

Regulation of Medical Devices involving Software in Australia – an Overview

John Jamieson

Conformity Assessment Branch
Therapeutic Goods Administration
PO Box 100, Woden ACT 2606

John.Jamieson@health.gov.au

Abstract

The Therapeutic Goods Administration (TGA) regulates the supply of therapeutic goods in Australia – including medical devices. Many medical devices are not programmable, electronic, or even electrical. However more devices are becoming programmable, and existing medical device software is becoming more complex.

Currently in Australia, certain types of medical devices are subjected to extensive pre-market documentary evaluation by the TGA. However most devices have less scrutiny.

It is proposed that medical device regulation in Australia will harmonise with the European Union Medical Device Directive. It is thereby hoped to: enhance requirements for many devices that are currently subject to few or no controls; reduce duplication for devices previously assessed by an overseas regulatory body; and to place increased emphasis on manufacturer quality and risk management systems and on post-market surveillance.

The intention is to address the safety of medical device software in its environmental context, and as a part of the device as a whole.

1 Introduction

Medical devices in Australia are regulated under the federal Therapeutic Goods Act 1989. The Act is administered by the Therapeutic Goods Administration (TGA), a Division of the Commonwealth Department of Health and Aged Care. The TGA regulates the supply of therapeutic goods, including medicines and medical devices, in order to ensure quality, safety and efficacy. At the same time the TGA aims to ensure the Australian community access, within a reasonable time, to therapeutic advances. The TGA does not regulate medical practice. Control over the supply of therapeutic goods is exercised through pre-market assessment, licensing of manufacturers, and post-market vigilance.

Medical devices may be defined as therapeutic goods that do not achieve the principal intended action by pharmacological, chemical, immunological or metabolic means (the definition excludes medicines) but that:

- prevent, diagnose, cure or alleviate a disease, ailment, defect or injury;

- influence, inhibit or modify a physiological process;
- test susceptibility to a disease or ailment;
- influence, control or prevent conception;
- test for pregnancy; or
- replace or modify parts of the anatomy.

By definition, a medical device includes any software necessary for its proper application. However software not associated with a medical device, such as medical record and information technology systems, are not considered medical devices.

2 Medical Devices Involving Software

Many medical devices are not electrical, even fewer are electronic, and even fewer involve software. However medical device software is becoming increasingly prominent. As described by others (e.g. Wallace and Kuhn, 1999, and Wood, 1999), more devices are becoming programmable and the complexity of medical device software is increasing.

Medical devices with software include those that are supplied and used entirely in hospitals and other health facilities, as well as consumer items such as blood pressure monitors. Some are used by patients themselves, but others are specifically for use by trained health professionals.

Many medical devices, and their software, operate in real time - monitoring, diagnosing, or controlling a physiological process as it changes. Many others perform off-line diagnosis without real time constraints. The software may be integral to the device, or it may be an accessory. The software may be part of a “closed” proprietary system, or it may run on a generic personal computer using off-the-shelf software. Security considerations are quite different in either case. See Wood (1999) for a discussion of some of these issues.

The device may be a stand-alone device, interacting with the user via a hardware interface only, or it may be networked in some way to allow remote monitoring, or even remote control. The device and its software may be implanted in a patient, or the software may simply allow the physician to communicate with, or to program, the device and its operation.

The complexity and risk profile of medical devices involving software can vary widely. The following examples illustrate some of this variety:

- a consumer digital thermometer for minor diagnosis – each unit used by a few relatively untrained people

but all units of a given model may be used by hundreds or thousands of people;

- an implanted artificial heart that is absolutely critical to preserving an individual patient's life and which may operate with infrequent clinical supervision; and
- a therapeutic X-Ray machine with a computer user interface, programmable software controlled therapy, and anatomical and biophysical modelling in the software, which is operated under a high level of professional staff supervision and maintenance, but that may be used to serially treat many patients.

Medical devices are becoming increasingly programmable – with screen, keypad, and graphical user interfaces - and are storing more information about the patient, their medical condition, their use of the device, and the device status and operation. Software is becoming important as an information (and sometimes diagnostic) tool: assimilating large amounts of patient and device data for presentation to the patient, health professional, or device supplier. The ergonomics and human engineering factors associated with the user interface are also becoming increasingly important.

A recent analysis of medical device recalls (Wallace and Kuhn, 1999) highlighted the diverse nature of medical device software failures. However trends were apparent, particularly in the relatively high incidence of poorly defined or implemented software algorithms. However the study also confirmed the importance of recognised software quality management practices as a means to prevent failures.

3 An Illustrative Example

A recent medical device problem from the implantable pacemaker industry will serve to illustrate some of the trends and kinds of problems currently being faced by manufacturers and by the TGA.

Some recent pacemaker failures have involved corruption of Random Access Memory (RAM) used to store program code or critical variables. Typically a single bit is "flipped", but multiple bit flips have occurred. The source of the corruption has not been conclusively determined, but it has been shown (Bradley and Normand, 1999) that cosmic neutron radiation would account for the nature and incidence of the problem. Another possible source of corruption may be alpha particles emitted by the electronic component packaging, but qualification testing of components is generally effective in nullifying this.

Different microcomputer elements are susceptible to this kind of failure to varying extents, because of different levels of stored charge. Microprocessor elements and Read-Only Memory (ROM) are considered less susceptible than RAM (Bradley and Normand, 1999). Different types of RAM are expected to perform differently but in general, devices with critical variables and control software stored in RAM are considered most susceptible to this failure mode.

Pacemakers have decreased in size considerably over recent years. A modern implantable pacemaker is typically less than 10 cc in volume. Battery size is the

limiting factor, and the electronic components have been integrated and miniaturised. The operating voltage and physical size of the electronic elements in the pacemaker circuitry have decreased. This has contributed to susceptibility to "bit-flip" errors.

The implantable pacemaker market is highly competitive and this has placed pressure on manufacturers to lower production costs. Different pacemaker models were once made on separate production lines or with hardware "jumpers". Now there is often a single production line, with distinct models configured entirely in software. The entire installed program code may be different for each model, or a model identification variable or lookup table may be used. This is now programmed as one of the final manufacturing steps. The RAM in the implanted pacemaker may also be upgraded in the field via a radio frequency telemetry link.

Fortunately these devices perform memory error detection and have a backup pacing mode, configured entirely in hardware, that acts as a fail-safe. Life is generally not threatened by this kind of failure, but quality of life may be impaired. The backup mode lacks features that enable the pacing therapy to be tailored to the needs of the individual patient. Pacemakers affected by this kind of failure require reprogramming, and it has sometimes been necessary to issue revised programming software.

This kind of problem rarely presented itself when pacemakers were less programmable. This example serves to highlight the current trend for medical devices with software to rapidly increase in complexity, sometimes with unpredicted consequences.

This example also points to the importance of redundancy at the system level for higher risk devices. The backup pacing mode may have actually saved several patients' lives, although there is no proof that this was the case. However the absence or failure of risk control mechanisms at the modular level is also suggested by these device failures. The lookup table data security and/or redundancy may require improvement. Improved memory component selection and shielding and error correction algorithms may help to reduce the frequency of these problems. If the critical memory was less corruptible, the affected patients' quality of life may have been less compromised and the resources allocated to pacemaker reprogramming may have been reduced.

4 Current Regulatory Framework

Medical devices in Australia have generally been dealt with within the same overall framework as medicines. Certain types of devices have been considered high risk and therefore subject to extensive documentary review by the TGA prior to supply. There are several such device types, but those that may involve software include: active implants, drug infusion systems, extracorporeal therapy systems, and some *in vitro* diagnostics. Other medical devices involving software are generally not subject to documentary review prior to supply, except for basic requirements including compliance with electromedical safety and electromagnetic compatibility standards.

Quality management systems certification is also required for manufacturers of the designated high risk device types. The certification process is extensive and manufacturing process control software issues are generally addressed, as well as design control of the device. Some lower risk device manufacturers also require quality management system certification, but design control for the device need not be covered.

In summary, device software is reviewed for only some high risk device types. However for most medical devices involving software, software issues are currently not addressed.

5 Harmonisation Proposal

The Commonwealth Government is currently considering a proposal to change the way medical devices are regulated in Australia. The intention is to harmonise Australian requirements with those currently in place in the European Union under the Medical Device Directives, and as part of a global harmonisation effort. In so doing, it is hoped to:

- reduce regulatory duplication for devices previously assessed by an overseas regulatory body;
- to enhance the requirements for many devices that are currently subject to few or no controls in Australia – including many devices involving software; and
- to place increased emphasis on manufacturer quality systems and post-market surveillance.

The heart of the new regulatory framework is a set of essential safety and performance principles. All medical devices, including those involving software, would be required to conform with these principles prior to supply. However some essential principles are applicable to a limited subset of devices.

A risk classification system would define the level and nature of TGA involvement in premarket conformity assessment required for particular medical devices. High risk devices, such as implantable defibrillators, may require extensive TGA involvement. TGA involvement with lower risk devices would be less, but for devices with software there would be more controls than under the current environment. For example, quality systems certification for the manufacturer, and a documented safety case for the device would generally be required. Under this scheme, medical device software inherits the same risk classification as any device that it controls or influences. Software may also be considered a medical device in its own right, with an independent risk classification.

Rather than designate particular types of device into particular risk classes, the proposed risk classification is based on a set of generic classification rules. The rules address the device in terms of: its level of invasiveness; duration of use; relationship to the central cardiovascular and nervous systems of the body; whether or not the device administers substances or energy to the body; whether or not the device is used in diagnosis; and other aspects of the device. The risk classification would generally determine the nature of regulatory body

involvement, but regardless of the risk class, all medical devices would be required to conform to the Essential Principles.

The new regime would not initially change the regulation of *in vitro* diagnostics, but controls for other diagnostic devices would be generally enhanced.

The new regulatory regime would place more responsibility for compliance in the hands of the manufacturer, but the TGA would have a critical role in the pre-market supply chain of higher risk devices. The new risk classification would place many devices currently designated as low risk, including many that involve software, into higher risk classes requiring greater scrutiny.

The new system is also expected to support the post-market activity of the TGA. More suppliers and manufacturers will be required to develop and maintain systems for responding to user problems and failures. The TGA's capabilities for market surveillance and post-market device problems are also expected to be enhanced.

For most manufacturers of medical devices involving software, the harmonisation proposal involves changes to the way those devices would be regulated in Australia. There should be little difference however, between Australian requirements and those required in Europe and other parts of the world.

Quality management systems, currently required for relatively few medical devices involving software, would need to be applied for a wider range of devices. The increased importance of quality systems may help to reduce the incidence of software failures (Wallace and Kuhn, 1999).

For high risk devices, the associated quality system audit would cover product design, production and regulatory requirements. For lower risk devices, a quality systems audit may not be required, or its scope may be limited to certain aspects. For low risk devices with a measuring function, for example, the design and production audit would focus on processes affecting measurement accuracy, precision, and stability.

6 The Essential Principles

The essential safety and performance principles are the basic reference point for the proposed system (see *Draft Medical Devices Regulations*, 2001). These are developed from the "Essential Requirements" of the European Medical Device Directive. This is one of the "New Approach" directives that are based on general requirements, and in which technical content has been delegated to standards. The intention is that the system will be better able to keep up with rapid technological change. Standards are considered easier to adapt to changing situations than is legislation.

The essential principle most directly applicable to medical devices involving software is:

"A medical device that incorporates an electronic programmable system must be designed and manufactured in a way that ensures that:

- a) *the performance, reliability, and repeatability of the system are appropriate for the intended purpose of the device; and*
- b) *any consequential risks associated with a single fault condition in the system are minimised.”*

Another essential principle relates to medical devices with a measuring function. Requirements include:

“The device must be designed and manufactured in a way that ensures that the device provides accurate, precise and stable measurements within the limits indicated by the manufacturer and having regard to the intended purpose of the device”; and

The measurement, monitoring and display scale of the device must be designed and manufactured in accordance with ergonomic principles, having regard to the intended purpose of the device”.

For software, or any other medical device, intended to be used in combination with other devices or equipment:

“A medical device that is intended by the manufacturer to be used in combination with another medical device or other equipment (including a connection system) must be designed and manufactured in a way that ensures that:

- a) *the medical device, and any other device or equipment with which it is used, operate in a safe way; and*
- b) *the intended performance of the device, and any other device or equipment with which it is used, is not impaired.”*

Devices monitoring clinical parameters also require appropriate alarms to warn of severe deterioration in the patient’s health.

There are also general requirements for:

- risk management activities, including risk analysis and disclosure of residual risk;
- conformity with safety principles generally acknowledged as state of the art;
- minimisation of undesirable side effects;
- benefits to outweigh residual side effects;
- appropriate transport and storage;
- infection and microbial contamination controls;
- electrical safety, and protection against electromagnetic and ionic radiation and other environmental influences;
- information to be provided with the device; and
- clinical evaluation of the device.

7 The Role of Standards

In principle, the role of technical standards changes dramatically under the harmonisation proposal. However in practical terms, the importance of currently enforced standards should not be diminished. There would be more formally recognised standards covering a greater range of devices and medical device issues than under the current system.

These “gazetted” standards would be used in assessing conformity with the essential principles. Generally, clauses of such standards would be mapped to specific essential principles, and compliance with requirements of

the standard would be used to assume conformity with those essential principles.

The real change is that standards now take “second-place” to the Essential Principles, which would be compulsory general safety and performance requirements. It is expected that the easiest way for manufacturers to illustrate conformity with these principles would be to obtain certification, by an accredited test house, to appropriate “gazetted” standards.

However this would not be the only way to demonstrate conformity. The manufacturer could use gazetted standards without formal certification, but conformity to the standard would need to be demonstrated in detail. If there was no applicable gazetted standard, or the manufacturer wished to do so, non-gazetted standards or in-house methods could instead be used. However any such method or test would need to be demonstrated as valid. In practice this would generally mean demonstrating that the in-house method was equivalent or superior to the standard. This is not a relaxation of requirements and in comparison to the current Australian system, technical requirements would actually be enhanced for most devices.

The standards currently under consideration for gazettal in Australia include those currently serving this purpose in the European Union (the so-called “harmonised standards”). The main such standard that is applicable to devices involving software is EN 60601-1-4. This standard is part of the IEC “601” family of electromedical safety standards which also include numerous device specific standards. Many of the other IEC “601” standards are also under consideration for gazettal.

EN 60601-1-4 goes beyond traditional testing and assessment of medical devices (dealt with by other standards in the “601” family) to include requirements for the processes by which the device is developed. The standard focuses on the integration of risk management activities with the device/ software development life cycle and quality management system, as described in ISO 9000-3 *Guidelines for the application of ISO 9001:1994 to the development, supply, installation and maintenance of computer software*, and ISO/IEC 12207 *Information technology – Software development processes*.

However EN 60601-1-4 does not address all of the relevant essential principles, particularly in relation to failure controls.

The TGA is also considering the gazettal of other standards relating to medical devices involving software. Standards potentially under consideration include: ISO 9000-3; ISO/IEC 12207; the software process assessment family of standards: AS 15504 *Information technology – Software process assessment*; and the safety critical systems standards: AS 61508 *Functional safety of electrical/ electronic/ programmable electronic safety-related systems*. Prior to gazettal, the scope of any such standards would need to be explicitly linked to relevant essential principles, and the impact on harmonisation with overseas requirements would also need to be considered.

8 The Summary Technical File

Under the harmonisation proposal, medical device manufacturers would require a Summary Technical File (STF) for each device, in which conformity with the essential principles would be documented. This would apply to all medical devices regardless of the risk classification, nature of TGA involvement, or whether or not the device involved software. The STF would need to be accessible for audit by the TGA throughout the product life cycle. The STF would be reviewed by the TGA prior to market entry for high risk devices only. The amount and detail of information included in the STF may vary considerably, depending on the risk classification, the applicable essential principles, and the complexity of the device.

The STF would formulate the safety case for the device, including any software. It would summarise the technical information related to the device in a format acceptable to both the TGA, and overseas regulatory bodies. It may form part of the manufacturer's complete technical file, but is not intended to contain all product details.

The STF for a medical device involving software would:

- describe the device - including its intended purpose, and indications and contraindications for use;
- summarise the technical requirements for the device, including significant software specifications;
- document risk management activities, including risk analysis, performed for the device and its software;
- summarise the manufacturing process for the device, including quality assurance measures;
- summarise design quality assurance activities and documents, including software verification and validation;
- summarise relevant clinical data;
- identify the essential safety principles relevant to the device and document appropriate conformity, by way of reference to a gazetted or other standard or other validated method.
- contain declarations or certificates of conformity to gazetted standards used to determine conformity;
- summarise tests and evaluations performed that were based on non-gazetted standards or in-house methods;
- describe device/ software variants;
- include a record of significant changes (eg software upgrades) along with reasons for believing these achieve the desired effect and that conformity continues; and
- contain labelling and instructions for use, installation, and maintenance.

9 What about the FDA?

The harmonisation proposal is intended to reduce barriers to trade whilst maintaining or enhancing the TGA's role. The system would be quite similar to that of Europe. There are some infrastructure differences between Europe and Australia that would need to be taken into account. There would also be some other differences, as the proposal actually mirrors the requirements of the Global Harmonisation Task Force (GHTF) which are based

largely on the European system. The GHTF is supported by all of the major international medical device regulators – including the TGA, regulators in Europe, Japan, and Canada, and the Food and Drug Administration (FDA) in the USA.

Although national differences are likely to remain for some time, the members of the GHTF are committed to global harmonisation of medical device regulation, and this includes the FDA. The FDA utilises similar regulatory controls as those used in both Australia and Europe. The FDA places similar emphasis on Quality systems certification, manufacturer risk management systems, pre-market review for higher risk devices, and post-market surveillance. The details regarding specific devices are sometimes different, but the overall approach is quite similar.

For medical devices containing software, the FDA has similar requirements to those expected in the harmonisation proposal for Australia. The risk and quality management issues described in the standard EN 60601-1-4, for example, are also emphasised explicitly by the FDA. The Summary Technical File described here, for a medical device with software under the proposed Australian requirements, expresses similar software issues to those required in a premarket submission to the FDA (see FDA guidance document, 1998).

10 Conclusion

Software is becoming an increasingly important aspect of medical devices, and medical device regulation. The way that the TGA regulates medical devices in Australia, including those involving software, is expected to change rapidly over the next few years. Medical devices with software are expected to be subject to more controls.

The TGA intends to approach medical device software from a perspective based on the intended purpose for the device and its intended user environment, and that views the device in its entirety including hardware, software and accessories.

In so doing, it is hoped to improve medical device regulation in Australia by reducing unnecessary regulatory requirements, enhancing public health and safety, and by developing a system that is in step with international requirements.

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