	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/2.5.5/Rec3**

Title:	**Conformity Assessment of Annex II, IVD's designed and evaluated prior to adoption of Common Technical Specifications (CTS)**
Chapter:	**2.5.5 Conformity assessment for particular product groups**

Text:	**"..."**
Key words:	**CTS,**

1 INTRODUCTION

This recommendation has been prepared to provide guidance for Notified Bodies and manufacturers, for use in connection with the conformity assessment for CE marking purposes of those IVD medical devices to which Annex II, relates but which had been designed and evaluated before final adoption of the CTS.

As provided for in article 5.3, for devices which are covered by Annex II, List A, and which are going to bear the CE marking, common technical specifications (CTS) for the evaluation of their performance have been drafted by governmental, professional and industry experts. In due course, the CTS will be formally adopted by the Standing Committee on Medical Devices in accordance with the Article 7 procedure and will be published in the Official Journal of the European Communities. In the meantime, the draft CTS may be used by Notified Bodies and Industry. No such device can be CE marked unless it meets the appropriate essential requirements including the CTS applicable to it at the date it is placed on the market or if, for duly justified reasons, the manufacturer does not comply with those specifications he must adopt solutions of a level at least equivalent thereto.

As regard the conformity assessment for the purpose of the CE marking of such devices that were evaluated and placed on the market under pre-existing regulatory arrangements, it may be that they do not comply in all respects with the applicable

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

Reference to Directives:	**Article/ Annex:**	**Reference to standards:**
AIMD		
MDD		
IVDD	Article 5.3, 22.4; Annex II	

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CTS see also NB-MED/2.13/Rec2. It may be, for example, that the exact number of patient samples as defined in the CTS is not met. In such cases, it is necessary to consider whether, nevertheless, the device meets the relevant essential requirements because the manufacturer had adopted solutions that provide a level of safety equivalent to that provided by the applicable CTS.

It is the purpose of this document to provide guidance for the acceptability of evidence to be provided by the manufacturer as regards such compliance.

2 Compliance Analysis

Manufacturers should analyse their data in comparison with the CTS. Performance evaluation data generated in connection with the development of these pre-existing Annex II, devices may be useful in showing compliance with the CTS even if these data may have been generated some years ago. For example, this may be possible by using data generated in-house or externally for other evaluation and validation studies or by using data submitted to national authorities for the national approval of an established device. In this context it is important to note that, by Article 22.4, Notified Bodies will have to take account of any such information and earlier approvals. If summarised data, e.g. data in scientific publications, are provided for showing compliance with the CTS the Notified Body must have access to the relevant information including underlying data so the Notified Body may be in a position to assess the validity of the performance evaluation. Differences between the available data and the requirements of the CTS may need to be filled by additional studies or by documented scientific justification.

3 Experience with established IVD-devices

Manufacturers may wish to CE mark IVD medical devices that are already established on the European market NB-MED/2.13/Rec2 applies. Historical data are valuable as long as test populations and test specimens are sufficiently characterised. Data from final release testing by the manufacturer and/or regular verification of manufactured product by an independent party may be used as evidence of high production consistency, but does not in itself prove compliance with the CTS.

4 Devices used for comparison

The purpose of the device used for comparison is to confirm the diagnostic status of the samples to be used in the performance evaluation. Data from studies which have been completed prior to the adoption of the CTS, without the use of a device used for comparison may be considered, for example for specificity (>99,5 in blood donor populations for blood screening assays) or geno/subtype sensitivity (detection of defined types), provided that the diagnostic status of the samples has been unequivocally established.

5 Flexibility

For certain populations, the CTS define the minimum numbers of samples to be tested, the criteria for the selection of respective samples and the criteria for interpretation and acceptance of results. As stated before, the Directive states "Manufacturers shall as a general rule be required to comply with the common technical specifications; if for duly justified reasons manufacturers do not comply with those specifications they must adopt solutions of a level at least equivalent thereto.". For example,

i) Diagnostic Specificity

Specificity studies using a smaller number of blood donor specimens than that proposed in the CTS may be considered equivalent to the CTS if the specificity of the device is statistically comparable to the minimal specificity required by the CTS. Furthermore the donor specificity data are supported by additional data based on a higher than the proposed number of samples from challenging populations such as specificity studies from populations with an increased risk for non-specific results, e.g. potentially cross- reacting specimens or samples of hospitalised patients. Regardless of the deficiency of data compared to the CTS requirements, the conclusions from studies performed with smaller than the proposed minimum numbers of specimens must be on a sound scientific and statistical basis.

ii) Diagnostic Sensitivity

Diagnostic sensitivity is important because of the detection of infection in the early stages of infection. For blood screening assays for viral infections, the

current public and regulatory attention focuses on the detection of infected blood donors / patients during all stages of infection so as to provide a high level of protection of public health. In the past, conclusions from regular sensitivity studies, performed by some national authorities, have resulted in the withdrawal of some IVD's from national markets where sensitivity was proved inadequate. Because of the importance of these criteria there is little room for flexibility in comparison with the sensitivity requirements of the CTS.

Low titre panels comprised of several single specimens from the early infection phase, could be considered as being equivalent to complete seroconversion panels of individual donors.

Geno/subtype detection as defined in the CTS may be considered as proven by respective data on prevalence for certain virus types in the test population instead of typing each single specimen.

iii) Whole system failure rate, robustness

Whole system failure is defined in the CTS as "the frequency of failures when the entire process is performed as prescribed by the manufacturer".

This can be established by the performance of specific validations or the use of data from the post production phase.

NB-MED	**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/2.5.5/Rec3**
Title:	**Conformity Assessment of Annex II, IVD's designed and evaluated prior to adoption of Common Technical Specifications (CTS)**	

Rev. 1: Notified Body Meeting, Brussels, November, 2 & 3, 1999:
The NBRG was asked to elaborate new NB-MED Recommendations in light of the IVD-directive if needed.

A small task force on NBRG-IVDD was established and met several times (on 03.12.99 at PEI and on 24.01.2000 at LRQA). First draft documents were elaborated (see also minutes NBRG/166/00 and NBRG/167/00).

Meeting of NBR Group, Brussels, March 2, 2000:
The work results of the small task force (elaborate new NB-MED Recommendations in light of IVDD) were presented to that NBRG-meeting.
The tabled revised working document (without revision no.) on "Conformity Assessment of Annex II, IVD's designed and evaluated prior to adoption of Common Technical Specifications (CTS)" was discussed and some comments for improvement were made. It was agreed that further development will be made by the task force group.

Meeting of NBR Group, Brussels, April 10 &11, 2000:
A new draft document was presented to that meeting (without rev. no.). NBRG reworked the document within an intensive discussion. It was decided to fit the document in the *recommendations nomenclature system* under chapter 2.5.5 *Conformity assessment for particular product groups*. Therefore the recommendation gets the number **NB-MED/2.5.5/Rec3**.
NBRG agreed that the document, as discussed and - during the meeting - revised, should be presented for formal adoption at the June NB-MED Plenary meeting **but could find application/knowledge in the meanwhile**.
Revision no: 1
stage 2

Notified Body Meeting, Brussels, June 6 & 7, 2000:
The document (NBM/62/00) was approved by the NB-MED plenary.
Confirmed at stage 3.
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