New European Guidance on **Borderline Products**

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The European Commission has recently updated an important guidance document on determining whether or not a medical product is subject to medical device or medicinal product regulations. In addition, a new manual that provides practical examples has also been issued. This article discusses these documents.

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Updated MEDDEV guidance

In July 2009, the European Commission (EC) issued a guidance document titled, "Borderline Products, Drug-Delivery Products and Medical Devices Incorporating, As An Integral Part, An Ancillary Medicinal Substance or An Ancillary Human Blood Derivative (MEDDEV 2.1/3 rev3)." The document can be obtained from the EC's website.[1] It replaces a previous version issued in 2001 and titled, "Demarcation Between: Directive 90/385/EEC on Active Implantable Medical Devices, Directive 93/42/EEC on Medical Devices, and Directive 65/65/EEC Relating to Medicinal Products, and Related Directives."

The purpose of the latest version of the document is to provide explanations and examples to aid the determination of whether a product falls under the Medical Device Directive (93/42/EEC) (MDD) or the Active Implantable Medical Devices Directive (90/385/EEC) (AIMDD) on the one hand, or under the Medicinal Products Directive (2001/83/EC) on the other. Readers familiar with the previous version will note that important changes have been made in the new version.

For example, the organisation and titles of the sections have been modified, which makes it easier to find explanations on borderline issues, drug delivery products and medical devices incorporating as an integral part a substance, which if used separately may be considered a medicinal product or a human blood derivative. Also, the current version includes advice regarding human blood derivatives. Another improvement is that the electronic version of the document contains hyperlinks. For example, the table of contents section titles are hyperlinked to the relevant sections in the document and there are also several hyperlinks to relevant websites and referenced documents.

Of significant importance is the fact that the current version of the guidance document incorporates the revisions made by Directive 2007/47/EC, which amends the MDD and the AIMDD. The amendments come into force on 21 March 2010.

Nonexhaustive list of examples

A useful feature of the previous version of the guidance document was the inclusion of lists of product examples for each of the following categories:

- medical devices
- medicinal devices
- medical devices incorporating a medicinal substance with ancillary action
- accessories to medical devices
- drug delivery medical devices
- medicinal products where the device and medicinal substance form a single integral product.

The updated guidance document also contains product examples; however, it points out that the list is not exhaustive and that other examples can be found in the "Manual on Borderline and Classification in the Community Regulatory Framework for Medical Devices (Version 1.4, 05-2009), which was developed by the Medical Devices Expert Group (MDEG) on Borderline and Classification. This manual can be obtained from the EC's website[2] and is discussed later.

Devices incorporating ancillary substances

The advice on medical devices incorporating as an integral part, a substance, which if used separately may be considered a medicinal product, has been expanded to include human blood derivatives and additional advice. It emphasises, based on the language in the Directives, that a product will be →

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considered a medical device providing the substance incorporated in the device meets the following three conditions:

- the substance, if used separately, may be considered to be a medicinal product or a human blood derivative
- the substance is liable to act upon the human body
- the action of this substance is ancillary to that of the device.

Another helpful addition is a statement that a medical device incorporates a medicinal substance as an integral part, within the meaning of Article 1 (4) of the MDD and Article 1 (4) of the AIMDD, if, and only if, the device and the substance are physically or chemically combined at the time of administration to the patient (such as use, implantation or application).

This means that if a medical device and a substance that is considered to be a medicinal product or human blood derivative that is liable to act upon the human body are placed on the market separately, but at the time of administration are physically or chemically combined, then Article 1 (4) of the MDD or Article 1 (4) of the AIMDD applies. Thus, the combination will be regulated as a single medical device, providing the action of the medicinal substance or human blood derivative is ancillary to that of the device. It is interesting to note that no such distinction is made in the section on drug delivery products regulated as medicinal products or medical devices.

Consultation process

For medical devices incorporating as an integral part an ancillary medicinal substance, the Notified Body must verify the usefulness of the substance as part of the medical device, taking account the intended purpose of the device. The Notified Body must then seek a scientific opinion from one of the Competent Authorities designated by a European Member State or the European Medicines Agency (EMEA) on the quality and safety of the substance, including the clinical benefit/risk profile of the incorporation of the substance into the device. The same actions must be taken with regard to human blood derivatives, except that the Notified Body is obligated to seek a scientific opinion from the EMEA. This process is termed the "consultation process."

The section in the revised guidance document on the consultation process has been reorganised, expanded and updated. For example, in the new section C.3, Documentation to be Provided by the Notified Body to the Competent Authority, reference is made to an EMEA guidance document, "EMEA Recommendation on the Procedural Aspects and Dossier Requirements for the Consultation to the EMEA by a Notified Body on an Ancillary Medicinal Substance or an Ancillary Human Blood Derivative Incorporated in a Medical Device (EMEA/CHMP/401993/2005)."[3]

This EMEA document clarifies that consultation with EMEA on ancillary medicinal substances is voluntary; however, it is mandatory with regard to human blood derivatives. This document was adopted in April 2008 and came into effect in July 2008. It states that "the changes introduced by Directive 2007/47/EC will apply from 21 March 2010 and will be implemented in this recommendation by that date." Readers should note that the current version does not incorporate the changes made to the MDD by Directive 2007/47/EC and also does not mention the AIMDD, although the advice provided can also be applied to devices requiring consultation that fall under the AIMDD. In addition, because the document was issued in 2008, it refers only to MEDDEV 2.1/3 rev 2.

Manual on borderline and classification

As mentioned previously, the MDEG has published a manual on borderline and classification issues. The document was issued in May 2009 and provides the views of the MDEG on products or categories of products that have raised doubts about whether or not they are medical devices, in vitro diagnostic medical devices, active implantable medical devices, medicinal products, biocides or cosmetic products. It also covers certain classification issues under the MDD.

The introduction of the manual makes twelve points regarding the purpose and use of the manual. For example, the first point states that borderline cases are considered to be those cases where it is not clear from the outset whether or not a product is a medical device, an in vitro diagnostic medical device or an active implantable medical device. Readers should refer to the manual for the full text of this point. The second point states that classification cases can be described as those cases where there exists a difficulty in the uniform application of the classification rules as laid down in the MDD (or where, depending on interpretation of the rules, different classifications can occur for a device).

Point eight states that the views expressed in the manual are not legally binding, because only the European Court of Justice ("the Court") can give an authoritative interpretation of Community law. Furthermore, point nine states that the manual does not relieve national Competent Authorities from their obligation to render decisions in these areas for any individual product, on a case-by-case basis. National authorities, acting under the supervision of the courts, must proceed on a case-by-case basis, taking account of all the characteristics of the product.

The manual is organised into sections such as Medical Device/In Vitro Diagnostic Medical Device – Medical Intended Purpose, Borderline In Vitro Diagnostic Medical Device and Borderline Medical Device – Medicinal Product. Each section includes an introduction and several examples of products that have been the subject of questions raised. The introduction provides the relevant definitions such as those of a medical device, in vitro diagnostic product, medicinal product or other product category, which are specified in the relevant European Directive. It also refers to relevant Directives and MEDDEV guidance documents. The examples include a description of a particular product type, background information and an "outcome," which is the opinion on the regulatory category or classification reached by MDEG.

Start early

The ability to determine the correct regulatory category of some of the more innovative medical devices is becoming more difficult. Therefore, the information provided in the new guidance document and the manual developed by the MDEG

are welcome. Another important guidance document, the discussion of which is beyond the scope of this article, is "IVD Guidances: Borderline issues, A Guide for Manufacturers and Notified Bodies (2.14/1 rev. 1, January 2004), which should be consulted for information on IVD borderline issues. This document can be obtained from the EC's website.[4] Prudent companies will identify the regulatory category of their products at the very beginning of new product projects to avoid significant and unpleasant regulatory problems that can jeopardise the success of the project. They will also identify any differences in the regions where the product will be marketed, because the regulatory category of the product in one region does not guarantee that it will be the same worldwide.

References

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