no evil

Mike Murphy on how the CE Mark compares with FDA approval for medical/cosmetic lasers and IPL devices

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Mike Murphy has been involved with lasers and IPL systems since 1986 when he worked with plastic surgeons in the Plastic and Reconstructive Surgery Unit, Canniesburn Hospital, Glasgow. He is a physicist and was involved in clinical research into the removal of vascular and pigmented lesions and tattoos using lasers and was also the laser safety officer in the hospital's laser unit. He has published a number of clinical reports in peer-reviewed journals across the world in both clinical and theoretical aspects of laser/IPL treatments in skin. In the last few years he has worked as an independent consultant in both lasers and IPLs around the world.

There appears to be some confusion about FDA approval and how it compares with the CE Mark in the cosmetic/medical arena. Many people in Europe mistakenly believe that FDA approval is a 'higher standard' than the CE Mark. Certainly, many manufacturers (particularly American suppliers and their distributors) use this confusion to imply that their equipment is, somehow, superior to the European-based competition. Hopefully this article will help to shed some light on the subject.

FDA Approval – What is it?

The FDA, or Food and Drug Administration, is a US government body which "regulates companies who manufacture, repackage, re-label and/or import medical devices which are sold into the US market, including lasers, IPLs, ultrasound and x-ray equipment", according to their web site.

Under the FDA's classification system medical/aesthetic devices are divided into three regulatory (risk) classes - I, II and III. Devices are classified according to the level of control necessary to ensure the safety and the effectiveness of the device. Regulatory control increases from class I to class III and these define the regulatory requirements that must be satisfied before the device may be sold on the open US market.
Under current regulations any electrical medical/aesthetic device must be approved under either a Premarket Approval (PMA) submission or a Premarket Notification 510(k) (or, if it is a low risk device, it may be classed as 'exempt').

Device Type	FDA Regulatory Requirements
Class I	'Low Risk' - may only require a 510(k)
Class II	'Medium Risk' - may only require a 510(k)
Class III	'High Risk' - requires a PMA approval

PMA submission

A PMA submission is the most stringent type of device marketing application required by the FDA. A device manufacturer/supplier must obtain approval of its PMA application before marketing the device into the US market. Devices which require PMAs are Class III products which are deemed to be of 'high risk' in that they may pose a significant risk of injury or illness, such as lasers or IPL units. The approval process for a PMA is much more rigorous than a 510(k) submission (see below) and must include clinical data to substantiate any claims made by the manufacturer.
The evidence submitted to support a PMA must show that the device is not only safe to use, but also effective for its intended use(s). Hence, a PMA approval is an actual 'approval' which is based on clinical results.

Premarket Notification 510(k) submission

A 510(k) submission is significantly different from a PMA in that it merely requires the manufacturer to show 'substantial equivalence' to a similar, existing device which is "legally in commercial distribution in the US market". It does not mean that it has been FDA approved – it is essentially a paper exercise. Indeed, some devices achieve a 510(k) against another system which itself only has a 510(k).
Such a submission does not require clinical evidence to substantiate its claims. However, some FDA reviewers may request evidence, if they feel it necessary.

In fact, when a manufacturer receives a 510(k) 'approval' letter from the FDA they are specifically instructed not to use the terms 'safe' or 'effective' in their marketing literature or web sites because the FDA do not endorse such claims based on this assessment. It is merely 'substantially equivalent.'

Many US companies offer devices which have a number of clinical claims to broaden their market appeal. However, a 510(k) only requires that ONE of these claims is actually met. This is now commonplace within the US market, and, consequently, internationally. Hence, a device which claims to treat hair, blood vessels and pigmented skin marks may actually have only been tested on hair or blood vessels or brown skin marks, but not necessarily all three.

Before a company is allowed to market a device in the US under a 510(k) they must receive a written 'order' from the FDA which states that the device has been 'cleared' for commercial distribution in the US – it does NOT mean that the device is 'approved' by the FDA. Merely that it is 'substantially equivalent' to an existing device.

Finally, a 510(k) submission may only take 90 days to clear while a PMA submission could take six months or more plus the time for clinical trials (which themselves could take years.) This fact alone should raise some concerns about any device cleared under the 510(k) process.

I recently spoke to a very well-known American investigator who does a lot of work for companies seeking FDA approval for their equipment. His words were that "they (the FDA) are all over the place." When asked what he meant he replied that the process depended entirely on which FDA official reviewed the submission. Often, under a 510(k), one reviewer may just want to see the specification sheet, while another may ask for three or six months' clinical results. However, he did admit that the FDA are "becoming more hard-nosed now."

A conversation with an American medical laser industry consultant confirmed these comments. Recently, a report1 was published which investigated the 'recall' rate on medical devices by the FDA. The authors found that there had been 113 recalls in the period 2005 to 2009 based on high risk devices which could 'cause serious health problems or death.' Out of these 113 devices 71% had been cleared through the 510(k) process which indicates a serious, potential problem with this particular route. Interestingly, 19% of these devices had been processed via the PMA route which is, perhaps, more worrying, since this is supposed to be a much more rigorous process. (7% were devices which had been considered 'exempt' from FDA regulation – and yet were subsequently found to be dangerous.). The authors concluded that a reform of the regulatory process should be undertaken to ensure future safety of medical devices. I would say that understatement is clearly evident here.

Clearly, this shows that not all FDA 'approvals' are the same. While a PMA submission is more stringent than the 510(k) process, it is obvious that there is a significant efficacy and safety (or device risk) difference between the two procedures. In other words, 'FDA approval' in itself is meaningless without further explanation as to which type of 'approval'.

In summary, FDA approval basically relates to studies proving that claimed clinical results of any device are shown to be statistically significant (compared with the original state) and that any side effects of the clinical procedure(s) are "reasonable" and not life threatening.

CE Mark (Declaration of Conformity)

The CE Mark is a legal requirement for virtually every product sold within the EU. Before any medical/aesthetic product can be placed on the European market they must meet the requirements of the relevant EU product Directives. These Directives are joint rules that have been put in place to simplify trade to and between the member countries of the European Union.

The CE Mark has specific meanings including the following:

1. It is a manufacturer's declaration that their product complies with the required health and safety regulations under Article 100A, European health, safety and environmental legislation, known as the Product Directives;
2. The product may be legally placed into the market of any EU country;
3. It shows users that the product meets the designated minimum safety standards and a minimum quality level
4. It allows for the withdrawal of non-conforming products by customs or enforcement authorities.

As with the American FDA system such products are usually classified under the following scheme: The CE mark means that a manufacturer is satisfied that his product conforms with the relevant Essential Requirements in the 93/42/EEC Directives and that it is fit for its intended purpose. However, they do not need to submit clinical data to support their claims. It also means that the product can be freely marketed anywhere in the EU without further control.

Unlike the FDA processes, the requirements of the CE Mark are clearly established in the Directives. These are quite precise and minimise the vagueness which appears to plague the FDA processes. That's not to say that the CE regulatory process is perfect – there is something of a grey area in the definitions of whether a procedure is 'medical' or 'cosmetic'.

The CE Medical Mark

The CE Medical mark is a requirement for all medical devices used in 'medical applications' – this applies to most Class III products, but not necessarily to the other classes. Regulations dictate that extensive data from clinical trials are provided as part of any submission to support any claims. Any device used in hospitals and similar clinical settings must have the CE Medical mark to ensure no interference with other life-sustaining equipment, such as respirators.

Many medical and aesthetic devices fall into the Class II category – these include lasers, IPL and RF systems, ultrasound and similar devices. Class II devices do not require clinical investigation data to be provided as part of the submission, but it is recommended that any clinical claims are supported by a "compilation of the relevant scientific literature."

For example, an IPL system which is sold for hair removal only is classed as a 'cosmetic device' and therefore does not require the CE Medical mark – the CE mark is sufficient. However, if the same unit is used to treat haemangiomas/port wine stains then it will be classed as a 'medical' unit and hence require the CE Medical mark, since these are judged to be vascular abnormalities. But, the treatment of 'thread veins' is regarded as an aesthetic procedure in many European countries and hence there is no need for the CE Medical mark.

Device Type	CE Regulatory Requirements
Class I	devices with low risk such as external patient support products
Class IIa / IIb or IPL devices	devices with medium risk such as laser
Class III	devices with high risk such as cardiovascular catheters

Interestingly, the CQC no longer requires registration (in England and Wales, as of October 2010) of IPL units used solely for hair removal, while they do require registration for devices used to treat blood vessels.. They do require registration for all

CE Medical Mark	Equipment must satisfy EU medical devices directive - clinical data evidence required only for Class III devices, but not necessarily for IPLs or lasers.	Legally required for all 'Medical Devices' sold within the EU – not valid in the US. Required for all hospital-based electrical equipment
CE Mark	Equipment must satisfy general EU safety Directives – no clinical evidence required	Legally required for virtually everything sold within the EU – not valid in the US
Premarket Approval (PMA)	Equipment must satisfy FDA requirements including data to support clinical claims	Required for distribution and use in the US – not required in the EU
Premarket Notification 510(k)	Equipment must be 'substantially equivalent' to an existing device on the US market	Required for distribution and use in the US – not required in the EU

medical/aesthetic lasers used in England and Wales regardless of their clinical applications (including hair.).

However, light-emitting devices, such as IPLs or lasers, can be granted the CE Medical mark without clinical results being submitted during the application process. Hence these systems are not necessarily more reliable in terms of efficacy, contrary to widely believed misconceptions.

In conclusion, what I am trying to say here is that neither CE nor FDA approval guarantees that medical/aesthetic equipment will deliver good clinical results. They are essentially safety tests with large variations in clinical efficacy. The main difference is that medical/aesthetic devices cannot be sold legally in Europe without the CE mark while there is no legal requirement for any FDA approval in the European markets.

So, when a salesman tells you his equipment 'has FDA approval' be sure to ask him 'is that a PMA or a 510(k) approval?' Because, as we now know, PMA is a real approval with reference to actual clinical results while a 510(k) is not. And, be absolutely sure the equipment has the CE or CE Medical mark – it MUST appear on the body of the equipment – otherwise you could end up in serious trouble if something goes wrong.

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Summary of Regulatory Approvals

One final word of warning; many products are now manufactured in China at a fraction of the cost of EU-manufactured devices. I have learned, via a manufacturer who has factories in Europe, South America and China, that CE certification may be easily 'bought' in China without the proper requirements being met. A 'real' CE Mark should show the identification of the Notified Body – a company licensed to ensure compliance with the Directives.

Since any importer into Europe bears responsibility for the safety of their imported products, they should satisfy themselves that their equipment truly does meet the various Directives required under the CE Mark. Otherwise they might get an unexpected knock on their door one night.

REFERENCES

(1) Medical Device Recalls and the FDA Approval Process Archives of Internal Medicine, Vol. 171, No. 11, June 13, 2011

Note: The author has personal experience of 510(k) submissions to the FDA with medical lasers in the past.