;
- c. packaging of the finished medical device.

**Assessment score concerning the manufacturing processes**

Good:	a+b+c
Moderate:	good minus 1 item
Insufficient:	good minus $\geq 2$ items

**8. Design and manufacturing sites**

Availability options:

Absent: the technical documentation does not contain information concerning the design and/or manufacturing site(s).

Present: the address(es) of the design and/or manufacturing site(s) are present. If quality management system certificates, or the equivalent, exist for these sites, they should be annexed to the documentation.

Contents:

- a. design site(s);
- b. manufacturing site(s);
- c. quality management system certificate(s);
- d. manufacturer's statement: quality management system is not applicable, no certificate(s) submitted.

**Assessment score concerning the manufacturing and design sites**

Good:	(a+b+c) or (a+b+d)
Moderate:	good minus 1 item
Insufficient:	good minus 2 items

**9. Checklist essential requirements**

Availability options:

Absent: the technical documentation does not contain information to indicate how the essential requirements are fulfilled.

Present: the technical documentation does not contain information to indicate how the essential requirements are fulfilled. Most commonly, a checklist essential requirements is used to show compliance with the essential requirements.

Contents:

- a. the identity of the device;
- b. the identify of the various variants/configurations, if applicable;
- c. checklist dated;
- d. applicability whether each essential requirement applies to the device;
- e. type of method(s) used to demonstrate conformity with each essential requirement that applies, e.g. recognized standard, in-house test method, or other methods;
- f. title and reference of the recognized standard, in-house test method, or other methods;
- g. reference to the actual technical documentation, i.e. certificates, test reports, validation reports, study reports, or other reports.

<b>Assessment score concerning the checklist essential requirements</b>	
Good:	$a+[b]+c+d+e+f+g$
Moderate:	good minus 1-2 items
Insufficient:	good minus $\geq 3$ items

**10. Risk analysis**

Availability options:

Absent: the technical documentation does not contain a report identifying the risk associated with the device concerned.

Present: the technical documentation contains a full report of the risks identified during the risk analysis process and how these risks have been controlled to an acceptable level.

Contents:

- a. risk analysis dated;
- b. risk analysis according to current standard, i.e. EN ISO 14971;
- c. all hazards identified or, appropriately, declared not applicable;
- d. risk estimated;
- e. risk control, i.e. control measures are consistently described in line with essential requirement 2 (MDD 93/42/EEC, Annex I);
- f. (overall) justification/acceptability of residual risks in relation to anticipated benefits;
- g. warnings/precautions on label are mentioned in risk analysis:
  - 1. no/few, i.e. <20%;
  - 2. considerable, i.e. between 20% and 80%;
  - 3. most/all, i.e. >80%;
- h. warnings/precautions/contraindications/side effects in instructions for use are mentioned in risk analysis:
  - 1. no/few, i.e. <20%;
  - 2. considerable, i.e. between 20% and 80%;
  - 3. most/all, i.e. >80%.

<b>Assessment sub-score1 concerning the risk analysis (a-f)</b>	
Good-1:	$a+b+c+d+e+f$
Moderate-1:	good-1 minus 1 item
Insufficient-1:	good-1 minus $\geq 2$ items

<b>Assessment <i>sub-score</i>2 concerning the coherence between user information and risk analysis (g-h)</b>	
Good-2:	g3+h3
Moderate-2:	(g2+h3) <b>or</b> (g3+h2) <b>or</b> (g2+h2)
Insufficient-2:	other combinations of items than used for good-2 or moderate-2 score

<b>Assessment score concerning the risk analysis</b>	
Good:	good-1+good-2
Moderate:	(moderate-1+good-2) <b>or</b> (good-1+moderate-2) <b>or</b> (moderate-1+moderate-2)
Insufficient:	other combinations of sub-scores

## 11. Product verification and validation - General

### Availability options:

Absent: the technical documentation does not contain general information about the product verification and validation performed.

Present: the technical documentation contains general information about the product verification and validation performed.

### Contents:

- a. technical tests, e.g. engineering tests, laboratory tests, simulated use testing;
- b. any animal tests for demonstrating feasibility or proof of concept of the finished device;
- c. any published literature regarding the device or substantially similar devices.

<b>Assessment score concerning the product verification and validation – general</b>
No assessment

## 12. Product verification and validation - Biocompatibility

### Availability options:

Absent: the technical documentation does not contain information concerning biocompatibility.

Present: the technical documentation contains information concerning biocompatibility.

### Contents:

- a. tests conducted;
- b. standards applied;
- c. test protocols;
- d. analysis of data;
- e. a summary of results;
- f. a systematic evaluation using Annex B of ISO 10993-1, including assessment and summary/conclusion (i.e. further testing is not deemed necessary because of established implant material).

Note: if a subsequent part of the EN 10993-series is used for biocompatibility studies, this can be considered to be a test protocol.

Note: at a minimum tests should be conducted on samples from the finished, sterilised (when supplied sterile) device.

<b>Assessment score concerning the biocompatibility</b>	
Good:	(a+b+c+d+e) <b>or</b> f
Moderate:	good (i.e. a+b+c+d+e) minus 1 item
Insufficient:	good (i.e. a+b+c+d+e) minus $\geq 2$ items

**13. Product verification and validation – Medicinal substances**

Availability options:

Absent: the technical documentation does not contain information concerning medicinal substances.

Present: the technical documentation contains information concerning medicinal substances.

Contents:

- a. the identity and source of the medical substance;
- b. the intended reason for its presence;
- c. the safety and performance of the medical substance in the intended application;
- d. the scientific opinion of the national competent authority or the European Medicines Agency.

<b>Assessment score concerning the medicinal substances</b>	
Good:	a+b+c+d
Moderate:	good minus 1 item
Insufficient:	good minus $\geq 2$ items

**14. Product verification and validation – Biological safety**

Availability options:

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

Present: a document containing information on biological safety is present.

Contents:

- a. list of materials;
- b. manufacturing flow chart, including certificates;
- c. validation report;
- d. traceability system.

<b>Assessment score concerning the biological safety</b>	
Good:	a+b+c+d
Moderate:	good minus 1 item
Insufficient:	good minus $\geq 2$ items

**15. Product verification and validation – Sterilisation**

Availability options:

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

Present: a document containing information on sterilisation is present.

Contents:

- a. detailed information of the initial sterilisation validation including bioburden testing, pyrogen testing, testing for sterilant residues (if applicable);
- b. packaging validation;
- c. the method used;
- d. sterility assurance level attained;
- e. standards applied;
- f. sterilisation protocol developed in accordance with those standards;
- g. summary of results;
- h. revalidation of the packaging;
- i. revalidation of the sterilisation processes.

Note: bioburden testing is not necessary when overkill process is used.



<b>Assessment score concerning the sterilisation</b>	
Good:	a+b+c+d+e+f+g+i
Moderate:	good minus 1-3 item(s)
Insufficient:	good minus $\geq 4$ items

## **16. Product verification and validation – Animal studies**

### Availability options:

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

Present: a document containing information on animal studies is present.

Not applicable: the manufacturer states that animal studies are not applicable.

### Contents:

- a. the study objectives;
- b. description of the methodology and analysis;
- c. results;
- d. conclusions;
- e. document conformity with Good Laboratory Practices;
- f. a discussion on the rationale for (and limitations of) selecting the particular animal model;
- g. a well-founded statement that animal studies are not applicable, e.g. the effects of the device or materials is well known, animal studies are not possible or do not give relevant information about the product (hip implants).

<b>Assessment score concerning the animal studies</b>	
Good:	a+b+c+d+e+f
Moderate:	good minus 1-2 items
Insufficient:	good minus $\geq 3$ items
Not applicable:	g

## **17. Product verification and validation – Clinical evaluation**

### Availability options:

Absent: the technical documentation does not contain a document or well-founded statement concerning the requested aspect of clinical evaluation.

Present: a statement or document is present. A clinical evaluation report based on equivalency has to demonstrate the safety and performance of the device in relation to previously clinically tested materials and/or devices.

### Contents:

- a. the proprietary name of the medical device and any code names assigned during device development;
- b. identification of the manufacturer of the medical device;
- c. description of the medical device and its intended application;
- d. intended therapeutic and/or diagnostic indications;
- e. safety and performance claims made for the medical device;
- f. context of the evaluation;
- g. choice of clinical data types;
- h. summary of the clinical data and appraisal;
- i. performance analysis of the medical device;
- j. safety analysis of the medical device;
- k. statement whether instructions for use and product literature are consistent with clinical data;
- l. conclusions.

<b>Assessment score concerning the clinical evaluation</b>	
Good:	a+b+c+d+e+f+g+h+i+j+k+l
Moderate:	good minus 1-3 item(s)
Insufficient:	good minus $\geq 4$ items

**18. Declaration of conformity**

<b>Assessment score concerning the declaration of conformity</b>
No assessment

**19. Post-market surveillance procedure**

Availability options:

Absent: the technical documentation does not contain information with regard to a post-market surveillance.

Present: procedure(s) with regard to post-market surveillance.

Contents:

- a. a procedure for *proactive* collection and review of experiences (e.g., customer satisfaction questionnaire/survey);
- b. a procedure for *passive* collection and review of experiences (i.e., customer/user complaints);
- c. a description of sources to collect experiences other than (customer/user) complaints (number of sources  $\geq 2$ );
- d. risk management activities will be taken, e.g. update of the results of risk analysis is mentioned;
- e. corrective and preventive actions will be taken;
- f. MEDDEV 2.12-2 Guidelines on post-market clinical follow-up (May 2004) is mentioned.

<b>Assessment score concerning the post-market surveillance procedure(s)</b>	
Good:	a+b+c+d+e
Moderate:	other combinations of items used than for good or insufficient score
Insufficient:	b <b>or</b> (b+e) <b>or</b> (b+d)

**20. Post-market surveillance-related procedure(s)**

<b>Assessment score concerning post market-surveillance-related procedure(s)</b>
No assessment

**21. Vigilance procedure**

Availability options:

Absent: the technical documentation does not contain procedure(s) with regard to vigilance.

Present: procedure(s) with regard to vigilance and/or procedure for field safety corrective action (formerly recall).

Contents:

- a. procedure for incident reporting;
- b. obligation to notify any malfunction or shortcoming of the medical device to competent authority is mentioned in a procedure;
- c. procedure for field safety corrective action (formerly recall)/field safety notice is mentioned or described, or the concept of field safety corrective action (recall) is described;

- d. risk management activities will be taken, e.g. update of the risk analysis is mentioned;
- e. (internal) corrective actions will be taken;
- f. MEDDEV 2.12-1 rev 5 Guidelines on a medical devices vigilance system (April 2007) is mentioned.

<b>Assessment score concerning the vigilance procedure(s)</b>	
Good:	a+b+c+d+e
Moderate:	good minus 1-2 item(s)
Insufficient:	good minus $\geq 3$ items

## 22. Vigilance-related procedure(s)

<b>Assessment score concerning vigilance-related procedure(s)</b>
No assessment

## 23. EC design / type examination certificate

<b>Assessment score concerning EC design / type examination certificate</b>
No assessment

## Appendix III Tables

**Table A1. Availability of technical documentation items – Coronary stent**

Technical documentation item	Identification number									
	101	103	104	105	106	107	108	110	111	
1. Device description	p-i	p-i	p-i	p-i	p-i	p-i	p-i	p-i	p-i	p-i
2. Device specification	p-i	p-i	p-i	p-i	p-i	p-i	p-i	p-i	p-i	p-i
3. Previous generation of device or similar device	p-i	p-i	p-i	p-i	p-i	p-i	p-f	p-i	p-i	
4. Label	p-i	p-i	p-i	p-f	p-i	p-i	p-i	p-i	p-i	
5. Instructions for use	p-i	p-i	p-i	p-i	p-i	p-i	p-i	p-i	p-f	
6. Design processes	p-f	p-i	p-i	p-i	p-i	p-i	p-f	p-i	p-f	
7. Manufacturing processes	p-i	p-i	p-i	p-i	p-i	p-i	p-f	p-i	p-i	
8. Design and manufacturing sites	p-i	p-i	p-i	p-i	p-i	p-i	p-i	p-i	p-i	
9. Checklist essential requirements	p-i	p-i	p-i	p-i	p-i	p-i	p-f	p-i	p-i	
10. Risk analysis	p-i	p-i	p-i	p-f	p-i	p-i	p-f	p-i	p-i	
11. Product verification and validation – General	p-i	p-i	p-i	p-i	p-i	p-i	p-f	p-i	p-i	
12. Biocompatibility	p-i	p-i	p-i	p-i	p-i	p-i	p-f	p-i	p-i	
13. Medicinal substances	na	na	na	na	na	na	na	na	na	
14. Biological safety	na	na	na	na	na	na	na	na	na	
15. Sterilisation	p-i	p-i	p-i	p-i	p-i	p-i	p-f	p-i	p-i	
16. Animal studies	p-i	p-i	p-i	p-f	p-i	p-f	p-f	p-i	p-i	
17. Clinical evaluation	p-i	p-i	p-i	p-i	p-i	p-i	p-f	p-i	p-i	
18. Declaration of conformity	p-i	p-i	p-i	p-i	p-i	p-i	p-i	p-i	p-i	
19. Post-market surveillance procedure(s)	p-i	p-i	p-f	p-i	p-i	p-i	p-i	p-i	p-i	
20. Post-market surveillance-related procedure(s)	p-f	p-f	p-f	p-f	p-f	p-f	p-i	p-f	p-f	
21. Vigilance procedure	p-i	p-i	p-f	p-i	p-i	p-i	p-i	p-i	p-i	
22. Vigilance-related procedure(s)	p-f	p-f	p-f	p-f	p-f	p-f	p-i	p-f	p-f	
23. EC design / type examination certificate	p-f	p-i	p-i	p-i	p-i	p-i	p-i	p-i	p-i	

na: not applicable; p-i: present – initial; p-f: present – final.

**Table A2. Availability of technical documentation items – Total hip prosthesis**

Technical documentation item	Identification number						
	204	205	206	207	210	213	215
1. Device description	p-i	p-i	p-i	p-i	p-i	p-i	p-i
2. Device specification	p-i	p-i	p-i	p-i	p-i	p-i	p-i
3. Previous generation of device or similar device	p-i	p-i	p-i	p-i	p-i	p-i	p-i
4. Label	p-i	p-i	p-i	p-f	p-i	p-i	p-f
5. Instructions for use	p-i	p-i	p-i	p-f	p-i	p-i	p-i
6. Design processes	p-i	p-i	p-i	p-f	p-i	p-i	p-i
7. Manufacturing processes	p-i	p-i	p-i	p-i	p-i	p-i	p-i
8. Design and manufacturing sites	p-i	p-i	p-i	p-f	p-i	p-f	p-i
9. Checklist essential requirements	p-i	p-i	p-i	p-i	p-i	p-i	p-i
10. Risk analysis	p-i	p-i	p-i	p-i	p-i	p-i	p-i
11. Product verification and validation – General	p-i	p-i	p-i	p-i	p-i	p-i	p-i
12. Biocompatibility	p-f	p-i	p-i	p-f	p-i	p-i	p-i
13. Medicinal substances	na	na	na	na	na	na	na
14. Biological safety	na	na	na	na	na	na	na
15. Sterilisation	p-i	p-i	p-i	p-f	p-i	p-i	p-i
16. Animal studies	na	na	na	na	na	na	na
17. Clinical evaluation	p-i	p-i	p-i	p-f	p-i	p-i	p-i
18. Declaration of conformity	p-i	p-i	p-i	p-i	p-i	p-i	p-i
19. Post-market surveillance procedure(s)	p-f	p-i	p-i	p-f	p-i	a	p-i
20. Post-market surveillance-related procedure(s)	p-f	p-f	p-f	p-f	p-f	a	p-f
21. Vigilance procedure	p-f	p-i	p-i	p-f	p-i	p-f	p-i
22. Vigilance-related procedure(s)	p-f	p-f	p-f	p-f	p-f	a	p-f
23. EC design / type examination certificate	p-i	p-i	p-f	p-i	p-i	p-f	p-i

a: absent; na: not applicable; p-i: present – initial; p-f: present – final.

**Table A3. Availability of technical documentation items – Silver-containing wound dressing**

Technical documentation item	Identification number									
	302	303	304	305	306	307	308	309	310	
1. Device description	p-i	p-i	p-i	p-i	p-i	p-i	p-i	p-i	p-i	p-i
2. Device specification	p-i	p-i	p-i	p-i	p-i	p-i	p-i	p-i	p-i	p-i
3. Previous generation of device or similar device	p-i	p-i	p-i	p-i	p-i	p-i	p-i	p-i	p-i	p-i
4. Label	p-i	p-i	p-i	p-i	p-i	p-i	p-i	p-i	p-i	p-f
5. Instructions for use	p-i	p-i	p-i	p-i	p-i	p-i	p-i	p-i	p-i	p-i
6. Design processes	p-i	p-f	p-i	p-i	p-f	p-f	p-i	p-f	p-i	p-i
7. Manufacturing processes	p-i	p-f	p-i	p-i	p-i	p-i	p-i	p-i	p-i	p-i
8. Design and manufacturing sites	p-i	p-i	p-i	p-i	p-i	p-i	p-i	p-i	p-i	p-i
9. Checklist essential requirements	p-i	p-i	p-i	p-i	p-i	p-i	p-i	p-i	p-i	p-i
10. Risk analysis	p-i	p-i	p-i	p-i	p-i	p-i	p-i	p-i	p-i	p-i
11. Product verification and validation – General	p-i	p-f	p-i	p-i	p-i	p-i	p-i	p-i	p-i	p-i
12. Biocompatibility	p-i	p-i	p-i	p-i	p-i	p-i	p-i	p-i	p-i	p-i
13. Medicinal substances	p-i	p-f	p-i	p-i	p-i	p-f	p-i	p-i	p-i	p-i
14. Biological safety	na	na	na	na	na	na	na	na	p-i	na
15. Sterilisation	p-i	na	p-i	p-i	p-i	p-i	p-i	p-i	na	p-i
16. Animal studies	p-i	p-f	p-i	p-i	p-i	p-f	p-i	p-f	p-i	p-i
17. Clinical evaluation	p-i	p-i	p-i	p-i	p-i	p-i	p-i	p-i	p-i	p-i
18. Declaration of conformity	p-i	p-i	p-i	p-i	p-f	p-i	p-i	p-i	p-i	p-i
19. Post-market surveillance procedure(s)	p-i	p-f	p-i	p-i	p-i	p-f	p-i	p-i	p-i	p-i
20. Post-market surveillance-related procedure(s)	p-f	p-f	p-f	p-i	a	p-f	p-f	p-f	p-f	p-f
21. Vigilance procedure	p-i	p-f	p-i	p-i	p-i	p-f	p-i	p-i	p-i	p-i
22. Vigilance-related procedure(s)	p-f	p-f	p-f	p-f	a	p-f	p-f	p-f	p-f	p-i
23. EC design / type examination certificate	p-f	p-f	p-i	p-i	p-i	p-i	p-i	p-i	p-i	p-f

a: absent; na: not applicable; p-i: present – initial; p-f: present – final.

**Table A4. Quality of technical documentation items – Coronary stent**

Technical documentation item	Identification number									
	101	103	104	105	106	107	108	110	111	
1. Device description	m	m	g	g	m	m	g	m	g	
2. Device specification	g	g	g	g	g	g	g	g	g	
3. Previous generation of device or similar device	m	g	g	g	g	g	g	m	g	
4. Label	g	g	g	g	g	g	g	g	m	
5. Instructions for use	g	g	g	g	g	g	m	g	m	
6. Design processes	g	m	g	m	g	m	i	m	g	
7. Manufacturing processes	g	g	g	g	g	g	g	g	g	
8. Design and manufacturing sites	m	g	g	g	g	g	m	m	g	
9. Checklist essential requirements	m	g	m	m	m	m	m	m	m	
10. Risk analysis	i	i	i	i	m	i	m	i	m	
11. Biocompatibility	i	g	m	g	g	g	g	i	g	
12. Medicinal substances	na	na	na	na	na	na	na	na	na	
13. Biological safety	na	na	na	na	na	na	na	na	na	
14. Sterilisation	g	g	m	g	m	g	m	m	i	
15. Animal studies	i	g	g	g	na	na	m	m	na	
16. Clinical evaluation	m	g	i	m	i	m	g	m	i	
17. Post-market surveillance procedure(s)	m	m	g	g	g	m	g	m	g	
18. Vigilance procedure	g	g	g	g	m	m	m	m	g	

na – not applicable; i – insufficient; m – moderate; g – good.

**Table A5. Quality of technical documentation items – Total hip implant**

Technical documentation item	Identification number						
	204	205	206	207	210	213	215
1. Device description	g	g	g	m	g	g	g
2. Device specification	g	g	g	g	m	g	g
3. Previous generation of device or similar device	g	g	m	m	m	g	g
4. Label	g	m	m	g	g	m	g
5. Instructions for use	m	m	m	g	m	m	g
6. Design processes	i	m	g	g	g	g	g
7. Manufacturing processes	g	m	g	m	g	m	g
8. Design and manufacturing sites	g	g	m	m	g	g	i
9. Checklist essential requirements	m	g	g	g	m	m	m
10. Risk analysis	m	i	m	i	i	m	m
11. Biocompatibility	i	g	g	i	i	g	g
12. Medicinal substances	na	na	na	na	na	na	na
13. Biological safety	na	na	na	na	na	na	na
14. Sterilisation	g	i	i	i	g	m	g
15. Animal studies	na	na	na	na	na	na	na
16. Clinical evaluation	m	m	m	i	i	g	i
17. Post-market surveillance procedure(s)	g	g	m	g	m	a	g
18. Vigilance procedure	g	g	g	g	m	g	g

na – not applicable; a – absent; i – insufficient; m – moderate; g – good.



**Table A6. Quality of technical documentation items – Silver-containing wound dressing**

Technical documentation item	Identification number									
	302	303	304	305	306	307	308	309	310	
1. Device description	g	g	g	g	g	g	g	g	g	g
2. Device specification	g	g	g	g	g	g	g	g	g	g
3. Previous generation of device or similar device	g	g	g	g	g	m	g	m	g	g
4. Label	g	i	g	m	m	g	m	g	g	g
5. Instructions for use	m	m	g	m	m	m	m	m	g	g
6. Design processes	g	g	i	m	i	g	g	g	g	g
7. Manufacturing processes	g	m	g	g	g	m	g	g	g	g
8. Design and manufacturing sites	g	g	g	g	g	g	g	m	g	g
9. Checklist essential requirements	g	m	g	g	m	m	m	g	m	m
10. Risk analysis	m	i	m	m	i	m	m	m	m	m
11. Biocompatibility	g	g	g	m	g	g	g	g	g	g
12. Medicinal substances	g	g	m	g	m	g	i	m	m	m
13. Biological safety	na	na	na	na	na	na	na	m	na	na
14. Sterilisation	i	na	m	i	m	m	m	na	i	i
15. Animal studies	m	m	g	g	m	g	m	g	i	i
16. Clinical evaluation	m	m	m	m	i	m	m	i	m	m
17. Post-market surveillance procedure(s)	m	i	m	m	i	m	g	g	g	g
18. Vigilance procedure	g	m	g	g	m	m	g	m	m	m

na – not applicable; i – insufficient; m – moderate; g – good.

**RIVM**

National Institute  
for Public Health  
and the Environment

P.O. Box 1  
3720 BA Bilthoven  
The Netherlands  
[www.rivm.com](http://www.rivm.com)

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National Institute  
for Public Health  
and the Environment

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B. Roszek | A.C.P. de Bruijn | J.W.G.A. Pot | A.W. van Drongelen

# Assessment of technical documentation of Class III medical devices