Medical Device Serviceability4.1 INTRODUCTION

6.1 Effective post-market surveillance

In order to comply with the European Union (EU) Medical Device Directives – 90/385/EEC Active Implantable Medical Directives (AIMD), 93/42/EEC Medical Device Directive (MDD) and 98/79/EC In Vitro Diagnostics Device Directive (IVDD) (referred to as 'The directives' hereafter), manufacturers must conduct post-market surveillance (PMS). As outlined in the quality assurance area of the annexes of these directives, PMS requires:

1. that the manufacturer institute and maintain an up-to-date systematic procedure to review experience gained from devices in the post-production phase, which include provisions referred to in Annex X (93/42/EEC), or Annex VII (90/385/EEC) and;
2. the implementation of appropriate means to apply any necessary corrective action.

The directives, in conjunction with the harmonized standards, form a framework for manufacturers to develop a comprehensive feedback system intended to ensure the continued safe-use of a device for the manufacturer's intended purpose.

6.1 The Requirements of Post-Market Surveillance (PMS)

PMS is a collection of processes and activities used to monitor the performance of a medical device. These activities are designed to generate information regarding use of the device to expediently identify device design and/or usage problems and accurately characterize the real-world device

behavior and clinical outcomes. The need for PMS arises immediately upon commercialization of the device.

- Ensuring adequate medical input into the risk management process during product development will help manufacturers characterize possible product safety issues. The risk profile of the device evolves from these efforts and can be used to effectively develop the PMS strategy for the device.
- The manufacturer has a long history of development and marketing of similar device types, they are likely to have a clear understanding of the patient population and the reasonably foreseeable risk associated with the device.
- Available data regarding state-of-the-art market experience for similar products and technology may be adequate for low-risk devices with a long history of clinical use.
- In the case of new technology, manufacturers often have a limited understanding of the patient population and the complexities of the disease state, which may affect the performance of the device. This limited knowledge may result in under or over representation of risks in the pre-market assessment of the device design and its interaction with the patient/user.

As shown in Table 1, the flow of information into risk management comes from a wide variety of activities and individuals including patients, physicians, healthcare facilities, regulatory authorities, professional societies, researchers and internal personnel.

Table 1 – Examples of PMS data and their respective action types

Proactive	Reactive
• Customer surveys • Post CE mark clinical trials, including PMCF • Manufacturer sponsored device tracking/implant registries • Expert user groups (focus groups)	• Customer complaints • Unsolicited user feedback (other than complaints) • Maintenance/service reports • In-house testing (routine) • Failure analysis • Social media • Literature reviews • Regional or national device registries (non-manufacturer sponsored trials)

6.2 The vigilance guidance document

These guidelines describe the European system for notification and evaluation of Incidents and Field Safety Corrective Actions (FSCA) regarding medical devices; this is known as the Medical Device Vigilance System (MDVS). The scope of these guidelines is relevant to 'incidents' occurring within the member states of the EEA, Switzerland and Turkey with regard to the following:

a) Devices which carry the CE mark.

b) Devices that do not carry the CE mark but fall under the scope of the directives (e.g. custom-made devices).

c) Devices that do not carry the CE mark because they were placed on the market prior to the implementation of the directives.

d) Devices that do not carry the CE mark but where such 'incidents' lead to (a) corrective action(s) relevant to the devices mentioned in a), b) and c).

A serious deterioration of health is defined as a:

- life-threatening illness;

- permanent impairment of a body function or permanent damage to a body structure;
- a condition necessitating medical or surgical intervention to prevent the above;
- fetal distress, fetal death or any congenital abnormality or birth defect.

Manufacturers should not be quick to dismiss events in which actual harm was not caused. Device malfunctions which could cause or contribute to a death or serious deterioration in health must be reported.

As common among regulatory authorities, required timelines for reporting correspond to the risks associated with public health. Timelines for the initial reporting of an incident is interpreted as 'immediately, without any unjustified delay'. Timelines for the three main incident categories are:

- serious public health threat – two calendar days after event discovery by the manufacturer;
- death or unanticipated serious deterioration in health – 10 elapsed calendar days following the date of event discovery;
- others – not later than 30 days elapsed calendar days following the date of event discovery.

6.3 An overview of the PMCF guidance document

It is important to note that Post-market clinical follow-up (PMCF) plans are not only relevant for high-risk devices. For example, residual risk (risk that remains after control measures have been taken during the pre-market phase or at other steps) is the primary type of risk that is addressed in the post-marketing phase. Residual risk includes known or emerging risks and potential risks due to statistical limitations.8 PMCF plans are beneficial for any class of device that is affected by defined parameters known to contribute to residual risk. the

circumstances under which PMCF may be necessary, include but are not limited to:

- novel medical technology;
- high product-related risk;
- high-risk anatomical locations;
- high-risk target populations (e.g. children, elderly);
- severity of disease/treatment challenges;
- unanswered questions of long-term safety and performance;
- identification of previously unstudied subpopulations which may exhibit different benefit/risk-ratio (i.e. hip implants in different ethnic populations);
- verification of safety and performance of device when exposed to a larger or a more varied population of clinical users.

Elements of PMCF studies include:

- clearly stated objective(s);
- scientifically sound design with an appropriate rationale;
- logical study plan and implementation;
- appropriate statistical analysis of data, interpretation, and conclusion.

6.4 Balancing pre-market and post-market clinical data guidelines

To help manufacturers determine when pre-market data is not sufficient to fulfill the need for a PMCF, the (revisions to the PMCF guidance document MEDDEV 2.12 Rev. 2) outlines the 'limitations in the clinical data available in the pre-market phase,' including:

- a limited number of subjects;
- a narrow diversity in study population;

- relative homogeneity of subjects and investigators (users);
- an imbalance between use under controlled variables versus use under a full range of conditions encountered in general medical practice.

The guidelines further suggest 'complete characterization of all risks may not always be possible or practical in the pre-market phase.' It may also be prudent for manufacturers to ask themselves the following questions to help guide the justification for either conducting or foregoing a PMCF:

- Does pre-market clinical data reveal any unanswered questions about safety or effectiveness?
- Did any adverse events occur that warrant further investigation?
- Was pre-market clinical data improperly generalized?
- Does the lifespan of the device extend beyond the time frame that pre-market clinical data was collected?
- Has new information emerged that affects pre-market data?
- Has the use of the device been extended to populations that were not included in clinical trials?
- Has the product been altered in any way from the product that was used to gather pre-market clinical data?

6.5 Communication with notified bodies (NB)

Given the presence of several interacting and authoritative guidance documents and standards, all of which create a set of larger, more comprehensive guiding principles for PMCF, good communication between the manufacturer and the NB is essential. Manufacturers should confer with their NB on the adequacy of the PMCF design to ensure compliance with all ERs.

When working with NBs to review a PMCF plan, the process is most efficient and beneficial to manufacturers when it is initiated during the early stages of development. Early feedback on proposed plans allows NBs to challenge any elements that will not stand up to scrutiny, thereby eliminating delays during the final review process. An experienced and knowledgeable NB will clearly communicate with manufacturers and provide reasons why a plan fails to meet requirements. Common examples of problem areas include:

- insufficient clinical measures (e.g. assessment time intervals and overall duration; assessed outcome measures);
- insufficient patient enrolment numbers, which would not account for potential loss to follow-up over the study duration;
- covering all indications;
- covering all devices related to the design dossier or technical documentation.

6.6 The need for PMCF data

The purpose of any medical device is to make significant improvements to a patient's quality of life, and manufacturers are facing increasing pressures to provide detailed technical documentation of clinical data, beyond pre-market findings, that demonstrate continued safe, effective use. This evidence should support any and all claims and indications regarding the device.

Real-market situations provide a good illustration of the need for this focus. For example, after recent complications with PIP breast implants and metal-on-metal hip implant devices, the EU Commission urged member states to tighten controls, increase surveillance, and restore full confidence in the EU CE marking regulatory system. The commission proposed the following:

- Verify that NBs are designated only for the assessment of medical devices and technologies that correspond to their proven expertise and competence.

- Ensure that all NBs exercise the authority given to them by law to ensure that manufacturers conform to regulations through assessment (e.g. power to conduct unannounced inspections).
- Reinforce market surveillance by national authorities (e.g. spot checks for certain types of devices).
- Improve the impact of the vigilance system for medical devices:
  - Provide systematic access for NBs to reports of adverse events.
  - Encourage healthcare professionals and patients to report adverse events.
  - Enhance coordination in analyzing reported incidents in order to pool expertise and speed up necessary corrective actions.
- Support the development of tools to ensure the traceability of medical devices and their long-term safety and performance monitoring (e.g. Unique device identification systems and implant registries).

These objectives, however, are not isolated to the EU. In 2012, the Center for Devices and Radiological Health (under USFDA13 jurisdiction) released its strategic priorities, the first of which emphasizes the complete implementation of a 'total product lifecycle approach' and includes the following post-market goals:

- Develop a comprehensive strategy to assess real-world device performance.
- Post a proposed strategy (accessible online) to assess real world device performance and seek public input.
- Develop a comprehensive framework for the timely evaluation and management of significant post-market signals.

6.7 Final thoughts – Translating the value of clinical data beyond compliance

A robust PMS program provides:

- real-world experience with a broad spectrum of physicians and patients, outside the confines of pre-market trial(s);
- early warning of a problem;
  - reveals low frequency events,
  - long-term performance of device,
  - monitors effect of design changes,
- early corrective action;
- compliance with relevant legislation;
- additional value beyond compliance (e.g. marketing, legal).