The Critical Task of Selecting a Notified Body, Part One

Since the dawn of the European medical device directives over 20 years ago, the process of selecting a Notified Body has been an important undertaking. In the current regulatory environment, this process is even more critical. Part one of this article discusses Notified Body regulatory requirements and the Notified Body Operations Group. Part two will cover important criteria to consider in selecting a Notified Body.

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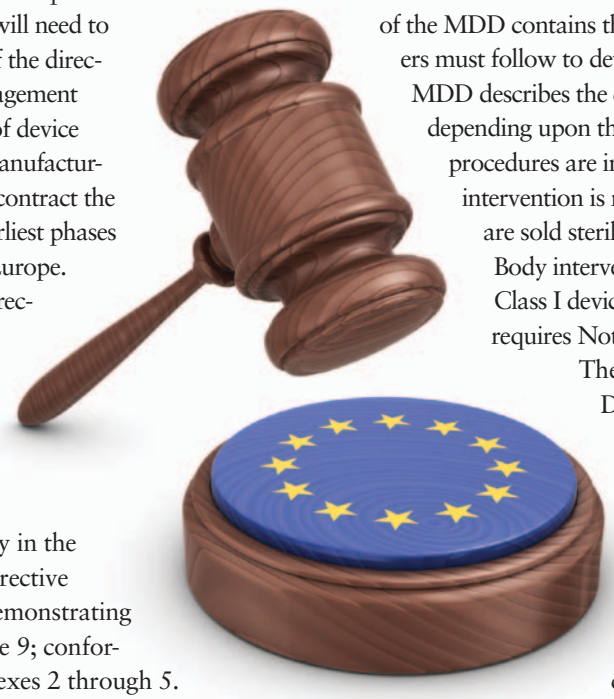
A Notified Body is a public or private organisation designated by a Competent Authority of a member state to carry out certain conformity assessment tasks specified in the European directives. To do this, it will need to assess compliance with specific aspects of the directives, including those related to risk management and the demonstration that the benefits of device use outweigh the risks. Medical device manufacturers should determine if they will need to contract the services of a Notified Body during the earliest phases of planning to market their products in Europe. To do this, the relevant medical device directive must be identified together with the regulatory risk category or classification of the device. This is followed by a decision on the conformity assessment procedure that will be followed to obtain the CE mark.

There is only one device risk category in the Active Implantable Medical Devices Directive (AIMDD; 90/385/EEC). Options for demonstrating conformity to the AIMDD are in Article 9; conformity assessment procedures are in Annexes 2 through 5. Manufacturers need to decide on the conformity assessment procedure they wish to follow to CE mark their devices. Notified Body intervention is required for all devices covered by the AIMDD.



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The Medical Devices Directive (MDD; 93/42/EEC) specifies four risk-based classes of devices, which are Class I, IIa, IIb and III, with Class I the lowest risk category and Class III the highest. Annex IX of the MDD contains the classification rules that manufacturers must follow to determine the device class. Article 9 of the MDD describes the conformity assessment options available, depending upon the device class. The conformity assessment procedures are in Annexes II through VII. Notified Body intervention is required for Class I devices only if they are sold sterile or have a measuring function. Notified Body intervention is not needed for any other type of Class I device. For all other classes of devices, the MDD requires Notified Body intervention.

The *In Vitro* Diagnostic Medical Devices Directive (IVDD; 98/79/EC) places devices into the following risk-based groups: devices that are specified in Annex II, which consists of List A and List B; devices for self-testing that are not in Annex I; and all other devices. The conformity assessment options are described in Article 9 and the conformity assessment procedures are in Annexes III through VII. Notified Body intervention is not required for the vast majority of IVD devices, but only for those listed in Annex II and for self-test devices.

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Notified Body regulatory requirements

Manufacturers should be aware of the requirements Notified Bodies must fulfill, how they are designated and the oversight to which they are subjected. For example, each medical device directive contains an annex that describes the criteria that Notified Bodies must meet in order to be designated (Annex 8 in the AIMDD, Annex XI in the MDD, and Annex IX in the IVDD). In addition, the European guidance document, "Designation and Monitoring of Notified Bodies within the Framework of EC Directives on Medical Devices" (MEDDEV 2.10-2 Rev. 1)[1] describes in more detail the criteria and conditions for the designation and operation of Notified Bodies. However, this 2001 document is in need of important updating so that it refers to current versions of the directives and standards and incorporates requirements for IVD Notified Bodies, which are excluded from the guidance.

One of the criteria that Notified Bodies must meet concerns subcontracting. In some cases, a Notified Body may not have specific in-house expertise and will require the services of a subcontractor. If so, the Notified Body must ensure that the subcontractor meets relevant criteria and has the requisite qualifications. In some cases, knowledge of the regulations is particularly critical.

For example, some Notified Bodies may need to subcontract certain types of clinical expertise, which is understandable given the vast range of clinical areas that medical devices cover. The subcontracted clinical expertise may be needed for assessing a manufacturer's clinical data, including clinical evaluation reports and associated documentation. Manufacturers should be assured that the clinical experts contracted for these services not only have the clinical expertise needed, but also a basic understanding of the regulatory framework for which the assessment is being performed. Otherwise, inappropriate conclusions that are inconsistent with the regulations may result. This happened with one particular subcontracted clinical expert who was convinced that a manufacturer was required to conduct a clinical study in each member state where the device was to be marketed; in fact, this is not required by European medical device regulations. Another subcontracted clinical expert insisted that a literature search was required as the basis for demonstrating device safety and performance in a clinical evaluation report, even though the manufacturer had carried out multiple clinical studies, including a very large randomised controlled study with convincing results. This could have been avoided had these experts been properly trained on the European device regulations before being employed in the assessment process. This may not be a common problem, but a check on hiring and training policies of external experts is a worthwhile discussion to have with a potential Notified Body.

Notified Body Operations Group (NBOG)

The NBOG was established in July 2000 by member states and the European Commission in response to widespread concern over variability and inconsistency in the performance of Notified Bodies in the medical device sector and their individual designations for specific device types. NBOG's terms of reference are to improve the overall performance of Notified Bodies in the medical device sector by primarily identifying and promulgating examples of best practices to be adopted by both Notified Bodies and organisations responsible for their designation and control. NBOG membership includes the European Commission and nominees from the member states' Designating and Competent Authorities, and is open to EFTA/EEA Competent Authorities as well as candidate and accession countries.

The NBOG website (www.nbog.eu) indicates the current chair and vice chair, work programme and methods, reports and news items, and, most importantly, a link to NBOG documents, including a detailed *Designating Authorities Handbook*, designed as a best practices guide for authorities responsible for the designation of Notified Bodies. Other documents that may be of interest to readers are the NBOG's Best Practice Guides, which are shown in Table I. They provide guidance on specific aspects related to the activities of Notified Bodies. For example, the change of a Notified Body, either voluntarily by the manufacturer or if the Notified Body is no longer able to operate or provide a required service, is an important event that should be managed carefully and in an organised manner. The NBOG guide on this subject contains helpful information on how to do this.

Another useful document is the "Checklist for audit of Notified Body's review of Clinical Data/Clinical Evaluation" (NBOG CL 2010-1, March 2010). The document is intended to be used by Designating Authorities to determine a Notified Body's capability for assessing clinical evaluation documents and specific clinical data to support compliance with clinical data and clinical evaluation requirements. The document is divided into two main sections: resource requirements and process requirements. The section on process requirements contains a detailed set of questions concerning the clinical data procedures and documentation that is expected to be checked during a quality system audit and technical file evaluation. A manufacturer reviewing these questions will know what is expected of a Notified Body and will be better prepared to respond to the questions that Notified Bodies will ask if they follow this best practice guide. Although not the subject of this article, it should be pointed out that the "Clinical Evaluation Guidelines" (MEDDEV 2.7.1 Rev 3, December 2009), also contain a checklist that Notified Bodies are expected to use for the assessment of clinical data; although, the questions are not identical to those contained in the NBOG guide, there is some overlap.

NBOG also makes available on its website reports of work, including the current activities of the Designating Authorities to effectively monitor and control their Notified Bodies. They are found on the Reports and News webpage, www.nbog.eu/5.html.

TABLE I: NBOG Best Practice Guides

Number	Title	Date
NBOG BPG 2006-1	Change of Notified Body	Nov 2008
NBOG BPG 2009-1	Guidance on Design-Dossier Examination and Report Content	Mar 2009
NBOG BPG 2009-2	Role of Notified Bodies in the Medical Device Vigilance System	Mar 2009
NBOG BPG 2009-3	Guideline for Designating Authorities to Define the Notification Scope of a Notified Body Conducting Medical Devices Assessment	Mar 2009
NBOG BPG 2009-4	Guidance on Notified Body's Tasks of Technical Documentation Assessment on a Representative Basis	Jul 2009
NBOG BPG 2010-1	Guidance for Notified Bodies auditing suppliers to medical device manufacturers	Mar 2010
NBOG BPG 2010-2	Guidance on Audit Report Content	Mar 2010
NBOG BPG 2010-3	Certificates issued by Notified Bodies with reference to Council Directives 93/42/EEC, 98/79/EC, and 90/385/EEC	Mar 2010

For example, the report of 14/15 January 2013 on the outcome of three meetings held in 2012, discusses key aspects of the meetings, which included measures to improve audits in light of the Pip breast implant scandal and the status of work to revise several NBOG guides.

Longstanding concerns

A report from the European Medical Devices Expert Group, "Report on the Functioning of the Medical Devices Directive" (2002),[2] describes generally accepted concerns regarding the competence of Notified Bodies to perform the tasks for which they are designated, differences in interpretation between Notified Bodies and lack of transparency in the performance and control of their activities. Directive 2007/47/EC that revised the MDD and AIMDD addressed these concerns. From the time that those revisions became mandatory in March 2010, efforts to improve the functioning of Notified Bodies continued at a relatively steady pace. More recently, the Pip breast implant scandal has led to additional measures being considered for the designation and control of Notified Bodies.

In consideration of the critical role that Notified Bodies play in the European regulatory system, manufacturers need to understand how they are monitored and controlled and how that could change. Part two of this article will discuss Team-NB, a Notified Body organisation, and important criteria to consider in selecting a Notified Body.

References

1. http://ec.europa.eu/health/medical-devices/files/meddev/2_10_2date04_2001_en.pdf.
2. www.team-nb.org/documents/2008/finalreport5-6-02cor1_3-july02.pdf.