**EUCOMED comments on the implications of some aspects of the adoption of the new pharma directive on existing and future medical devices**

## I. Introduction

Certain provisions of the revised version of the pharma directive (Directive 2001/83/EC on the Community Code relating to medicinal products for human use, as amended by Directive 2004/27/EC) may create substantial uncertainty in the medical devices and other non pharmaceutical sectors. Eucomed welcomes the Commission initiative to organize the hearing announced by Commissioner Liikanen in December 2003 at the Plenary of the European Parliament on this matter,

Technical development and the publication and existence of various sector specific directives, which contain a variety of product definitions, have created or contributed to create a situation where the number of borderline situations is increasing.

## II The Medical Devices Directive already deals with products that are not "pure" medical devices

A number of emerging new products, such as drug-eluting stents are combinations of medical devices with medicinal products. They are neither "pure" medical devices nor "pure" medicinal products. The current medical devices legislation has however been carefully drafted to provide an appropriate regulatory framework to accommodate technological innovation and guaranteeing a thorough review of the quality, safety and usefulness of the pharmaceutical component of such products prior to their placing on the market.

In summary, the principle intended purpose[1] of the product and the way in which this is achieved determines which legislation should apply. If the pharmacological, immunological or metabolic action of the combined product is ancillary to that of the medical device, the medical devices legislation will prevail. If, on the other hand, the primary intended mode of action is pharmacological, immunological or metabolic, then the medicinal products legislation will apply.

The definition of Medical Devices (Art. 1.2a of Council Directive 93/42/EEC of 14 June 1993 concerning medical devices, hereinafter also referred to as the "MDD") was to that effect carefully drafted as to minimise uncertainties in the field of application of the directive:

> *"a) 'medical device' means any instrument, apparatus, appliance, material or other article, whether used alone or in combination, including the software necessary for its proper application intended by the manufacturer to be used for human beings for the purpose of:*
> *— Diagnosis, prevention, monitoring, treatment or alleviation of disease,*
> *— Diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap,*
> *— Investigation, replacement or modification of the anatomy or of a physiological process,*
> *— control of conception,*

[1] The MDD defines principal intended purpose as follows (Article 1(2), g): *"the use for which the device is intended according to the data supplied by the manufacturer on the labelling, in the instructions and/ or in promotional material"*.

***and which does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means**;"*

## III. The provisions at stake in the Pharmaceuticals directive

A revision of the pharmaceuticals legislation was launched in November 2001. One of the proposals of the Commission was to change the definition of "medicinal products" in such a way that it would potentially accommodate some of the combined pharmaceuticals-medical devices and some, if not all, human tissue products. The European Parliament resisted this attempt, but the final outcome of the legislative procedure was the adoption by the European Parliament and the Council of Ministers of a new definition of medicinal product and the insertion in the recitals of the new directive of a sentence indicating that, where a product falls clearly under the definition of, for example, "medical device", it shall be covered by the Medical Devices Directive. At the same time, the European Parliament and the Council decided to maintain an article which states that "in case of doubt" the pharmaceutical legislation shall apply.

The definition in the revised pharma directive provides that a medicinal product is:

*"**Any** substance or combination of substances which may be **used in** or administered to human beings either with a view to restoring, correcting or modifying physiological functions **by exerting a pharmacological, immunological or metabolic action**, or to making a medical diagnosis*."

Trying to avoid the unintentional shifting of several medical devices from the scope of the MDD to the pharmaceuticals directive, the legislator included in the recitals of the new Pharmaceutical directive the following:

"Recital 7
*With the same objective of clarifying situations, where a given product comes under the definition of medicinal product but could also fall within the definition of other regulated products, it is necessary, in case of doubt and in order to ensure legal certainty, to state explicitly which provisions have to be complied with. **Where a product comes clearly under the definition of other product categories**, in particular food, food supplements, **medical devices**, biocides or cosmetics, **this Directive should not apply**."*
This wording fully and rightly acknowledges the application of the *lex specialis* principle.

An additional area of uncertainty arose from the subsequent (re-) introduction of article 2.2, which reads[2]:

*"**In cases of doubt**, where, taking into account all its characteristics, a product may fall within the definition of a 'medicinal product' and within the definition of a product covered by other Community legislation, **the provisions of this Directive shall apply**."*

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[2] Article 2.2 was originally not retained in the first reading of the European Parliament. It was also rejected by the Environment committee in the second reading, but "reappeared" during the negotiations between the European Parliament and the Council prior to the Plenary vote at the Parliament

This provision is based on the assumption that a given product can fall under two different product definitions. Whilst a combination product can indeed contain for instance a medicinal product element and a medical device element, a combination product cannot be at the same time a medicinal product and a medical device. This is why the MDD deals with products that are not "pure" medical devices (*supra*).

**IV. The medicinal products directive has created legal uncertainty, whilst the MDD gives clear guidance in the event of combination products**

Let us see where these provisions could create confusion:

First of all the wording of recital 7 and article 2.2 do not match: in the preamble it is indicated that, under certain circumstances, "*this Directive should not apply*", whereas in article 2(2), it is indicated that, under certain circumstances, "*the provisions of this Directive shall apply*".

Second, the question arises as to when the "in case of doubt" clause can be triggered?

A relatively simple example is represented by the above-mentioned drug-eluting stents. Stents are, generally, intended to keep blood vessels open in a mechanical manner. As most foreign objects introduced in the body, the body itself tends to react by creating scar tissue, which, sooner or later, in the case of the stents may reduce the lumen of the opened vessel (re-stenosis). Studies have demonstrated that the presence of particular substances on the stent can delay or even prevent the scar tissue growth, therefore improving the performance of the stent.

One may also consider the situation where there could be a need to deliver a specific substance in a specific location and that the most convenient means is to place it on a stent as carrier to allow slow delivery at that specific location.

These two scenarios both involve medical devices, having as an integral part, a substance, which, if used alone and under certain conditions, could be considered a medicinal product.

Both might fall under the definition of medicinal product, since they "*…may be used in human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action*".

However, taking into account the principal intended purpose of the product, in one case, the product falls clearly under the scope of the MDD. The clauses of the MDD which allow to make the above conclusion are contained in Article 1, paragraphs 3 and 4:

> *"3. If a device (in tended to administer a substance) is placed on the market in such a way that the device and the medicinal product form a single integral product which is intended exclusively for use in the given combination and which is not reusable, that single product shall be governed by Directive 65/65/EEC. The relevant essential requirements of Annex I to the present Directive shall apply as far as safety and performance related device features are concerned.*
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> *4. Where a device incorporates, as an integral part, a substance which, if used separately, may be considered to be a medicinal product within the meaning of Article 1 of Directive 65/65/EEC and which is liable to act upon the body with action ancillary to that of the device, that device must be assessed and authorized in accordance with this Directive."*

It follows from the above, that the MDD gives clear guidance on how to benefit from the relevant legislation when the two elements are present at the same time, thus avoiding the impossible concomitant application of the two legislative measures to the product.

In the above example, the manufacturer shall evaluate the role of the medicinal product which coats the stent and, depending whether the action of the medicinal product is ancillary[3] to the action of the device or not, the combination shall be treated as a medical device or as a medicinal product.

## V. Need for clarification

Another aspect of Article 2(2) deserving further clarification relates to the statement in that article *"taking into account all its characteristics"*. In the case of the borderline between medicinal products and medical devices, Eucomed understands this statement to imply for all stakeholders that only **after** having thoroughly analysed **the principal intended purpose** of the product, a doubt, may, in very exceptional cases, subsist. Indeed it is Eucomed's understanding that this text puts an obligation on all stakeholders (including the manufacturer, competent authority, notified body and eventually also the courts) to first review all the characteristics of the product, and for the border between drugs and devices, the legislation prescribes that the substantive test to be applied is the principle intended purpose as follows from the MDD. Only if there would still be a doubt after that test, Article 2(2) of the pharma directive could be triggered.

## VI Concluding remarks

Eucomed therefore respectfully requests that the Commission, in order to clarify the situation that has been created following adoption of the new medicinal products directive, issue a guidance along the lines of the present paper In other words, Eucomed calls for a guidance that states that art. 2/2 will be applicable only in cases that cannot be resolved on the basis of the medical devices legislation.

[3] Which means: the principal intended action of the product in or on the human body is not achieved by pharmacological, immunological or metabolic means, but the product may be assisted in its function by such means (art.1.2.a of the 93/42/EC).