The regulation of software
Medicines, biologicals, blood, tissues, and devices

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Presentation to MSIA and MTAA
Presentation to:

- the Medical Software Industry Association (MSIA) of Australia
- the Medical Technology Association of Australia (MTAA)
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A systems approach

IMDRF SaMD Project

Key messages and Q&A
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Legislation

- **Therapeutic Goods Act 1989**
- Therapeutic Goods Regulations 1990
- Therapeutic Goods (Medical Devices) Regulations 2002
- Other legislative instruments including excluded and exempt goods orders
Software used in manufacturing
Software with a therapeutic purpose (medical device software)
Software for maintaining quality management systems
Software, systems, and toolsets applicable to all

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Software with a therapeutic purpose (medical device software)

- Infusion pumps and blood-pressure monitors
- IVD instruments and equipment (e.g., analysers, pregnancy testers)
- Portable electronic devices, e.g., pacemakers, hearing aids, defibrillators
- Patient monitors, ECGs, MRIs, and radiation-therapy machines
- And many more…
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Software with a therapeutic purpose (medical device software)

- Embedded software (firmware, EPROM, etc)
- Mobile, server (incl. cloud), desktop programs and apps
- Programmable hardware (e.g., FPGAs)
- Software that drives or controls other medical devices
Software used in manufacturing

Building-management systems

Production, sterilisation, water, and cleaning systems...

Statistical-process control systems

Lab equipment used in manufacturing

Applies only to systems used for or affecting production (manufacture)
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Software for maintaining quality management systems

- Enterprise resource planning systems
- Documentation management systems
- Corrective Action Preventive Action systems
- Training and record-keeping systems
- Other compliance systems

Applies only to QMS/GMP/compliance (not divorced business) systems
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Software, systems, and toolsets applicable to all

- Backup, fail-over, and redundant systems
- Infrastructure and security systems (networks, firewalls, etc.)
- Software-development toolsets (IDEs, compilers, etc.)
- Monitoring and management systems (including load, performance, analysis)

Easily overlooked but important aspects of QMS/GMP, performance, and safety
Medical devices

*Therapeutic Goods Act 1989*, section 41BD:

(1) A medical device is:

a) any instrument, apparatus, appliance, material or other article (whether used alone or in combination, and including the software necessary for its proper application) intended, by the person under whose name it is or is to be supplied, to be used for human beings for the purpose of one or more of the following:

i. diagnosis, prevention, monitoring, treatment or alleviation of disease;

ii. diagnosis, monitoring, treatment, alleviation of or compensation for an injury or disability;

cont(…)}
The intended purpose

Section 41BD (2) states that the intended purpose is to be derived from labelling, instructions, advertising material, and technical documentation provided by the legal manufacturer.

NOTE:

• The Secretary may declare particular things, devices, classes, types, or articles to be medical devices or not.

• Such a declaration under this section does not stop articles from being therapeutic goods.
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Software with a therapeutic purpose (medical device software)

When software becomes a medical device

Software becomes a medical device when it meets the definition, that is, when the legal manufacturer intends for the software to be used in:

- diagnosis;
- prevention;
- monitoring;
- treatment; or
- alleviation of disease, disability, etc.

The manner, form, material not relevant to whether an item meets the definition.
Software with a therapeutic purpose (medical device software)

How medical device software is regulated in Australia

Software is regulated under the medical devices regulatory framework

- Regulation is risk based
- Manufacturers are required to demonstrate that their devices meet the Essential Principles of Safety and Performance
- Manufacturers apply Conformity Assessment procedures
- Different classes require different Conformity Assessment procedures to be applied by the manufacturer

For further information, refer to:
- the Australian Regulatory Guidelines for Medical Devices (ARGMD)
- Regulation of medical software and mobile medical 'apps'.
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Key messages and Q&A
Software as a Medical Device guidance documents

1. Software as a Medical Device (SaMD): Key Definition

2. Software as a Medical Device: Possible Framework for Risk Categorization and Corresponding Considerations

3. Software as a Medical Device (SaMD): Application of Quality Management System (consultation underway)
1. IMDRF definition of Software as a Medical Device

Software as a Medical Device (SaMD) is defined as software intended to be used for one or more medical purposes that perform these purposes without being part of a hardware medical device.

This includes:
- mobile phone and tablet apps,
- desktop applications (e.g., radiation treatment planning SW),
- software that runs in the cloud (e.g., Web applications), and
- software that runs on any other general-purpose computing platform (smart watches, smart eyewear, etc.)
1. IMDRF definition of Software as a Medical Device

The SaMD definition excludes:

- embedded device SW
- SW that controls or drives hardware devices
- SW used for maintaining quality systems
- SW for manufacturing control & monitoring systems
  - production, sterilisation, and cleaning systems
  - building management systems
  - etc.
The definition of SaMD in context
1. IMDRF definition of *Software as a Medical Device*

SaMDs predominantly manage information rather than (directly) controlling the administration of energy or substances to or from a patient.

The information is then used directly for diagnosis or indirectly for treatment*.

The GHTF/IMDRF regulatory model makes minimal reference to information as a potential source of harm.

*Cognitive behavioural therapy applied by an SaMD would be considered by the TGA to be direct treatment.*
2. Proposed risk categorisation and considerations document

Objective is to introduce:

• a foundational approach,
• establish a common understanding for SaMD,
• harmonised vocabulary, and
• general and specific considerations
  for manufacturers, regulators, and users

Notes
• No intention to replace or modify existing regulatory classification schemes or requirements. Further efforts required prior to regulatory use.
2. Proposed risk categorisation and considerations document

Contents

• Introduction
• Scope (including objectives)
• Definitions
• SaMD Definition Statement
• Framework principles
• General considerations
  • Design and development
  • Changes
• Specific considerations
  • Socio-technical environment
• Technology and system environment
• Information security with respect to safety
• Appendices
  • Clarification of definition of SaMD
  • Analysis of SaMD framework with existing classifications
• References
Some challenges with software
Highly connected and dependent nature of software means that disruption in the ecosystem can result in loss of information, delayed, corrupted, or mixed patient information, or inaccurate information which may lead to incorrect or inaccurate diagnoses and/or treatments.

Recent example:
A change to the firewall rules on a hospital network made by IT staff resulted in the alarm signals from patient monitors in ICU not being delivered to the nurses’ station.
Software-related ‘failures’ => Where software is involved in an adverse event

• Most relate to problems with requirements (incomplete or flawed assumptions)
• Changes in socio-technical environment
• System errors mis-attributed as ‘user errors’ (errors following user actions)
• Insufficient controls for maintaining safety
• The software behaved exactly as designed…
• Traditional safety engineering approaches based on probability analysis (FMEA, FTA, HAZOP, etc.) have limited applicability to complex systems
• Emergent properties (safety is an emergent property)
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2. Proposed risk categorisation and considerations document

**SaMD Categories**

<table>
<thead>
<tr>
<th>State of Healthcare situation or condition</th>
<th>Significance of information provided by SaMD to Healthcare decision</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Treats or Diagnoses</td>
</tr>
<tr>
<td>Critical</td>
<td>IV</td>
</tr>
<tr>
<td>Serious</td>
<td>III</td>
</tr>
<tr>
<td>Non-Serious</td>
<td>II</td>
</tr>
</tbody>
</table>
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2. Proposed risk categorisation and considerations document

- SaMD Definition Statement
- Socio-technical environments
- Technology and system environments
- Information security with respect to safety
- Reduced (external) verification options
- Importance of a methodical and systematic development process
The proper and safe functioning of SaMD is highly dependent on a sufficient and common understanding of the socio-technical environment that includes the manufacturer and the user.

Software that is highly reliable and correct can be unsafe.
3. Software as a Medical Device (SaMD) mapped to ISO 13485

The objective of this third document is to provide guidance on the application of existing, standardised, and generally accepted quality management system (QMS) practices to SaMD.

Consultation out now (closes Monday 1 June 2015)
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Key messages and Q&A
The TGA approaches inspections and reviews by:

- taking a holistic rather than reductionist view
- treating safety and performance as a dynamic control problem rather than a reliability problem
- identifying system behaviour safety constraints
- assessing the sufficiency and adequacy of controls put in place by manufacturers

May include specific performance requirements (e.g., timing in a pacemaker)
The TGA looks to see that the manufacturer:
- **designs** for safety and performance
- **develops** for quality, robustness, resilience, and predictability
- **monitors, reports, and improves** using appropriate, sufficient, robust, and defensible tools, approaches, and methods.

With sufficient breadth and depth of expertise.
Safe state(s)

Safety-constraint examples:
• Temperature limits
• Toxicity limits
• Timing limits
• Accuracy, specificity
• Voltage, current, frequency of applied energy

Types of controls:
• technical,
• process (e.g., procedures),
• social (people),
• environmental,
• etc.

Example controls:
• Visual inspection procedures for steps in manufacture
• PCDs, monitoring of temperature, humidity, and vacuum for EtO sterilisation machine
• Real-time ECG monitoring for patient monitor
• Database integrity constraints

A systems approach
Review of safety controls

The TGA will look at controls that might affect safety, e.g.:
1. An unsafe control action is provided that creates a hazard
2. A required control action is not provided to avoid a hazard
3. A potentially safe control action is provided too late, too early, or in the wrong order
4. A continuous safe control action is provided too long or is stopped too soon
5. A control action required to enforce a safety constraint (avoid a hazard) is provided but not followed (e.g., a procedure or instruction provided by the manufacturer).
Where applicable, the TGA might look for:

- Necessary and sufficient technical (including clinical) competence
- Understanding of safe system states and constraints
- Resilience engineering (robust, resilient designs)
- Use of appropriate and sufficient risk-management tools, e.g., STPA
- Methodical and systematic design and development (e.g., design patterns and contracts)

Designs for safety and performance

—ISO/IEC/IEEE 29148; IEC 62304; ISO 14971; IEC/TR 80002-1; and IEC 62366.
Where applicable, the TGA might look for:

- Lifecycle development of software (i.e., IEC 62304)
- Use of good software- and systems-engineering practice
- Understanding of benefits and limitations of chosen development tools
- Use of appropriate and sufficient risk-management tools
- Methodical and systematic design and development (e.g., design patterns and contracts)

Development for quality, predictability

—ISO 13485; ISO/IEC/IEEE 29148; IEC 62304; ISO 14971; and IEC/TR 80002-1.
The TGA might also look for:

- Signal monitoring and analysis (ISO 13485, leading safety indicators)
- Understanding of limitations of monitoring processes (shadow faults, medical and domain context of use)
- Adverse-event and fault reporting (transparency) and investigations
- Trends analysis
- Corrections, corrective actions, and preventive actions

Monitoring, reporting, and continual improvement

— ISO 13485; ISO/IEC/IEEE 29148; IEC 62304; ISO 14971; and IEC/TR 80002-1.
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Post-market monitoring, surveillance, and action

• Capturing and tracking incidents and complaints involving software is a significant challenge.

• Manufacturers are expected to identify leading safety indicators and are required to link incidents to CAPA and risk management activities—closing of the feedback loop…

• Recognise, Retain, and Report campaign
Please report adverse events (incidents)...

In addition to the direct management of safety issues, the data reported to us helps us to see trends and better understand the causes of adverse events where software is involved.

Your reporting helps us to identify and respond to safety matters.

Large datasets are needed for the identification of shadow faults.

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Key messages and Q&A
The TGA regulates a broad range of software systems.

A holistic systems-engineering approach is used.

Many factors may be reviewed during an inspection or review.

Lifecycle, design and development, monitoring, and reporting are very important elements for safety.

Please help by reporting adverse events.

Recap

Key messages and Q&A
Key messages and Q&A

TGA information services:
- Safety alerts
- Recall actions
- Medicines Safety Update
- Medical Devices Safety Update
- Consultations
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