	Co-ordination of Notified Bodies Medical Devices (NB-MED) on Council Directives 90/385/EEC, 93/42/EEC and 98/79/EC	**Recommendation** **NB-MED/2.2/Rec3**

Title:	**"Use-by" date for Medical Devices**
Chapter:	**2.2 Essential Requirements**

Text:	**---**
Key words:	**"Use-by" date**

1 Requirements

The medical devices directives (MDD, AIMD, draft IVDD) each require a statement given on the label and/or the information provided with the device on any time limitation on the safe use of the device. Although the wording differs, each addresses the need to provide this information:

MDD, annex I, 13.3:	**AIMD, annex 1, 14:**	**IVDD, annex I, Part B, 8.4:**
"The label must bear the following particulars: ... (e) where appropriate, an indication of the date by which the device should be used, in safety, expressed as the year and month; ..."	"Every device must bear ... : ... - an indication of the time limit for implanting a device safely."	"The label must bear the following particulars ... : ... (e) if necessary, an indication of the date by which the device or part of it should be used, in safety, expressed as the year, the month and, where relevant, the day, in that order; ..."

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

Reference to Directives:	**Article/ Annex:**	**Reference to standards:**
AIMD	Annex: 1-14	EN 1441, prEN 1041
MDD	Annex: I-13.3	EN 1441, prEN 1041
IVDD	Annex: I, Part B, 8.4	EN 1441, prEN 1041

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2 Purpose of this recommendation

In the case of devices covered by the AIMD, a time limit must always be given.

In the case of devices covered by the MDD and the IVDD, a time limit is only required where "appropriate" or "necessary", respectively. The purpose of this recommendation is to

a) assist the manufacturer in deciding whether a "use-by" date is required for his particular device and

b) indicate what information is required to support his decision.

Note: The "use-by" time limit relates to the period before the first use of the device. It does not relate to the number or period of subsequent uses (the "lifetime" of the device).

If the device is reusable, the MDD separately requires (Annex I, 13.6 (h)) "... information on ... any restrictions on the number of reuses." The same requirement is laid down in the IVD Directive (Annex I, Part B, 8.4).

If the device is for single use, but over a prolonged period, any limitations on what would be the expected pattern of use would be required as "... special operating instructions" or "... warnings and/or precautions to take" (MDD, annex I, 13.3 (j) and (k) respectively).

Specifically for IVDs the Directive requires in its Annex I, Part B, 8.7(c) that "the storage conditions and shelf life following the first opening of the primary container, together with the storage conditions and stability of working reagents" shall be given.

Note: There is nothing in the medical devices directives which prohibits a manufacturer voluntarily recommending a "use-by" date, even though the performances and characteristics are not in fact affected by the passage of time.

3 How to decide if a "use-by" date is required

A "use-by" date is required where a safety-related characteristic or claimed performance is likely to deteriorate over time.

In deciding whether there is such a "safety-related" deterioration, the manufacturer must have regard to the results of the risk analysis and measures taken to manage risk.

a) The risk analysis should identify *those performances and characteristics* necessary for the safe use of the particular device.

   - For example, the risk analysis may indicate that sterility is necessary for safe use. Equally, the risk analysis would not cover the colour of the device if this is purely aesthetic, but it might cover the colour of the device if that colour has a purpose related to safe use of the device (e. g. the colour signifies the size of the device).

b) The risk analysis and measures taken to manage risk will also identify the *level or extent* of performance or characteristic but only in so far as they are relevant to safe use of the device.

   - For example, the level of resistance to gas flow or rate of leakage from a breathing system, or the probability of non-sterility.

c) The risk analysis and measures taken to manage risk will also identify the *period* over which the relevant performance or characteristic would be expected to be maintained for safe use, including the shelflife and intended period of use.

   - For example, the period over which a pacemaker battery maintains sufficient energy to function after implantation as long as intended by the manufacturer.

4 Information that is required to support the decision

4.1 Information necessary if a "use-by" date *is* given

The manufacturer must demonstrate that the claimed performances and characteristics of the device are maintained over the claimed shelf life which the "use-by" date reflects.

This may be achieved by

a) prospective studies using accelerated ageing, validated with real time degradation correlation; or

b) retrospective studies using real time experience, involving e.g. testing of stored samples, review of the complaints history or published literature etc.; or

c) a combination of a) and b).

4.2 Information necessary if a "use-by" date *is not* given

As the absence of a "use-by" date constitutes an implicit claim of an infinite shelf life, the manufacturer must demonstrate either

a) that there are *no* safety-related performances or characteristics which are likely to deteriorate over time (3a above), or

b) that the *extent* of any likely deterioration (3b above) does not represent an un-acceptable risk, or

c) that the *period* over which unacceptable deterioriation occurs is far beyond the likely time of the first use of the device (3c above), e.g. 30 years.

In doing so, the manufacturer must consider, amongst other matters

- materials of the device itself and those used in manufacture, including adhesives, coatings, packaging etc.

- methods of manufacturing, (e.g. attachment of components, package sealing process);

- methods of protecting the device or parts thereof from deterioration (e.g. packaging, storage instructions);

- if relevant, state in which the device is maintained prior to first use (e.g. without battery fitted)

- the potential for inherent time dependent material degradation (e.g. due to long term effects of sterilisation on materials such as that of free radicals from gamma irradiation leading to polymer degradation).

If the manufacturer cannot meet the requirements of either 4.2a or 4.2b or 4.2c above, a "use-by" date must be given.

5 Examples

5.1 Cardiac catheter with latex balloon

[Only aspect considered in this example: time-related deterioration of the balloon]

A cardiac catheter incorporates a latex balloon to locate the cather tip within, and temporarily occlude, a blood vessel. The ability of the balloon to withstand certain pressure is necessary for safe use. The latex of the balloon, however, deteroriates over time. The packaging and the storage instructions to protect the device from light reduce the rate of deteroriation, but do not prevent it. It is therefore necessary to give a "use-by" date.

The manufacturer must demonstrate that

- *the latex balloon remains able to withstand the relevant pressure over the claimed shelf life, when the device is stored in accordance with the manufacturer's instructions.*

5.2 Orthopaedic hip joint implant (supplied sterile)

[Only aspect considered in this example: time-related deterioration of the sterile packaging]

A metal and ceramic orthopaedic implant is supplied sterile in a composite plastic/paper unit container. The ability of the packaging to maintain sterility is necessary for safe use. Whilst the maintenance of sterility is in part event-related (i.e. a function of the actual storage and handling conditions), it is also a function of time, due to e.g. the reduction in flexibility and seal strength of the package material over a period rendering it more susceptible to the events which may compromise sterility.

Moreover, as such implants are available in a variety of sizes to suit different clinical applications, a particular device may remain in the store over a long time until needed for implantation.

It is therefore necessary to give a "use-by" date. In the case of maintenance of sterility, the "use-by" date will reflect a combination of

a) the time-related deterioration in the performance of the pack, e.g. seal strength, seal integrity and resistance to penetration of particles carrying micro-organisms,

b) the probability of events occurring during transport and storage which compromise sterility, but are not evident and therefore where the warning not to use the device when the package is opened or damaged will not assist.

The manufacturer must demonstrate that

- *the packaging material is able to maintain device sterility over the claimed shelf life, when stored in accordance with the manufacturer's instructions.*

5.3 Implantable cardiac pacemaker

[Only aspect considered in this example: battery lifetime]

An implantable cardiac pacemaker is supplied with a battery fitted and sealed into the device. Due to self-discharge, all batteries have a limited life even if not used. The period for which the battery maintains sufficient energy for the device to function as intended by the manufacturer following implantation is important to avoid the need for a surgical operation to explant and replace the device unnecessarily soon. It is therefore necessary to give a "use-by" date.

The manufacturer must demonstrate that

- *the battery retains sufficient energy to function for the manufacturer's claimed operating time even if implanted at the end of the claimed shelf life.*

5.4 IVD reagent kits

In the case of IVD kits which are composed of several reagents the "use-by date" of the kit should be that of the component of the kit having the shortest shelf-life.

	Co-ordination of Notified Bodies Medical Devices (NB-MED) on Council Directives 90/385/EEC, 93/42/EEC and 98/79/EC	**Rationale and history sheet to NB-MED/2.2/Rec3**
Title:	**"Use-by" date for Medical devices**	

Rev. 1: The subject has come up in the NB-MED meeting years ago, based on the "old" draft NB-MED recommendation 2.2/R4 *Expiry dating of medical devices* (stage hold). After long discussions in several meetings a decision was made in the NB-MED meeting on 11./12.09.95 (minutes item 7.1). Next step was a discussion in the Medical Devices Expert Group on 07.03.97, resulting in a statement in the minutes of that meeting. This is why NB-MED/2.2/R4 has been put on hold status.

Meeting of NBR Group, Brussels, June 26. & 27., 1997:
When reworking all draft NB-MED recommendations, also No. 2.2/R4 has been reviewed. It was decided that a thorough rework of this NB recommendation would be necessary. A small group with Jan Thalen, David Barrow and Johann Rader was installed for that task.

Meeting of task force, Munich, September 11., 1997:
This group has met on 11.90.97 in Munich (with Jan Thalen apologised) and prepared a draft. For this draft, the following documents have been considered:

- Draft NB-MED recommendation 2.2/R4 *Expiry dating of medical devices* (old numbering: 3.4.2e)
- Minutes of the Medical Devices Expert Group meeting on 07.03.96
- Minutes of NB-MED meeting on 11./12.09.95
- Minutes of NBR Group meeting on 26./27.06.97

The paper proposed to be taken into consideration "FDA Quality System Final Rule, October 7, 1996, pages 53/54" gives an explanation of the term "where appropriate". This paper has **not** been taken into consideration, as this explanation relates to the regulatory system of the FDA/USA and cannot be used in another regulatory system (EU/MDD) for which it has never been intended.
Confirmed at stage 0

Rev. 2: Meeting of NBR Group, Essen, September 29. & 30., 1997:
Discussion concerning the tabled stage 0 document. Some minor changes were proposed and adopted by NBRG.
It was decided to fit the document in the new *recommendations nomenclature system* (chapter 2.2 *Essential requirements*). Therefore the recommendation gets the number **NB-MED/2.2/R3**.
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.
Confirmed at stage 2
Revision 2

Rev.-Nr.	Rev. date	accepted	amended	withdrawn
	06.06.2000			

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Notified Body Meeting, Brussels, November 18 & 19, 1997:
The „old" draft NB-MED recommendation 2.2/R4 *Expiry dating of medical devices* (old numbering: 3.4.2e) will be withdrawn.
Confirmed to be at Stage: 3

Rev. 3: Medical Devices Expert Group Meeting, Brussels, February 9/10, 1998:
The stage 3 document on „Use-bye date" was presented to the Medical Devices Experts Group and was accepted provided that some changes will be done; proposals were given by the UK representative.

Meeting of NBR Group, Brussels, April 20 & 21, 1998:
By consideration the proposed and minuted changes out of the Medical Devices Experts Group meeting NBRG made the following reworking of the document:

„...
3 How to decide if a "use-by" date is required
...
c) The risk analysis and measures taken to manage risk will also identify the period over which the relevant performance or characteristic would be expected to be maintained for safe use, including the shelflife and intended period of use.
...
4 Information that is required to support the decision.
4.1 Information necessary if a "use-by" date is given
...
a) prospective studies using accelerated ageing, validated with real time degradation correlation; or
...
4.2 Information necessary if a "use-by" date is not given
...
- if relevant, state in which the device is maintained prior to first use (e.g. without battery fitted)
- the potential for inherent time dependent material degradation (e.g. due to long term effects of sterilisation on materials such as that of free radicals from gamma irradiation leading to polymer degradation).
..."

On occasion of the next NB-MED meeting on June these changes will be presented.
Confirmed at stage 4
New revision no: 3

Notified Body Meeting, Brussels, June 9 & 10, 1998:
NB-MED agreed with above proposed changes and this document will stay a stage 4 document because it was fully accepted at the Medical Devices Experts Group meeting on February.
Confirmed at stage 3

Rev. 4: Notified Body Meeting, Brussels, November, 2 & 3, 1999:
The NBRG was asked to rework the NB-MED Recommendations in light of the IVD-directive.

Meeting of NBR Group, Cologne, February 3, 2000:
The work results of a small task force (task: reworking the Recommendations in light of IVDD) were presented to that NBRG-meeting.
The tabled revised working document (without revision no.) was discussed and some criticism was made. Mr. Dalgetty promised to send his written comments to NBRG. NBRG agreed that the document should not be presented to the NB-MED Plenary meeting. Comments will be discussed on occasion of the next NBRG-meeting.

Meeting of NBR Group, Brussels, April 10 &11, 2000:
Dr. Dörr presented a new working document and explained the 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 - during the meeting - revised, should be presented for adoption at the June NB-MED Plenary meeting.
Revision no: 4
stage 2

Notified Body Meeting, Brussels, June 6 & 7, 2000:
The document (NBM/58/00) was approved by the NB-MED plenary.
Confirmed at stage 3.
Revision no: 4