	<p style="text-align: center;"><b>Co-ordination of Notified Bodies Medical Devices (NB-MED) on Council Directives 90/385/EEC, 93/42/EEC and 98/79/EC</b></p>	<p style="text-align: center;"><b>Recommendation NB-MED/2.5.2/Rec2</b></p>
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<b>Title:</b>	<b>Reporting of design changes and changes of the quality system</b>
<b>Chapter:</b>	<b>2.5.2</b> Conformity assessment procedures; <b>Quality assurance</b>

<b>Text:</b>	<b>Reporting of changes to the Notified Body According to the Directives substantial changes in the design and quality system must be reported</b>
<b>Key words:</b>	<b>changes, quality system, design</b>

## 1 Rationale


The Medical Devices Directives variously require in different Annexes that where a Notified Body has been involved in the approval of the quality system or the device design / type, the manufacturer must inform the Notified Body of “substantial” changes to the quality system and/or changes to the device which could affect compliance with the essential requirements or the intended use.

It is not practicable to specify in general terms what types of change are or are not “substantial”. For instance, a change in colour may be purely cosmetic in some cases, yet be “substantial” in other cases where it is the means for drawing attention to warnings, functions etc. Instead, it is recommended that the manufacturer have a system for categorising changes as substantial or not and informing the Notified Body as appropriate, and that the Notified Body reviews the operation of this system as part of routine surveillance.

*A rationale and history sheet is available; please contact Technical Secretariat.*

<b>Reference to Directives:</b>	<b>Article/ Annex:</b>	<b>Reference to standards:</b>
AIMD	Annex: 2-3.4, 2-4.4, 3-6, 5-3.4	EN 46001/2
MDD	Annex: II-3.4, II-4.4, III-6, V-3.4, VI-3.4	EN 46001/2
IVDD	Annex: III-6.3, IV-3.4, IV-4.4, V-6.1, VI-3.4	EN 46001/2

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## 2 Manufacturer decision on whether or not particular changes are substantial

The manufacturer should establish, maintain and apply a procedure for categorising and documenting any changes to the device design/type (including software) and/or quality system as either “substantial” or not substantial.

As set out in the MDD changes to the design of a device are relevant to conformity assessment under annex II, 4 (design examination) and annex III (type examination). Changes to the quality system are relevant to conformity assessment under annex II, 3 (full quality system), annex V (production quality assurance) and annex VI (product quality assurance).

As regards IVDs the corresponding provisions are set out in the Annexes III, IV, V and VII.

Note: Changes to the intended use may constitute a new device. Additionally, in the cases of devices covered by the MDD, this may alter the classification, and so affect the conformity assessment procedure.


Changes are “substantial” and (depending on the chosen conformity assessment route) the manufacturer must inform the Notified Body where:

- (i) for product changes, the change would affect conformity with (a) the essential requirements and/or (b) the conditions prescribed for the intended use of the device.
- (ii) for changes to the quality system, either (a) the change would affect compliance of the devices covered by the quality system with the essential requirements or the approved type / design or (b) the change means additions to the product-range covered by the quality system.

Note: The term “significant” as used in Annex III-6 of MDD and Annex III-6.3 of IVDD is considered equivalent to the term “substantial”.

The matters for the manufacturer to consider when deciding whether or not particular changes are “substantial” include the following:

- for device changes

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- does the change introduce new hazards which have not been previously addressed?
- does the change adversely affect the risk associated with existing hazards?
- does the change alter the details on intended use and/or compliance with the essential requirements given in the design / type approval dossier submitted to the Notified Body?
- does the change mean that the device will have different end users or be used in a different manner?
- does the change mean that the clinical data/performance evaluation data for the original device is not sufficient to confirm conformity of the changed device with the required characteristics and performance?
- for changes to the quality system

(see also "Global Harmonization Task Force *Guidelines for Regulatory Auditing of Quality Systems of Medical Device Manufacturers*", section *Special audits* (MedDev 2.5/2, latest revision))

- does the change alter the manufacturing technologies or product-range covered?
- does the change affect product conformity with the essential requirements or the approved type / design?
- does the change affect the continued compliance of the quality system with the relevant harmonized standards?
- does the change affect the arrangements (e.g. verification, validation, organizational structure) for ensuring continued compliance with the requirements of the Directive?

### 3 Manufacturer reporting of changes

The manufacturer should promptly inform the Notified Body of planned substantial changes.

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A notification of any substantial change in the design /device as well as in the quality system should include

- (i) a brief description of the modifications compared to the approved design / device or the approved quality system and
- (ii) the reason for the changes / modifications and
- (iii) in the case of design / device changes, a statement on the relevance to the compliance with the essential requirements.

#### 4 Notified Body surveillance and certification

(see also “Global Harmonization Task Force *Guidelines for Regulatory Auditing of Quality Systems of Medical Device Manufacturers*“, section *Special audits* (MedDev 2.5/2, latest revision))

The Notified Body should review during audit the operation of the manufacturers system to classify changes as “substantial“ and to inform the Notified Body.

The Notified Body should also review those changes considered by the manufacturer as non-substantial and which therefore have not been reported.

Where a „substantial“ change is reported and agreed either a new certificate or an addendum to an existing certificate can be issued or the existing certificate can remain valid.


#### 5 Examples

##### 5.1 Changes to EC-approved quality systems (MDD Annex II, V, VI; IVDD Annexes IV and VII respectively):

###### a) Reportable change:

Addition of a sterilisation subcontractor to the list of approved suppliers. Rationale: Sterilisation is a “special process“ requiring validation, therefore this is a substantial change.

###### b) Non-reportable change:

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<b>Title:</b>	<b>Reporting of design changes and changes of the quality system</b>	

Addition of an electrical components supplier, e.g. for resistors, to the list of approved suppliers as

- selection and approval of suppliers is part of the quality system of the manufacturer
- the components to be supplied
  - meet the manufacturer's existing specifications
  - do not fall within the manufacturer's classification of a "substantial change".

5.2 Changes to EC-approved medical devices design/type (including software) (MDD Annexes II, 4.4 and III; IVDD Annexes VI-4.2 and V, respectively):


a) Reportable change:

- Changes to the medical device included computer software (e.g. new functionalities, new algorithms for computing) which will change the specifications and / or performances of the device (e.g. changes of those materials which have to be biocompatible or changes of main components like power source, Central Processing Unit (CPU), defibrillator-capacitors etc.)
- new operating systems

are substantial changes.


Note: In the case of IVD reagents substantial changes are those which significantly influence the performance characteristics compared to those of the originally approved design. Where changes of the performance characteristics are due to changes of the manufacturing process, these may well be considered as substantial.

- Altering the intended use of the product (e.g. from Brady Implantable Pulse Generator (IPG) to Tachy IPG).
- Other changes which may affect the design or performance/characteristics of the device (e.g. new sterilisation method, new welding method, or in the case of computer software, new functionalities, new algorithms for computing, new operating system) are considered to be substantial changes.

	<p style="text-align: center;"><b>Co-ordination of Notified Bodies Medical Devices (NB-MED) on Council Directives 90/385/EEC, 93/42/EEC and 98/79/EC</b></p>	<p style="text-align: center;"><b>Recommendation NB-MED/2.5.2/Rec2</b></p>
<p><b>Title:</b></p>	<p style="text-align: center;"><b>Reporting of design changes and changes of the quality system</b></p>	

b) Non-reportable change:

A manufacturer is using a component which deviates from a component that he used before (e.g. electronic circuitry). However, he corrects this deviation with another component so that the finished product specification and performance are not changed and documents the actions taken. Upon review, the manufacturer determines and records that risks are not adversely affected and compliance with the essential requirements is maintained and so it is not considered to be a substantial change.

	<b>Co-ordination of Notified Bodies Medical Devices (NB-MED) on Council Directives 90/385/EEC, 93/42/EEC and 98/79/EC</b>	<u><b>Rationale and history sheet</b></u> to <b>NB-MED/2.5.2/Rec2</b>
<b>Title:</b>	<b>Reporting of design changes and changes of the quality system</b>	

**Rev 1:** Meeting of NBR Group, Cologne, Jan. 20 & 21. 1997:

It was decided that the previous text required major revision. An attempt was made to list which types of change did or did not need to be advised to the Notified Body. This proved to be impracticable since a particular type of change could be minor in one situation, yet "substantial" in another.

For instance, a change in colour may be purely cosmetic in some cases, yet be "substantial" in other cases where it is the means for drawing attention to warnings, functions etc.

Meeting of NBR Group, Essen, April 03. & 04. 1997:

It was decided to redraft the document to recommend that the manufacturer apply a systematic approach to evaluation and categorisation of changes. Lists are included of matters for the manufacturer to consider when categorising changes. In preparing the redraft, comments received in relation to the original text (from MDC and the German NB Group) were fully considered.

NBRG agreed to send the revised document, with its "Rationale and history" sheet to all member of NB-MED for commenting before presenting it for approval in the Plenary meeting in June 1997.

New revision no: 1

Confirmed to be at Stage: 2

**Rev 2:** Notified Body Meeting, Brussels, June. 24 & 25. 1997:

It was decided to accept this recommendation with some minor changes excluded the samples (chapter 5).

It was also decided **to give back this document to the NBRG** to rework the samples.

Meeting of NBR Group, Brussels, June 26. & 27. 1997:

The document (chapter 1 - 4) was reworked.

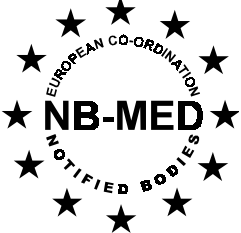
New revision no: 2

Confirmed to be at Stage: 3

The samples (chapter 5) was also reworked; new proposal (*in italics*, see next page):

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## 5 Examples

### 5.1 Changes to EC-approved quality systems (Annex II, V, VI):

#### a) Reportable change:

*Addition of a sterilisation subcontractor to the list of approved suppliers. Rationale: Sterilisation is a “special process“ requiring validation, therefore this is a substantial change.*

#### b) Non-reportable change:

*Addition of an electrical components supplier, e.g. for resistors, to the list of approved suppliers as*

- *selection and approval of suppliers is part of the quality system of the manufacturer*
- *the components to be supplied*
  - *meet the manufacturer’s existing specifications*
  - *do not fall within the manufacturer’s classification of a “substantial change“.*

*The change is not reportable.*

### 5.2 Changes to EC-approved medical devices design/type (Annex II, 4.2 and III):

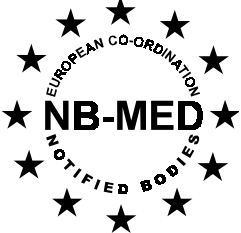
#### a) Reportable change:

- *Changes to the medical device (included software) which will change the specifications and / or performances of the device (e.g. changes of those materials which have to be biocompatible or changes of main components like power source, Central Processing Unit (CPU), defibrillator-capacitors etc.) are substantial changes.*
- *Altering the intended use of the product (e.g. from Brady Implantable Pulse Generator (IPG) to Tachy IPG) or other changes which may affect the design or performance/characteristics of the device (e.g. new sterilisation method, new welding method) are considered to be substantial changes.*

#### b) Non-reportable change:

*A manufacturer is using a component which deviates from a component that he used before (e.g. electronic circuitry). However, he corrects this deviation with another component so that the finished product specification and performance are not changed and documents the actions taken. Upon review, the manufacturer determines and records that risks are not adversely affected and compliance with the essential requirements is maintained and so it is not considered to be a substantial change.*



	<p style="text-align: center;"><b>Co-ordination of Notified Bodies Medical Devices (NB-MED) on Council Directives 90/385/EEC, 93/42/EEC and 98/79/EC</b></p>	<p style="text-align: center;"><b><u>Rationale and history sheet</u> to NB-MED/2.5.2/Rec2</b></p>
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NBRG agreed

- to fit in this document in the bundle of „stage 3-documents“ and
- to send it - concerning the acceptance of the proposal for the chapter „samples“ - with its "Rationale and history" sheet to all member of NB-MED for commenting before presenting it for approval (text plus samples) in the Plenary meeting in November 1997.

**Rev 3:** Meeting of NBR Group, Essen, September 29 & 30 1997:

It was decided to add the above mentioned proposal for examples into the recommendation and to fit the document in the new *recommendations nomenclature system* (chapter **2.5.2 Conformity assessment procedures; Quality assurance**). Therefore the recommendation gets the new number **NB-MED/2.5.2/R2**. NBRG agreed to send the document, with its "Rationale and history" sheet to all member of NB-MED for commenting before presenting it for approval in the Plenary meeting in November 1997.

Revision no: 3

Confirmed to be at stage: 2

Notified Body Meeting, Brussels, November 18 & 19, 1997:

Confirmed to be at Stage: 3

**Rev. 4:** Medical Devices Expert Group Meeting, Brussels, February 9/10, 1998:

The stage 3 document was presented to the Medical Devices Experts Group but not accepted because this document needs more clarification about „When exactly have changes to be indicated?“. The UK-representative will examine the document and will inform the NBR Group about the results.

Meeting of NBR Group, Brussels, April 20 & 21, 1998:

The NBRG reworked the document and made in light of above mentioned discussion in the MDEG some clarification:

„2 *Manufacturer decision on whether or not particular changes are substantial*  
*The manufacturer ... or not substantial.*

*Changes to the design of a device are relevant to conformity assessment under annex II, 4 (design examination) and annex III (type examination).*

*Changes to the quality system are relevant to conformity assessment under annex II, 3 (full quality system), annex V (production quality assurance) and annex VI (product quality assurance).*

*Note: Changes to the intended use may constitute a new device or alter the classification, and so affect the conformity assessment procedure.*

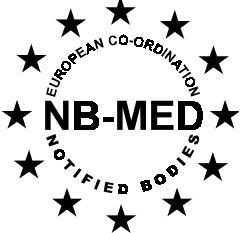
...

4 *Notified Body surveillance and certification*

...  
*The Notified Body should review ... to inform the Notified Body.*

*Where a „substantial“ change is reported and agreed either a new certificate or an addendum to an existing certificate can be issued or the existing certificate can remain valid.*

...“  
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	<p><b>Co-ordination of Notified Bodies Medical Devices (NB-MED) on Council Directives 90/385/EEC, 93/42/EEC and 98/79/EC</b></p>	<p><b><u>Rationale and history sheet</u> to NB-MED/2.5.2/Rec2</b></p>
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On occasion of the next NB-MED meeting on June NB-MED will be informed about this changes; further consideration will be done by the Medical Devices Experts Group.

Confirmed at stage 3

New revision no: 4

**Rev 5:** Notified Body Meeting, Brussels, November 3 & 4, 1998:

The NB-MED agreed the recommendation with this changes; also some minor editorial hints were given and will be considered. This document will remain a stage 3 document. Further development will take place in the Medical Devices Experts Group.

Confirmed to be at Stage: 3

New revision no: 5

**Rev 6:** Notified Body Meeting, Brussels, March 2 & 3, 1999:

Mr. Reincke introduced the document NBM/37/99 which could be considered as a further aspect to be included in the existing NB-MED Recommendation 2.5.2/Rec2 "Changes ...". The document should give within a list an answer to "What could be regarded as major changes if – in case of an approved product – some software- or hardware-changes appear with the requirement for notification by a Notified Body?". NBRG was asked to take this proposal on board within the NBRG for consideration to the above mentioned NB-MED Recommendation 2.5.2/Rec2 e. g. as a sample. But due to the workload within the NBRG it was not yet reached the possibility to work on this document. In the meanwhile **Mr. Reincke** was asked by the Technical Secretariat to make a concrete proposal for a revised Recommendation 2.5.2/Rec2.

Notified Body Meeting, Brussels, February 29, & March 1, 2000:

A proposal was sent to TS for further presentation to the NBRG meeting on 10./11. April 2000.

New revision no: 6

**Rev 7:** Meeting of NBR Group, Brussels, April 10 & 11, 2000:

Proposed changes - made by Mr. Reincke - were accepted and modified with minor editorial changes. Dr. Dörr brought in verbal form his view of changes which should be made in light of IVDD; in parallel he referred to the comments made by Mr. Dalgetty (see NBRG/176/00). After the discussion it was agreed that all comments were considered in the new revised draft document.

NBRG agreed that the document, as discussed and revised, should be presented for adoption at the June NB-MED Plenary meeting.

Revision no: 7

stage 2

Notified Body Meeting, Brussels, June 6 & 7, 2000:

The document (NBM/59/00) was approved by the NB-MED plenary.

Confirmed at stage 3.

Revision no: 7