LEADING ARTICLE

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Post-Marketing Surveillance and Vigilance for Medical Devices

The European Approach

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Abstract

The extent to which the medical device manufacturers are responsible for actively monitoring the performance of their products after they have successfully passed the rigorous pre-market approval process has always been a matter of diverse opinion. Within Europe, the law is unhelpfully vague on this point. While there are some comparatively clear obligations for reporting incidents to the authorities (known as the 'vigilance system'), little detail is given on how diligently the manufacturer should try to find out about such incidents.

In the early stages of the European Community Directives covering medical devices, there was much emphasis upon formulating guidance to help interpret the vigilance reporting requirements. It is, however, only recently that attention has turned to attempting to clarify what is expected from post-marketing surveillance (PMS) in its broader sense.

This article discuses both the vigilance and PMS processes and outlines the currently available European, and particularly UK, guidance documents which are aimed at promoting a more level playing field across industry where these activities are concerned. In particular, it explains the principle differences between vigilance and post-marketing surveillance: the former being the reporting of adverse incidents by manufacturers to the regulatory authorities and their subsequent sharing of key incident data between each other; the latter being the process by which information on overall devise performance is captured, analysed and acted upon. Nevertheless, it is still a struggle to gain widespread appreciation that these two activities are not in fact one and the same.

With the introduction of the Medical Devices Directives[1-3] in Europe during the 1990s, manufacturers and competent authorities (CAs) such as the UK Medical Devices Agency (MDA) assumed certain incident reporting obligations under the European Vigilance System. These are spelt out in the articles and annexes of the European Community (EC) Directives and are becoming better known and understood with the proliferation of pertinent guidance documents.

Most importantly, the revision of the EC Vigilance Guidelines[4] provided a number of much needed points of clarification, particularly for CAs, by drawing upon experience gained over the first 4 years of vigilance reporting.

1. The Vigilance System

The fundamental principal of vigilance is to reduce the chance of the same types of adverse incident being repeated in different places across the European Economic Area. This is achieved via a 2-part process whereby manufacturers are obliged

to report serious incident (known as 'vigilance cases') to relevant CAs, and the CAs then have to report a defined subset of these to each other and to the European Commission. Despite being a seemingly simple objective, it must be remembered that the success of the latter part of vigilance requires coordination of 19 different countries with different cultures and experience, not to mention different languages. Vigilance is as much a challenge for CAs as it is for industry.

The MDA has seen a striking improvement in the interpretation of the vigilance requirements both among industry and fellow CAs over the last few years. While the revision of the EC Vigilance Guidelines has undoubtedly improved consistency among CAs, the emergence of a number of UK device-specific vigilance guidance documents clarifying reportable events for industry, is also leading to greater uniformity of approach by manufacturers. While at present these guidance documents[5-8] (covering joint replacements, breast implants artificial heart valves and coronary stents) apply only in the UK, it is hoped that they may be adopted by other CAs at a European level, with any necessary amendments or modifications.

Although I have described vigilance as a 2-step process, it is well recognised that in reality its success relies on a previous step – the reporting of the adverse incidents by the device users to the manufactures and/or CAs. Since the EC Directives, however, were designed principally to facilitate free-trade across Europe, they do not provide for mandatory user reporting. Instead, this remains an issue of national variation, with some countries requiring such reporting under separate laws. Some countries, like the UK, call on the good will of users to cooperate under a voluntary system, and others make no provisions at all, thereby potentially jeopardising the success of the vigilance system.

Within the UK, we have operated a highly successful user reporting system for medical devices for more than 15 years, which has much in common with the better known UK 'yellow card' system for reporting adverse drug reactions. The reports from device users are submitted to MDA's 'Adverse Incident Centre' and then promulgated to the relevant device specialists, as is the case for the manufacturer incident reports. Although there is no statutory requirement for patients, clinicians and other medical device users to notify the MDA of device-related adverse events, in practice compliance is high and this provides an invaluable supplement to the manufacturer mandatory reporting system. These reports add value to the incident investigation process in 3 principle ways. First, they often provide a second, user perspective on the same event already reported by the manufacturer. Secondly, they provide a means of alerting the regulatory authority to certain device-related problems which may have been outside the scope of the statutory vigilance reporting requirements. These often involve user-device interface problems where the whole system of device-usage, its environment and practical utility, require attention to try to reduce risks. Thirdly, user reports provide the only means within Europe for the regulatory authorities to exercise a degree of audit on the compliance by manufacturers with their statutory vigilance reporting obligations.

2. Post-Marketing Surveillance

There has always been much talk about vigilance, a popular subject at conferences and meetings. It is only more recently that attention has turned to the fact that vigilance is only a small aspect of the manufacturer's wider post-marketing surveillance (PMS) obligations under the EC Directives. Within the annexes of the EC Directives it is stated that manufacturers must 'institute and keep up-to-date a systematic procedure to review experience gained from devices in the post-production phase'. The need to notify CAs of vigilance cases is 'included' within, but is not equal to, this PMS requirement. The MDA's experience has shown that this obligation is often poorly understood, and frequently underestimated by industry.

PMS is a 3-stage process (see fig. 1). The first and often most difficult stage is obtaining meaningful feedback on device performance to serve as the 'input' to the PMS process. The passive aspect

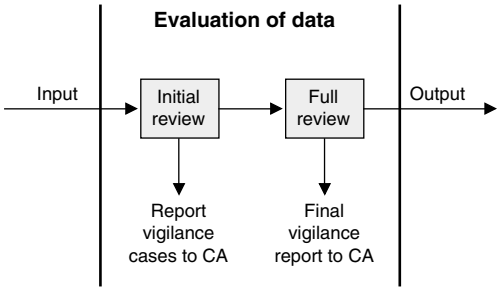

Fig. 1. The three phases of post-marketing surveillance. **CA** = competent authorities.

is achieved with minimal effort by the manufacturer, since, for example, customer complaints and problems encountered by field representatives or maintenance engineers, should readily come to the attention of the regulatory affairs manager. However, for other than the lowest risk devices, such a passive approach is seldom adequate. In addition, it is expected that a reasonable range of proactive activities will be initiated to solicit information from customers, to collect data from the literature, or to identify finer performance characteristics from ongoing in-house testing etc. In the case of implantable devices, systematic post-marketing clinical trials, device registries or explant evaluation studies should also be considered. The key to determining the nature and extent of PMS for any particular device, is a thorough understanding of the device's risk assessment, its previous clinical history and any remaining unanswered performance questions. No one set of PMS activities will be appropriate for all device types, of varying technological maturity, and made by companies with different infrastructures and priorities.

The second phase of PMS is the evaluation of data on device performance and the determination of the need for any form of (corrective) action. It is within this phase that reportable vigilance cases are identified and an initial report is filed with the CA. This phase then includes a thorough analysis of the performance issue or a full incident investigation, and subsequent final vigilance report to the CA confirming the company's conclusions.

The final 'output' phase of PMS comprises implementation of any actions to be taken as a result of the evaluation of input data. In many cases there will be no action, where the feedback serves primarily to confirm the anticipated level of performance of the device, but on occasions will include field action, or design or process changes, for example, to address identified risks.

As yet less guidance is available dedicated to PMS than to vigilance. To address this need, last year the EC Notified Bodies Experts Group produced some generic device guidance to expand upon the text within the EC Directives.[9] In the main, however, to find useful advice on PMS, one must recognise that above all, it forms as essential part of any complete quality system (see fig. 2). It is the last stage of the product development lifecycle. As with any cyclical process it follows that it also serves to provide vital input to the first stage of product development, design control. There are a number of standards dedicated to interpreting the quality system standards ISO 9000 and EN 46001,[10] which offer comments upon what is required of PMS. The most notable being ISO 9000-4[11] which states that the feedback system should 'permit the analysis on a continuing basis, of the degree to which the product satisfies customer requirements or expectations on quality, including safety and dependability', and EN 50103:1995[12] which references the important concept of detecting trends in device performance in order to identify problems. While this latter guidance specifically applies to active devices, the concept is fully transferable to other higher

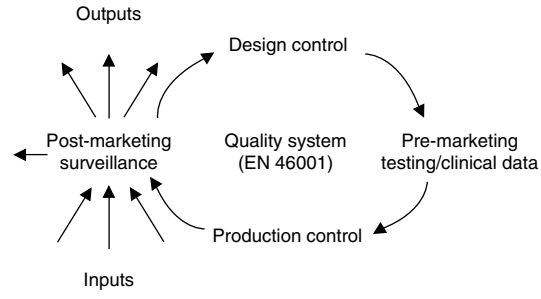

Fig. 2. Post-marketing surveillance: one part of a quality system.

risk products. Last year, the MDA also published the first UK device-specific guidance document on post-marketing surveillance.[13] This document details minimum expectations for the continued surveillance of the performance of joint replacements after they have received market approval, including the need to continue the follow-up of patients enrolled within any pre-marketing clinical investigations. It also highlights the value of structured post-marketing clinical studies, and emphasises that data collection within such studies should be to similar standards to those applied in the pre-marketing trials. It acknowledges the place of implant registries in tracking devices and their performance, and stresses the importance of forging good communication links with the medical profession to obtain expert, up-to-date feedback.

3. Conclusion

Notably, none of the referenced guidance documents specify the actual logistics or structure of an ideal PMS system. This may be a reflection of the fact that any company is free to develop whatever system best fits their needs, provided the scope of activity exceeds an acceptable minimum for each device type. However, one current goal of many regulatory authorities is simply to gain a common appreciation that PMS and vigilance are not one and the same. PMS involves casting the net widely to capture information which may lead to the submission of vigilance reports, in addition to meeting a number of other broader company objectives.

It is important to remember that PMS is not only there for the bad things in life. It is also the way in which manufacturers obtain positive feedback on device performance and ideas for product enhancements. While these aspects may be of less interest to the regulatory authority, they remain vital for the continued market viability of the product.

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