

RIVM report 265011003 / 2005

**Assessment of technical documentation of
Annex II medical devices**

B. Roszek¹, A.W. van Drongelen, R.E. Geertsma,
E.A.E. van Tienhoven

This investigation has been performed by order and for the account of the Dutch Health Care Inspectorate, within the framework of project V/265011 “Supporting the Health Care Inspectorate on Medical Technology” (research project number 8.04-05.7a).

¹ Corresponding author:

Dr. B. Roszek, Centre for Biological Medicines and Medical Technology, RIVM/BMT
P.O. Box 1, NL-3720 BA Bilthoven
E-mail: Boris.Roszek@rivm.nl

Abstract

Assessment of technical documentation of Annex II medical devices

An investigation was carried out on the availability and quality of the technical documentation (file) of medical devices. Manufacturers of medical devices are obliged to prepare and maintain documentation complying with the provisions in the Medical Device Directive (MDD). Manufacturers are legally required to affix a CE mark to their medical devices in order to gain access to the European market. Under the MDD several procedures are available for manufacturers enabling them to obtain CE marking. The investigation focused on the procedure described in Annex II of the MDD which includes a full quality system ranging from product design to post market surveillance. For this purpose manufacturers (national and international) were selected who reported (near) incidents involving medical devices to the Dutch Competent Authority. The investigation showed that in the sample the Annex II procedure is currently not functioning adequately. A considerable number of moderate and severe shortcomings was observed in the assessed documentation, while most files were incomplete when initially submitted for assessment. Most shortcomings were found in file items such as risk analysis, clinical evaluation, labelling, instructions for use, and post market surveillance and vigilance procedures (procedures to collect experiences with medical devices and to monitor performance). These items are essential for the continuous quality and safety of medical devices. Improvement of the availability and quality of the technical documentation is therefore necessary. The results of this investigation support the need for adjustments to Annex II of the MDD that have already been proposed during the current review process by the European Commission.

Keywords: Medical Device Directive; medical devices; technical documentation; assessment; conformity assessment procedure

Rapport in het kort

Beoordeling van technische documentatie van Annex II medische hulpmiddelen

Onderzoek werd verricht naar de beschikbaarheid en kwaliteit van de technische documentatie (dossier) van medische hulpmiddelen. Fabrikanten van medische hulpmiddelen zijn verplicht om documentatie beschikbaar te hebben die voldoet aan de bepalingen in de Europese Richtlijn Medische Hulpmiddelen (MDD). Voor toegang tot de Europese markt zijn fabrikanten wettelijk verplicht hun medische hulpmiddelen te voorzien van een CE markering. In de MDD staan verschillende procedures voor het verkrijgen van deze markering. Het onderzoek richtte zich op de procedure zoals beschreven in Annex II van de MDD, waarbinnen een volledig kwaliteitssysteem van productontwerp tot post marketing surveillance een sleutelpositie inneemt. Voor dit doel werden fabrikanten (nationaal en internationaal) geselecteerd die (bijna) incidenten hebben gemeld aan de Inspectie voor de Volksgezondheid. Het onderzoek toonde aan dat in de steekproef de Annex II procedure momenteel niet adequaat functioneert. Het merendeel van de dossiers was in eerste instantie incompleet en een aanzienlijk aantal ernstige en matige tekortkomingen is geconstateerd in de beoordeelde documentatie. De meeste tekortkomingen hadden betrekking op dossieronderdelen zoals risicoanalyse, klinische evaluatie, etikettering, gebruiksaanwijzing, en procedures voor post marketing surveillance en vigilante (procedures voor het verzamelen van ervaringen met medische hulpmiddelen en het monitoren van de werking). Deze onderdelen zijn van wezenlijk belang voor een continue kwaliteit en veiligheid van medische hulpmiddelen. Verbetering van de beschikbaarheid en kwaliteit van de technische documentatie is daarom noodzakelijk. De resultaten van dit onderzoek verschaffen aanvullende onderbouwing voor aanpassingen in Annex II van de MDD, zoals die reeds zijn voorgesteld tijdens het momenteel uitgevoerde herzieningsproces door de Europese Commissie.

Trefwoorden: Europese Richtlijn Medische Hulpmiddelen; medische hulpmiddelen; technische documentatie; beoordeling; conformiteitsbeoordelingsprocedure

Contents

1. INTRODUCTION	5
1.1 GENERAL	5
1.2 OBJECTIVES	5
2. METHODS	6
2.1 SELECTION OF MANUFACTURERS	6
2.2 REQUEST OF TECHNICAL DOCUMENTATION	6
2.3 ASSESSMENT OF TECHNICAL DOCUMENTATION	7
3. RESULTS	8
3.1 RESPONSE OF MANUFACTURERS	8
3.2 ASSESSMENT OF TECHNICAL DOCUMENTATION	9
3.2.1 <i>General description of the device</i>	10
3.2.2 <i>Variants</i>	10
3.2.3 <i>Design specifications</i>	10
3.2.4 <i>Results of the risk analysis</i>	11
3.2.5 <i>Standards applied</i>	11
3.2.6 <i>Design control and verification</i>	12
3.2.7 <i>Combination with other medical devices</i>	12
3.2.8 <i>Clinical data</i>	12
3.2.9 <i>Label</i>	13
3.2.10 <i>Instructions for use</i>	13
3.2.11 <i>Post market surveillance procedure</i>	13
3.2.12 <i>Vigilance procedure</i>	14
3.3 RECIPROCITY BETWEEN RISK ANALYSIS AND INSTRUCTIONS	14
3.4 OVERALL ASSESSMENT OF ALL FILE ITEMS	15
4. DISCUSSION AND CONCLUSIONS	16
4.1 DISCUSSION	16
4.2 CONCLUSIONS	17
REFERENCES	18
APPENDIX I: ASSESSED MEDICAL DEVICES	19
APPENDIX II: ASSESSMENT FORM	20
APPENDIX III: MANUAL FOR THE ASSESSMENT	22
APPENDIX IV: SOURCES OF INFORMATION FOR PMS	26

1. Introduction

1.1 General

In 1993, the Council of European Communities issued the Medical Device Directive (MDD) (1), which has been transposed into national laws 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 type of risks involved. For low risk medical devices (Class I, e.g. wheelchairs) the manufacturer can follow the procedure given in Annex VII of the MDD. After completing this procedure, he can affix the CE mark. Moreover, he shall register himself with the national Competent Authority. Manufacturers of medium risk (Class IIa, e.g. most electro-medical equipment for transient use), high risk (Class IIb, e.g. most long-term invasive and implantable devices) and highest risk medical devices (Class III, e.g. equipment and implants that are in contact with the central nervous system and the heart) can follow different procedures.

In this report we concentrate on the procedure in Annex II of the MDD. The key to this procedure is the presence of a full quality assurance system for the design, manufacture, and final inspection of the medical devices concerned. The quality system must ensure that the medical device complies with the Essential Requirements. Compliance is verified by a Notified Body, which is an independent commercial organisation accredited by national competent authorities. The Notified Body has the authority to issue the CE mark. Annex II only states that the Notified Body shall audit the quality system. However, it is regarded good practice that this audit includes the full evaluation of required technical documentation for several sample devices.

The Dutch Competent Authority, the Health Care Inspectorate (IGZ), supervises the enforcement of laws for health care, and regulations and decrees concerning medical devices. Recently, it has been shown that manufacturers of Class I medical devices (which procedures are referred to in Annex VII of the MDD) have major shortcomings in their technical file documentation (2, 3). The aim of the present study is to investigate the technical documentation as required in the Annex II procedure. The Centre of Biological Medicines and Medical Technology (BMT) of the Dutch National Institute for Public Health and the Environment (RIVM) carried out the assessment of this documentation at the request of IGZ.

1.2 Objectives

The primary objective of this investigation was to assess the quality of the technical documentation of medical devices, for which the conformity assessment procedure described in Annex II of the MDD was used to obtain CE marking. In order to carry out assessments in a consistent manner, the development of a tool for assessing technical documentation specified in Annex II was defined as a secondary goal.

2. Methods

2.1 Selection of manufacturers

According to the MDD, manufacturers are required to report serious (near) incidents involving medical devices to their national Competent Authority. Incidents reported to IGZ were used to obtain information about marketed medical devices, i.e. classification of the medical device and conformity assessment procedures for this study. Inclusion criteria for manufacturers were:

- manufacturers reported incidents involving Class IIa, IIb, or III medical devices in 2003 or 2004;
- manufacturers declared using the conformity assessment procedure described in Annex II of the MDD.

The enrolment of manufacturers started in September 2003 and was completed in October 2004. In total 30 manufacturers were selected.

2.2 Request of technical documentation

In Annex II it is stated that the manufacturer must document all the elements, requirements, and provisions for his quality system in a systematic and orderly manner in the form of procedures and policies. For this investigation, manufacturers received an initial request from IGZ to provide the following file items of their documentation (the related article in Annex II is given between brackets):

1. A general description of the medical device (3.2.c.1);
2. Any variants planned (3.2.c.1);
3. The design specifications (3.2.c.2);
4. The results of the risk analysis (3.2.c.2);
5. The standards which will be applied (3.2.c.2);
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 (3.2.c.2);
7. The techniques used to control and verify the design and the processes and systematic measures which will be used when the products are being designed (3.2.c.3);
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 (3.2.c.4);
9. The clinical data (3.2.c.6);
10. The draft label (3.2.c.7);
11. The instructions for use (3.2.c.7);
12. The post market surveillance (PMS) procedure (3.1.g.i);
13. The vigilance procedure (3.1.g.ii).

In the initial request send to the first 15 manufacturers enrolled in this study, they were requested to provide items 12 and 13 mentioning “the vigilance procedure as laid down in section 3.1.g.i and 3.1.g.ii” but not explicitly the term “post market surveillance procedure”. A substantial part of these manufacturers misinterpreted the phrasing and sent incomplete documentation. Consequently, manufacturers received a rectified phrasing as stated above.

If the manufacturer did not respond to the initial request, a reminder was sent. Upon receipt, the submitted documentation was first checked for availability of the requested file items. If any file item was absent, manufacturers received one final request to send the missing documentation. Manufacturers were withdrawn from this investigation if:

- the selected manufacturer was actually a distributor;

- manufacturers did not respond after sending a reminder;
- manufacturers did not send all applicable file items;
- manufacturers did not respond before November 6, 2004.

All documentation was regarded as strictly confidential.

2.3 Assessment of technical documentation

A dedicated form was developed for the assessments (see Appendix II). The form consisted of a general and an assessment part. The general part included a summary of the assessment. The second part contained a checklist for the requested file items and two additional questions concerning the reciprocity of residual risks in the risk analysis and warnings/precautions in the instructions for use. It was decided to use a three-level rating scale: insufficient, moderate and good. For each file item, there was a line for additional remarks on the form. Two assessors evaluated the documentation of each medical device. Individual assessors may subject the information in the files to different interpretations, yielding different scores. In order to facilitate objective and consistent assessment of the files as far as possible, a set of criteria for each file item was developed. The elements considered essential for a particular file item were listed. All these elements needed to be present in a file item for a good score. Combinations of elements leading to a moderate or to an insufficient score were also decided upon. This guidance on the scoring of each file item was entered into a manual (see Appendix III). The manual was updated according to new insights obtained during the investigation. In such cases previously assessed files were reassessed using the adjusted criteria.

To gain some insight in the applicable hazards and risks related to the included medical devices a search was performed on similar devices in the Manufacturer User Facility and Distributor Experience (MAUDE) database of the USA Food and Drug Administration (FDA), which contains reports of adverse events involving medical devices.

3. Results

3.1 Response of manufacturers

Thirty manufacturers received the initial request to send technical documentation to the RIVM (Figure 1). Twenty-three manufacturers sent in documentation, six responded late or not at all and one responder appeared to be a distributor. Of those twenty-three manufacturers, nineteen were requested to send absent file items. The final availability check revealed that twenty-one manufacturers sent all file items. The included medical devices were classified as Class IIa (n=11), IIb (n=9), and III (n=1) medical devices (see Appendix I). Nine Notified Bodies were involved.

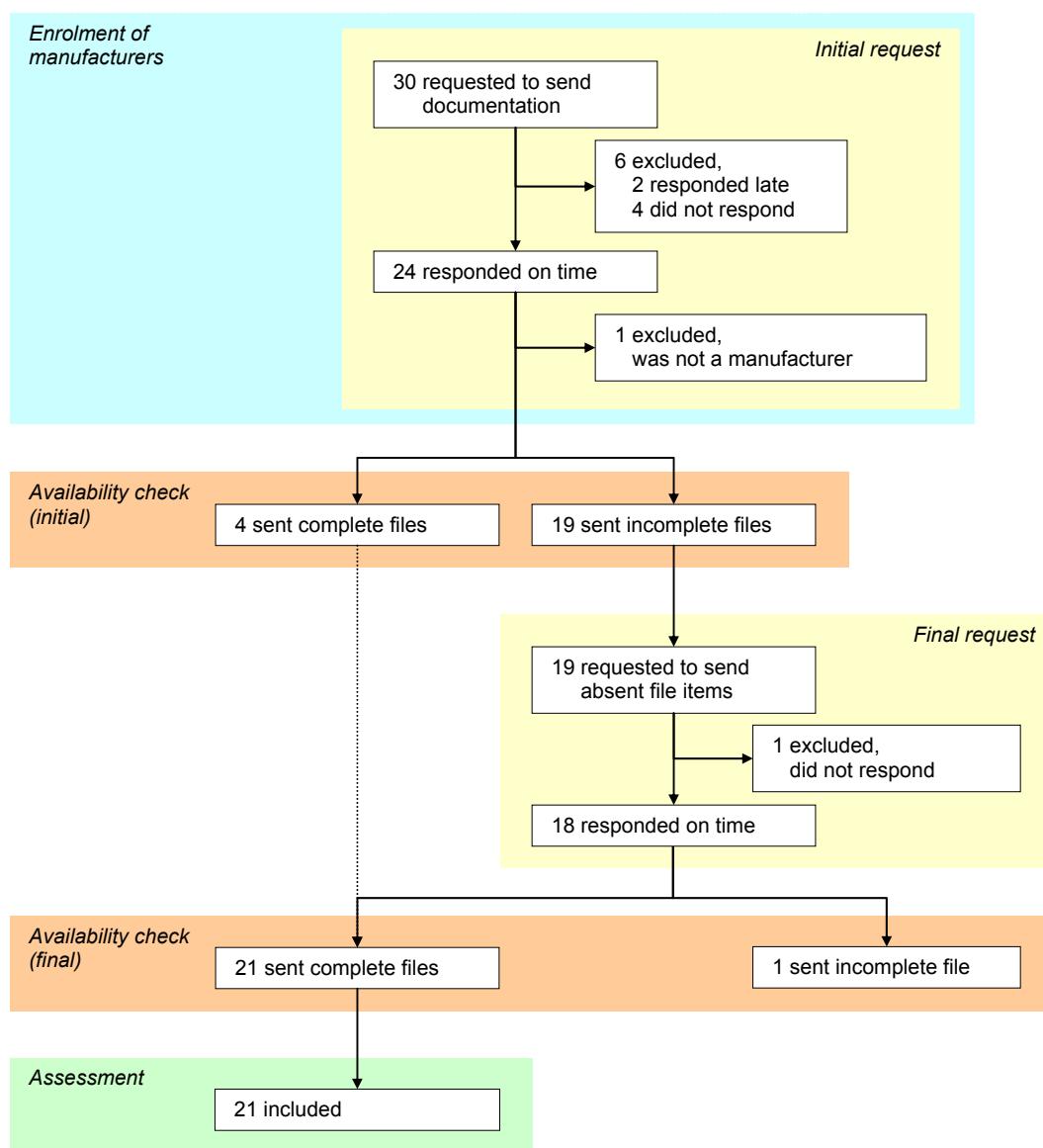


Figure 1. Flow diagram of manufacturers' responses in various stages of the investigation.

The majority of file items were either in Dutch, English, French, or German. One file item was in Danish (i.e., PMS procedure) and a second one in Latvian (i.e., master product formula including a schematic drawing).

Only the general description of the medical device was present for all medical devices after the initial request (Figure 2). Clinical data and the PMS procedure were often absent, as well as the solutions adopted to comply with the Essential Requirements when harmonised standards were not applied and conformity proof in case the device is intended to be used in combination with other devices. It should be noted that for the first fifteen files, the request for PMS and vigilance procedures was phrased in such a way, that manufacturers could misinterpret it to mean only vigilance procedures. Overall, 3% of all file items was not applicable, 17% was absent, and 80% was present initially.

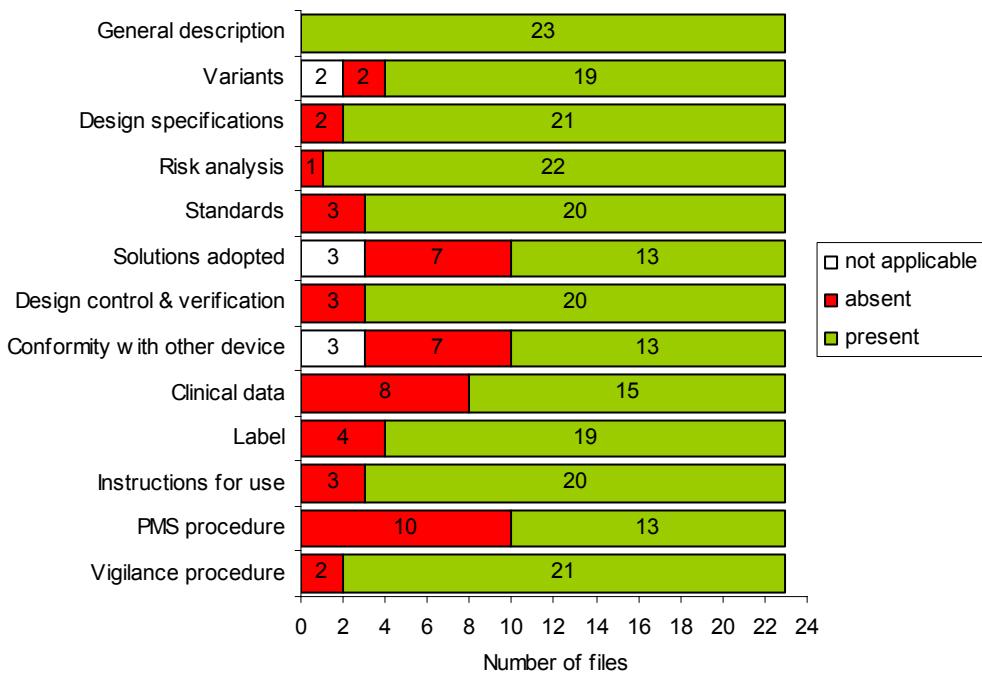


Figure 2. Availability of technical documentation of Annex II medical devices after the initial request. Total number of files received was 23.

3.2 Assessment of technical documentation

All file items were assessed by using the three-level rating system as described in the manual (see Appendix III) for all file items, except for the variants planned and the solutions adopted to comply with the Essential Requirements when harmonised standards were not applied. The documentation provided for this latter file item usually consisted of a checklist of the Essential Requirements containing a limited amount of information and references to further internal procedures and documentation. This was not an adequate basis to perform an assessment.

Shortcomings were observed for all file items (Figure 3). Minor shortcomings were only found for the general description of the medical device and standards applied, whereas major shortcomings were found for all other file items, i.e. variants, design specifications, risk analysis, design control & verification, conformity proof in case the device is intended to be used in combination with other devices, clinical data, labelling, instructions for use, PMS and vigilance procedures. In the following paragraphs, the results for the specific file items are discussed.

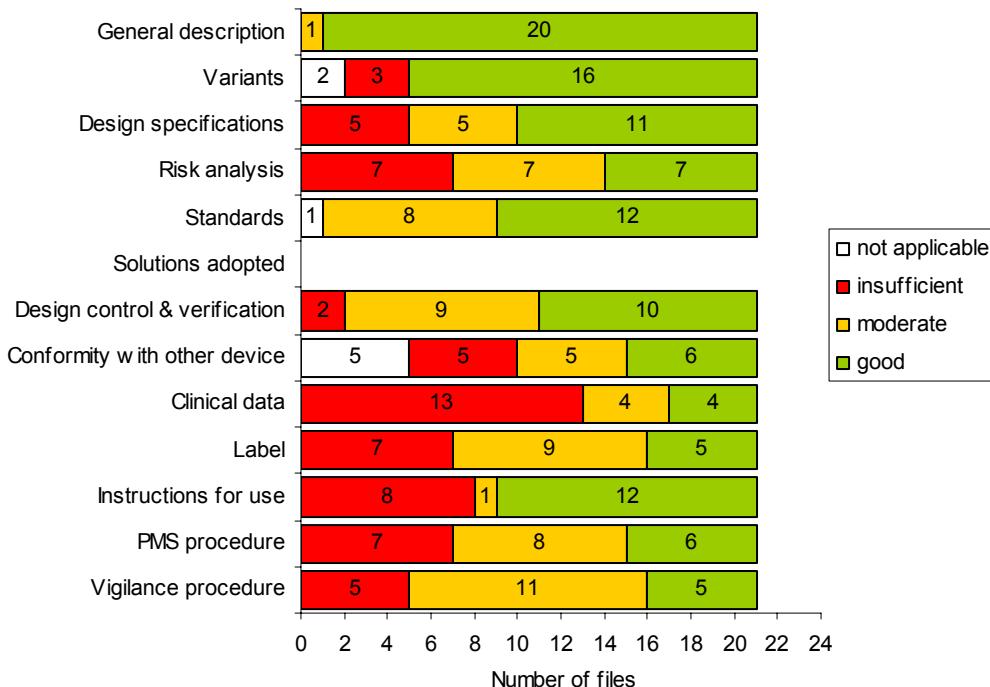


Figure 3. Assessment of technical documentation of Annex II medical devices. Solutions adopted when standards are not applied were not assessed. Total number of assessed files was 21.

3.2.1 General description of the device

A good general description consists of a (brief) physical description of the medical device, a short description of the mode of action, a short description of the intended use and a short description of the contra-indications, warnings, and precautions.

A physical description of medical devices was always present, as well as the description of the mode of action and the intended use. Contra-indications, warnings and precautions were usually found as part of the instructions for use, and not within the general description itself. This was considered adequate.

3.2.2 Variants

A good description of variants contains details including e.g. size, colour, length, weight, etc. The rationale for the variants should be mentioned if the reason is not immediately obvious.

In general, description of variants was adequately addressed in the files. The majority of planned variants included a description of physical dimensions or other characteristics (16/21). The rationale for variants was often obvious or was mentioned in the file. In three files presence of variants was mentioned without giving any description of characteristics.

3.2.3 Design specifications

A good design specification contains a (technical) drawing, a specification of the utilised materials or components and a specification of the mode of action.

Overall, the design specifications scored “good” in 11/21 files. In 10 cases the documentation was considered insufficient (5/21) or moderate (5/21) due to absence of drawings (7/21), no

specifications of materials (4/21) or mode of action (4/21). Although it is likely that manufacturers often have more information concerning design specifications than they actually provided, this is a reason for concern, because adequate information needs to be readily available, e.g. in case of incidents.

3.2.4 Results of the risk analysis

In a good risk analysis the identified hazards and estimated risks are listed thoroughly and the control measures taken are consistent (elimination of risks, adequate protection measures, informing the user of residual risks).

The risk analysis ranged from a document identifying a limited number of hazards and/or associated risks without adequate measures to a document giving an exhaustive list of hazards and associated risks followed by adequate measures and a history of changes made to the document on the basis of PMS activities. Sometimes, the risk analysis only focussed on failures of the device and did not concern the risks associated with the use of a device. In most cases, the assessors were no product specialists for the particular devices. However, using their basic knowledge of the devices, combined with knowledge and expertise on risk assessment techniques, judgements could be made. To gain additional insight in known or foreseeable risks for the particular devices, which should be addressed in the risk analysis, reported adverse events in the FDA MAUDE database were reviewed.

In only 10/21 of the files, the risk analysis appeared to cover most of the applicable risks. Adequate measures to reduce or eliminate risks imply inherently safe design, taking adequate protection measures including alarms, and informing users of the residual risks in instructions for use. Such measures were presented in approximately half of the files (11/21). Other factors which were weighed in the assessment of the risk analysis were the date and the reciprocity between risk analysis and instructions for use. Most risk analyses were signed and dated (19/21). More than 40% was dated before December 2000 (8/19), which raises serious questions about the functioning of their PMS system and the implementation of a cycle of continuous improvement, which would mean going back to the risk analysis whenever new information becomes available. Reciprocity from the instructions for use back to the risk analysis was incomplete in more than 70% of the files (see 3.3).

Overall, the risk analysis, which can be considered as the basis for a safe medical device, contained moderate to severe shortcomings in the majority of the medical devices.

3.2.5 Standards applied

The list of applied standards shall correspond to the list drawn up by the assessors.

In most files the manufacturers demonstrated conformity with particular essential requirements by claiming compliance with available published standards using an Essential Requirements checklist (18/21). A separate list with standards applied was supplied twice. One manufacturer declared not applying any standards and compliance with the Essential Requirements of the MDD was demonstrated in an Essential Requirements checklist referring to further internal documentation. Assessors drew up a list of relevant harmonised European standards and compared them with the supplied standards. In just over half of the files the list corresponded roughly with the manufacturer's list.

Four of the checklists were not dated, and four were dated before December 2000. Results suggest that a number of manufacturers do not update this document on a regular basis and do not check if newer versions of standards are available. This can be illustrated by the fact that only a limited number of manufacturers mentioned the important new standard EN/ISO 14971 for Risk Management, which was published in 2000 and superseded EN 1441, of which presumption of conformity ceased on April 1, 2004.

3.2.6 Design control and verification

For a good control and verification of design the techniques used (including any test results) and procedures shall be present.

Procedures related to the control and verification of the design of medical devices were present in most files (17/21). Many procedures included several review stages. Adequate techniques to control and verify the design were present in more than half of the files (12/21). However, several files included less adequate techniques providing little insight and understanding (6/21).

Overall, approximately half of the files scored “good”, whereas only 10% scored “insufficient” and 43% scored “moderate”. Half of the files scored “moderate” or “insufficient” because there were either no adequate procedures or no techniques present in the file. Manufacturers might be hesitant to send the techniques and test results, because of the amount of data involved. Description of techniques was considered adequate for our purposes.

3.2.7 Combination with other medical devices

For a good proof of the conformity when combined with other devices, the combination and extensive proof shall be given.

Conformity proof when the medical device is to be connected to other medical devices could be substantiated by a description of possible practical combinations and proof that the combination complies with the Essential Requirements.

Overall, approximately one quarter of the manufacturers gave adequate proof of the combination with other devices. Several manufacturers did not consider this item applicable, although their product was to be used in combination with other devices, e.g. a catheter introducer or a diagnostic device of which the software was designed in such a way that the resulting data can also be used as input for a therapeutic device. This is clearly a subject which is misinterpreted or underestimated by manufacturers.

3.2.8 Clinical data

Good clinical data shall contain (criteria obtained from MEDDEV guideline on clinical evaluation (4))

- a critical evaluation of literature regarding the device in question with results and conclusion **or**
- a critical evaluation of literature on similar devices with a demonstration of equivalency, results and conclusion **or**
- a clinical investigation with an adequate clinical investigation plan (possibly preceded by a literature study) with the device in question **or**
- for well-established or simple devices documented expert opinions and justification for not performing a clinical evaluation.

A literature compilation (e.g. references, abstracts) was present in approximately half of the files (11/21) of which only five included a critical evaluation of the literature. Clinical investigations were even scarcer (5/21). The clinical data (i.e., literature or investigation) focused on either the medical device in question (6/21) or equivalent devices (1/21), i.e. clinical, technical, and biological equivalency was demonstrated. Less than half of the literature evaluations and clinical investigations were signed and dated (9/21).

The MDD requires that a clinical evaluation should be performed as a general rule, in particular in the case of implantable devices and Class III medical devices. Several manufacturers (10/21) stated that, as their medical devices were not implantable and classified IIa or IIb, the provision was not applicable. Therefore, they did not feel obliged to undertake any clinical evaluation according to existing standards.

Overall, clinical data was insufficient in more than half of the files assessed, which can be explained by the different interpretation of the necessity of a clinical evaluation. This

situation is reason for great concern, and has already been identified as one of the major subjects of the current review of the MDD.

3.2.9 Label

A good label shall be in Dutch or a grant exemption from the Dutch language requirement shall be available. The essential requirements 13.3.a – 13.3.m shall be met.

Labelling was supplied either in Dutch (12/21) or another language (9/21). One grant exemption from the Dutch language requirement was present, allowing the manufacturer to supply the medical device with English labelling in the Netherlands. Many labels did not comply (16/21) with the Essential Requirements: incomplete address of the manufacturer (6/21), no EU representative (2/21), no lot number (2/21), no warnings (3/21), or generic label without name of the medical device (1/21).

Overall, only one quarter of all files scored “good”. The most frequent shortcomings were the language and the contact information, probably due to the limited space on the labels as used. Adequate contact information is an important part of the label, especially if there is a problem with a device. Correction of these shortcomings is relatively simple and should be performed as soon as possible.

3.2.10 Instructions for use

Good instructions for use shall be in Dutch or a grant exemption from the Dutch language requirement shall be available. The essential requirements 13.6.a – 13.6.j and 13.7.a – 13.7.f (if applicable for professional use) shall be met.

More than half of the instructions for use were in Dutch (12/21), and one was partially in Dutch, i.e. the addendum was in English. One grant exemption from the Dutch language requirement was present, allowing the supplied English version of the instructions for use instead of a Dutch translation. Instructions for use showed similar shortcomings as the labels: incomplete address (3/21), not in Dutch (8/21), unclear description for a connecting medical device (1/21). Another factor which was weighed in the assessment was the reciprocity between risk analysis and instructions for use. In almost 50% of the cases the instructions for use were not covering residual risks from the risk analysis in an adequate way (see 3.3).

Overall, approximately half of the instructions for use scored “good”. Considering the fact that the instructions for use are the communication medium between the manufacturer and the user, this was a disappointing score. The fact that almost 40% of the instructions for use were not in Dutch can also be regarded a major problem. For most products, not all users will be sufficiently fluent in English to understand the subtleties in English instructions for use.

3.2.11 Post market surveillance procedure

An adequate PMS procedure shall consist of

- active collection and review of experiences **and**
- the use of ≥ 3 sources of information **and**
- lessons to be learnt from experiences: corrective and preventive actions will be taken, e.g. PMS as the closing element of the cycle of continuous improvement.

The PMS procedure is based on the active role of the manufacturer to collect and review experiences gained from the actual or an equivalent medical device in the post production phase. Active PMS procedures were often absent (8/21). Most manufacturers did have a complaint procedure (19/21), which is considered a passive way of PMS. To collect experiences, the manufacturers can use different resources (see Appendix IV). Most manufacturers used more than three resources and only a few used less than two. Procedures

for corrective and preventive actions were present in 19/21 files, although most often less evident (13/21).

Overall, approximately one quarter of the files scored “good” on PMS procedures and one third of the files scored “insufficient”. An active PMS procedure using several sources will allow that the medical device and its accompanying information will be improved if new information becomes available. It is therefore a cause for concern that many manufacturers do not fulfil this requirement adequately.

3.2.12 Vigilance procedure

An adequate vigilance procedure shall consider

- incidents/complaints and recalls **and**
- notification duty to competent authorities **and**
- a complete cycle of continuous improvement: lessons learnt will lead to e.g. changes in the product, 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 might lead or might have led to the death of a patient or user or to a serious deterioration of his state of health. Manufacturers sent procedures for incidents/complaints (19/21) and recalls (13/21) in which the notification duty to competent authorities was mentioned (21/21). This 100% score is influenced by a selection bias, because only manufacturers who notified the Dutch Competent Authority were selected. In addition, a procedure for corrective and preventive actions in order to learn from incidents/complaints and recalls was often supplied (18/21). Good procedures incorporating actions taken with regard to design changes, risk analysis evaluation, intended use, and modifications of labelling and/or instructions for use were present in only a few files (5/21), which were the files scoring “good”.

Overall, the vigilance procedure showed similar results compared with the PMS procedure caused by the fact that the lessons to be learned from (near) incidents for the quality and safety of the product were not clear from the file. The PMS and vigilance procedures were often relatively short documents. Other documents (e.g. field corrective action procedures, and corrective and preventive action procedures) were often mentioned as related documents. However, manufacturers failed to supply these documents. Because the relationship between these documents and the PMS and vigilance procedures was often not mentioned, the score was negatively affected, although there might be a good structure behind these related documents.

3.3 Reciprocity between risk analysis and instructions

During the assessment of the files, the extent of reciprocity between the instructions for use and the risk analysis was taken into consideration. This score for reciprocity has a direct relation to the score for the assessment of those two separate file items. Table 1 gives the presence of the risks, which were not eliminated by the design of the device (residual risks), as warnings in the instructions for use. The results indicated that in 48% of the files not all residual risks were mentioned in the instructions for use. In all of these cases, the user will not be aware of those residual risks.

Table 1. Presence of residual risks from risk analysis in instructions for use.

Extent of reciprocity	Presence (n)
No or only several residuals risks present in instructions for use	6
Approximately 50% of the residuals risks present in instructions for use	4
All / nearly all residual risks present in instructions for use	11

Table 2 shows that the warnings from the instructions for use were not fully traceable in the risk analysis in 71% of the files. The presence of the warnings from the instructions for use in the risk analysis is an indication of the interaction between the different departments in a company working on different aspects of a product. It is also an indication of the cycle of continuous improvement. If problems occur during use and these are subsequently mentioned only in the instructions for use, without being included in the risk analysis, the PMS and the Risk Management procedures are inadequate. Apparently, there is insufficient communication between the respective responsible persons for risk analysis and instructions for use.

Table 2. Presence of warnings from instructions for use in risk analysis.

Extent of reciprocity	Presence (n)
No or only several warnings present in risk analysis	11
Approximately 50% of the warnings present in risk analysis	4
All / nearly all warnings present in risk analysis	6

3.4 Overall assessment of all file items

If the assessment of all file items is taken together, then half of the medical device file items yielded only the score “good” and the other half was either “insufficient” or “moderate” (Figure 4).

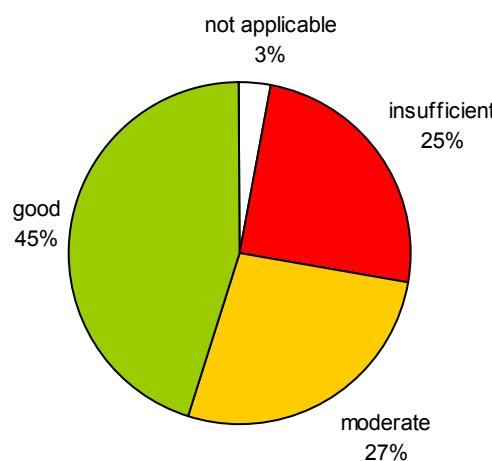


Figure 4. Overall assessment of documentation of Annex II medical devices. File items were assessed using a three-level rating score. Total number of assessed medical devices was 21.

4. Discussion and conclusions

4.1 Discussion

In our study, manufacturers were requested to send technical documentation regarding specific medical devices. After the initial request only 17% of the manufacturers (4/23) provided all requested information. After the final request this increased up to 95% (21/22) and nearly all file items were received. The same phenomenon was observed during our investigation of Class I technical files (2). This can be due to the fact that manufacturers do not have all the requested file items readily available, even if a reasonable time is allowed for handling the request. In general, manufacturers had three weeks to respond. Manufacturers should be prepared to present all relevant technical documentation on their devices within a short time, enabling both themselves and Competent Authorities to undertake appropriate action in cases of incidents or other reasons to doubt the quality and/or safety of the devices. Thus, the availability of the technical documentation needs to be improved.

With regard to method used to select the medical devices of which the technical documentation was assessed during this investigation, it could be argued that the results of this study might be negatively influenced by the fact that files were requested only from manufacturers reporting incidents. On the other hand, however, the manufacturers reporting incidents could very well be the manufacturers who strictly follow the requirements in the MDD. This would lead to a positive influence of the selection method on the quality of the assessed technical documentation. The overall effect of the selection method on the results of this study, if any, is therefore considered acceptable.

One of the objectives of this study was to develop criteria for an objective evaluation of the technical documentation. The choices for certain criteria have been discussed extensively before and during the actual evaluation of the files. Obviously, because of the unique aspects of each device, and the varying ways in which manufacturers build up their files, findings from the files did not always fit the criteria. However, in general, it was felt that the current set of criteria was useful in performing an objective and timely evaluation. It would be valuable to obtain feedback on these criteria from manufacturers, Notified Bodies and Competent Authorities in different Member States.

In most cases, the assessors were no product specialists for the particular devices. Especially for the assessment of the risk analysis this could be considered a limitation. However, using their basic knowledge of the devices, combined with knowledge and expertise on risk assessment techniques and the MAUDE search, judgements could be made.

The number of shortcomings in the assessed technical documentation is considerable. The quality of the files needs to be improved. It was observed that several file items were more frequently insufficient than other file items. These were notably the risk analysis, clinical data, label, instructions for use and PMS and vigilance procedures. These items are closely related to providing and maintaining a safe product. The cycle of continuous product improvement, embedded in the MDD, is therefore not guaranteed. Implementation of quality management and risk management systems according to currently available harmonised European and International Standards could help manufacturers to comply with these requirements. Apparently, the current text of the MDD leaves room for interpretation. The European Commission and the individual Member States have recognised this and are revising the text of the MDD. The conformity route through Annex II is one of the subjects which get particular attention in this process. The results of this investigation could serve as additional argumentation for already proposed changes. One of the solutions to improve the quality of technical documentation for Annex II devices could be a change in the way

manufacturers are audited by Notified Bodies. During the review of the Medical Device Directive (5), it was noted that “The assessment of whether a manufacturer has indeed the organisational capabilities to carry out a design activity for medical devices, cannot take place without the Notified Body examining - on a sampling basis - technical documentation in relation to design, including the technical files relating to the use of clinical data, risk analysis and design evaluation”.

4.2 Conclusions

- Out of thirty selected manufacturers only twenty-one provided all requested applicable technical documentation of Annex II medical devices.
- Technical documentation of Annex II medical devices showed major shortcomings.
- Most shortcomings were observed in the risk analysis, clinical evaluation, instructions for use and labelling, PMS and vigilance procedures. These are key aspects in enabling a continuous cycle of improvement.
- A considerable number of required items of the technical documentation were not readily available.
- The method used for this assessment was found to be adequate to gain insight into the quality of the technical documentation of Annex II devices.
- Improvement of the availability and quality of the technical documentation is necessary.
- The results of this investigation provide further argumentation for changes to Annex II of the MDD that have already been proposed during the current review process.

References

- (1) Medical Device Directive 93/42/EEC, Council Directive of June 14, 1993.
- (2) A.W. van Drongelen, A.C.P. de Bruijn, R.E. Geertsma and C. Wassenaar (2003). A method for the assessment of technical file documentation of Class I medical devices (in Dutch). RIVM report 318902010, Bilthoven. Downloadable from:
<http://www.rivm.nl/bibliotheek/rapporten/318902010.html>
- (3) Report on product documentation and vigilance of Class I medical devices (in Danish). Danish Medicines Agency, Copenhagen. Downloadable from:
http://www.medicinskudstyr.dk/db/filarkiv/4236/Rapport_overvagning_klasse_I_fabrikanter.pdf
- (4) Evaluation of clinical data: a guide for manufacturers and notified bodies, MEDDEV 2.7.1, April 2003. Downloadable from:
http://europa.eu.int/comm/enterprise/medical_devices/meddev/2_7.pdf
- (5) Report on the Functioning of the Medical Devices. Medical Device Expert Group, June 5, 2002. Downloadable from:
http://europa.eu.int/comm/enterprise/medical_devices/policy/final_report.pdf

Appendix I: Assessed medical devices

Class	Medical speciality	Medical device description	Number of devices
IIa	Anaesthesiology	Bacterial breathing filter	1
		Tracheostomy tube and cuff	1
	Cardiovascular	Catheter introducer	3
		PTA catheter [§]	1
	General hospital	Intravascular administration set	1
	Home care	Suction pump	1
	Obstetrics/gynaecology	Oocyte aspiration needle	1
	Ophthalmology	Ophthalmic refractometer	1
		Soft contact lens	1
IIb	Anaesthesiology	Heat and moisture condenser	1
	Cardiovascular	Angiographic injector	1
		Iliac stent	1
	General surgery	Manual stapler	1
	Home care	Infusion pump	1
	Orthopaedics	Bone fixation screw/plate	2
		Shoulder joint prosthesis	1
	Radiology	Angiographic X-ray system	1
III	Cardiovascular	Intra-aortic balloon system	1

[§] PTA: percutaneous transluminal angioplasty

Appendix II: Assessment form

Assessment form of technical files of Annex II medical devices

Identification code: MET/Class ...

Initials assessor(s): ...

Date assessment: ...

Is the product a medical device? yes / no

Class of MD (I, IIa, IIb or III)? Class ...

Classification rule number (Annex IX)? Rule ...

Conformity assessment procedure? Annex ...

Name of manufacturer¹: ...

Address: ...

Telephone: ...

Fax: ...

Name contact person: ...

Product name and type: ...

Short description of the product: ...

¹ Name of manufacturer / EU-representative as defined in MDD.

Summary

--

CHECKLIST

Selected file items of Annex II of the MDD

File items	NA	Availability		Assessment		
		absent	present	insufficient	moderate	good
1. General description of the product (3.2.c.1)		<input type="checkbox"/>				
2. Description of variants planned (3.2.c.1)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		<input type="checkbox"/>
3. Design specifications (3.2.c.2)		<input type="checkbox"/>				
4. Results of the risk analysis (3.2.c.2)		<input type="checkbox"/>				
5. List of applied standards (3.2.c.2)	<input type="checkbox"/>					
6. Solutions adopted (3.2.c.2)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			
7. Control and verify design (3.2.c.3)		<input type="checkbox"/>				
8. Conformity proof (3.2.c.4)	<input type="checkbox"/>					
9. Clinical data (3.2.c.6)		<input type="checkbox"/>				
10. Labelling (3.2.c.7)		<input type="checkbox"/>				
11. Instructions for use (3.2.c.7)		<input type="checkbox"/>				
12. Post market surveillance procedure (3.1.g.i)		<input type="checkbox"/>				
13. Vigilance procedure (3.1.g.ii)		<input type="checkbox"/>				
Reciprocity between risk analysis and instructions for use						
Are residual risks/hazards mentioned in the risk analysis also mentioned as warnings in the instructions for use/labelling?				<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Are warnings in the instructions for use/labelling also mentioned as risks/hazards in the risk analysis?				<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Appendix III: Manual for the assessment

On the assessment form a file item can be indicated as either present, absent or not applicable. If a file item is present, it shall be rated on a three-value scale, i.e. insufficient, moderate and good. This document gives information concerning the rating.

1. General description of the medical device (3.2.c.1)

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

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

Insufficient:

- physical description of the medical device without intended use **or**
- intended use without physical description of the medical device.

Moderate:

- physical description of the medical device **and**
- description of the mode of action of the medical device **and**
- short description of the intended use, e.g. patient population, medical condition of the patient, and/or intended professional use.

Good:

- physical description of the medical device **and**
- description of the mode of action of the medical device **and**
- short description of the intended use **and**
- short description of the contra-indications, warnings, precautions, and/or stop criteria.

2. Description of variants planned (3.2.c.1)

Not applicable: manufacturer declares that no variants are planned.

Absent: manufacturer does not explicitly mention the presence of variants.

Present:

Insufficient:

- variants are mentioned without physical description **or**
- variants are implicitly mentioned in a file item.

Good:

- variants are mentioned including e.g. size, colour, length, weight, etc. The rationale for the product variants should be mentioned if the reason is not obvious.

3. Design specifications (3.2.c.2)

Absent: the file does not contain items concerning design specifications.

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

Insufficient:

- a (design) drawing **or**
- specification of the used materials or components **or**
- specification of the mode of action.

Moderate:

- drawing and specification of the mode of action **or**
- drawing and specification of the used materials or components **or**
- specification of the used materials or components and the mode of action.

Good:

- drawing **and** specification of the used materials or components **and** specification of the mode of action.

NB: for contact lenses, no drawing is required if the optical parameters are clearly defined.

4. Results of the risk analysis (3.2.c.2)

Absent: the file does not contain the results of the risk analysis.

Present: a document containing the results of the risk analysis is present.

Note: check and record the date of the risk analysis.

Insufficient:

- not all hazards are identified and not all risks are estimated **and** the measures taken are poor.

Moderate:

- identified hazards and estimated risks are mentioned thoroughly **and** the measures taken are poor **or**
- not all hazards are identified and not all risks are estimated though the measures taken are adequate.

Good:

- identified hazards and estimated risks are mentioned thoroughly **and** the measures are consistently described in line with the essential requirement 2 (elimination of risks, adequate protection measures, informing the user of residual risks).

5. List of applied standards (3.2.c.2)

Not applicable: manufacturer declares that harmonised standards are not applicable.

Absent: the applied standards are not mentioned in the file. Make a note on the assessment form: no separate list of standards is present, no essential requirements checklist is present or an essential requirements checklist without standards is present.

Present: the MDD states that the manufacturer shall only list the applied standards. Check which standards can be applicable for the product (<http://www.newapproach.org/home.asp>). Only harmonised European standards are relevant. Present if a separate list of applied standards or an essential requirements checklist with applied standards is available. Check and record the date of the document.

Insufficient:

- the list of applied standards hardly corresponds to the list drawn up by the assessors.

Moderate:

- a considerable part of the list of applied standards corresponds to the list drawn up by the assessors.

Good:

- the list of applied standards corresponds to the list drawn up by the assessors.

6. Solutions adopted (3.2.c.2)

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

Not applicable: the manufacturer declares that only standards are applied.

Absent: the file does not contain a document with solutions adopted.

Present: a checklist essential requirements containing solutions adopted is present.

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 (3.2.c.3)

Absent: the file does not contain relevant documents.

Present:**Insufficient:**

- inadequate techniques providing little understanding **or**
- only test results are present.

Moderate:

- only procedures are present **or**
- only techniques are present **or**
- procedures are present and some examples of design verification techniques are given (the actual used techniques are not obvious).

Good:

- techniques used and procedures are present.

8. Proof of conformity to the essential requirements when connected to another medical device (3.2.c.4)

Not applicable: manufacturer declares that medical device cannot be connected to another medical device.

Absent: not mentioned in the file.

Present: the proof of conformity can be given in the checklist essential requirements (requirement 9.1)

Insufficient:

- manufacturer states the combination **or**
- proof is given.

Moderate:

- combination and limited proof is given.

Good:

- combination and extensive proof is given.

9. Clinical data (3.2.c.6)

Absent: the file does not contain a document concerning the clinical data.

Present:Insufficient:

- compilation of literature **and/or**
- statement of clinical/medical expert **and/or**
- merely a statement of manufacturer without any documented substantiation.

Moderate:

- critical evaluation of literature without equivalency, results and conclusion **or**
- critical evaluation of literature regarding of the device in question, without results and conclusion **or**
- clinical investigation with poor clinical investigation plan.

Good:

- a critical evaluation of literature regarding the device in question with results and conclusion **or**
- a critical evaluation of literature on similar devices with a demonstration of equivalency, results and conclusion **or**
- a clinical investigation with an adequate clinical investigation plan (possibly preceded by a literature study) with the device in question **or**
- for well-established or simple devices documented expert opinions and justification for not performing a clinical evaluation.

10. Labelling (3.2.c.7)Absent: the file does not contain a label.Present: an original label or a copy thereof is supplied. Note the identification number of the Notified Body (see CE mark on label)Insufficient:

- label is not in Dutch and grant exemption from the Dutch language requirement is **not** included in the file.

Moderate:

- Dutch label and label complies partially with the essential requirements (13.3.a – 13.3.m) **or**
- label in foreign language and label complies partially with essential requirements (13.3.a – 1.3.m) including grant exemption from the Dutch language requirement.

Good:

- Dutch label and label complies with the essential requirements (13.3.a – 13.3.m) **or**
- label in foreign language and label complies with essential requirements (13.3.a – 1.3.m) including grant exemption from the Dutch language requirement.

11. Instructions for use (3.2.c.7)Absent: the file does not contain instructions for use (IFU).Present: the original IFU or a copy thereof is supplied. Note the identification number of the Notified Body (see CE mark on IFU)Insufficient:

- IFU is not in Dutch and grant exemption from the Dutch language requirement is **not** included in the file.

Moderate:

- IFU in Dutch and IFU complies partially with the essential requirements (13.6.a – 13.6.j and 13.7.a – 13.7.f if applicable for professional use) **or**
- IFU in foreign language and IFU complies partially with the essential requirements (13.6.a – 13.6.j and 13.7.a – 13.7.f if applicable for professional use) including grant exemption from the Dutch language requirement.

Good:

- in Dutch and IFU complies with the essential requirements (13.6.a – 13.6.j and 13.7.a – 13.7.f if applicable for professional use) **or**
- IFU in foreign language and IFU complies with the essential requirements (13.6.a – 13.6.j and 13.7.a – 13.7.f if applicable for professional use) including grant exemption from the Dutch language requirement.

12. Post market surveillance procedure (3.1.g.i)Absent: the file does not contain a document that can be considered as a post market surveillance (PMS) procedure.Present: a procedure to review experiences gained from devices in the postproduction phase. For an adequate PMS system, an active role of the manufacturer is essential.

Insufficient:

- only a complaint procedure for users **or**
- a non-systematic approach (no procedure) is used or experiences are collected in an ad hoc manner.

Moderate:

- procedure for the *active* collection and review of experiences **and**
- manufacturer uses ≤ 2 sources of information (see appendix IV).

Good:

- procedure for the *active* collection and review of experiences **and**
- manufacturer uses ≥ 3 sources of information **and**
- procedure for the lessons to be learnt from experiences: corrective and preventive actions will be taken, e.g. PMS as the final element of the circle of continuous improvement.

13. Vigilance procedure (3.1.g.ii)

Absent: the file does not contain a procedure to notify competent authorities of incidents or a procedure identified as such by the manufacturer.

Present: there is a procedure to notify the 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.

Insufficient:

- only incident/complaint or recall procedure present without notification **or**
- only incident/complaint or recall procedure present with insufficient notification duty (i.e. notification duty for incidents is not mentioned).

Moderate:

- procedure for incidents/complaints and recalls present **and**
- notification duty to competent authorities is mentioned **and**
- procedure for the review of incidents and complaints is incomplete: the consequences for the product are not clearly stated in the procedure.

Good:

- procedure for incidents/complaints and recalls present **and**
- notification duty to competent authorities is mentioned **and**
- procedure for the review of incidents and complaints is complete: lessons learnt will lead could lead to e.g. changes in the product, risk analysis, intended use and labelling or instructions for use.

Reciprocity between risk analysis and instructions for use

Are residual risks/hazards mentioned in the risk analysis also mentioned as warnings in the instructions for use/labelling?

Insufficient:

- only a few or no residual risks/hazards are mentioned as warnings.

Moderate:

- roughly half of the residual risks/hazards are mentioned as warnings.

Good:

- most of the residual risks/hazards are mentioned as warnings.

Are warnings in the instructions for use/labelling also mentioned as risks/hazards in the risk analysis?

Insufficient:

- only a few or no warnings are mentioned as risks/hazards.

Moderate:

- roughly half of the warnings are mentioned as residual risks/hazards.

Good:

- most of the warnings are mentioned as residual risks/hazards.

Appendix IV: Sources of information for PMS

Sources of information are:

- expert users groups
- customer surveys
- customer complaints and warranty claims
- post CE-market clinical trials
- literature reviews
- user feedback other than complaints: surveys, customer satisfaction
- device tracking/ implant registries
- user reactions during training programs
- Competent Authority
- 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