Software as Medical Device (SaMD)
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Corporate Profile

Brandwood CKC is the premier regulatory, quality systems and commercialisation consultancy in Australia serving local and international healthscience innovators for more than 20 years. We are headquartered in Sydney with international offices in Los Angeles, Wellington, Beijing, Taipei and Hong Kong.

Through our merger in 2019, Brandwood CKC brings together two of Australia’s pre-eminent names in health science regulatory and technical consulting: Brandwood Biomedical and Capital K Consulting.

Brandwood CKC combines our complementary technical strengths and diversity with a shared commercial focus and global market view across all areas of therapeutics and diagnostics. Our multilingual team are positioned to deliver comprehensive support in major international markets. Whether your market ambitions are local or global, we are with you every step of the journey.
Got a Question?

Click on Q&A and type your question.

We will answer in the Q&A session at the end.
Agenda

- Context for SaMD
- Key Definitions
- Current SaMD Regulatory Environment
- Regulation of SaMDs
- QMS for SaMD
- Clinical Evidence
- Key take Aways and Conclusions
Agenda

Context for SaMD
Why is the Regulation of SaMD a “hot topic”? 

**Computing technology evolves faster than the Regulation**

- Shift from Hardware incorporating software to smart stand-alone software.
- Increased use of Smartphones and tablets apps which can be SaMDs.

**Spreading access to technology**

- Software is relatively easy to develop and publish by individuals (e.g. app stores, websites).
- A wide range of people have access to ‘cloud’.

**Growing interrelationships of Connected Health**

- Digital health, eHealth, mHealth, telecare, telehealth and telemedicine.

*Increasingly difficult to clearly interpret when a software product fits into the Medical Device framework...*
Key Regulatory Challenges

The non-physical nature of software brings some unique challenges, for example:

- What forms a Software Medical Device and what product is regulated?
- Who can develop a Medical Device and potentially become “Legal Manufacturer”?
- How to restrict access to certain users / who should use the device?
- How to evaluate software (Socio-technical) risks and determine (clinical) data requirements?
- How to control software specifications through its lifecycle?
  - Features that trigger a Medical Device function or change its risk classification
  - Use within compatible/incompatible platforms
  - Frequency and process for updates and maintenance
  - Copies / traceability
Key IMDRF Regulatory Developments

- **Definitions**
  • IMDRF/SaMD WG/N10 FINAL:2013 – Software as Medical Device (SaMD): Key Definitions

- **Risk Management**
  • IMDRF/SaMD WG/N12 FINAL:2014 – Software as Medical Device: Possible Framework for Risk Categorization and Corresponding Considerations

- **Quality Systems and SW development**
  • IMDRF/SaMD WG/N23 FINAL:2015 – Software as a Medical Device (SaMD): Application of Quality Management System

- **Clinical Evidence**
  • IMDRF/SaMD WG/N41 FINAL:2017 – Software as Medical Device (SaMD): Clinical Evaluation
Agenda

- Context for SaMD
- Key Definitions
Key Definitions - Some Important Distinctions

- SaMD vs. Medical Device Software
- SaMD vs. Consumer Product
When Does a Software Product Become a SaMD?

- Must have a Medical purpose – meets the definition for Medical Device
  Software intended to be used for:
  - Diagnosis or screening,
  - Prevention,
  - monitoring,
  - treatment or alleviation of disease.

- Issue with Medical Device “intended use” but particularly with SaMDs:
  - can be explicit: Product labelling, instructions for use
  - can be implicit: feature set, data presentations, expected or known use in the field, significance/criticality of
    information provided
  - can change over time!

- Always evaluate for Medical Device classification when:
  - The Software can benefit a patient
  - The Software generates information that influences or support medical care
Difference Between Medical Device Software and SaMD

- Part of a (hardware) Medical Device = **Medical Device Software**
  - Embedded
  - Programmable (PEMS)
  - Control Systems
  - Desktop app that directly interfaces with a hardware

- Stand-alone Software = **SaMD**
  - Computer software with medical purpose
  - Medical Apps
  - Web-based apps
### Examples of SaMDs

#### Likely SaMDs

- Rehab software which provides measures of changes in mobility and posture
- Desktop software to detect and track sleep disorder breathing
- Mobile app that analyses patient information and physiological parameters (e.g. heart rate, blood pressure) to determine a treatment plan

#### Usually Not SaMDs

- Software used in the manufacturing of a MD and which has no therapeutic purpose
- Software used to statistically evaluate clinical study results, registers etc
- “Health coaches” and Lifestyle apps, including databases that help maintaining a healthy lifestyle
- Software for reimbursement, resource management such as staff and patient visit scheduling or other non medical purpose

*Examples only. Always consider all factors when assessing the status of a device.*
Agenda

Some Context

Key definitions – Types of software

Current SaMD Regulatory Environment
Current Issue with SaMD Classification

- Under EU (MDD) and the AU/HC Regulations, focus is on “physical interaction with the device” hence most SaMDs are classified as low/moderate risks (i.e. Class I or IIa). Current rules do not always reflect an interpretation of actual device risk level.

(5) If a medical device is driven, or influenced, by an item of software, the software has the same classification as the medical device.

- EU MDR in contrast shows clear consideration of SaMD and their potential risks:

6.3. Rule 11

Software intended to provide information which is used to take decisions with diagnosis or therapeutic purposes is classified as class Ila, except if such decisions have an impact that may cause:

— death or an irreversible deterioration of a person’s state of health, in which case it is in class III; or

— a serious deterioration of a person’s state of health or a surgical intervention, in which case it is classified as class IIb.

Software intended to monitor physiological processes is classified as class Ila, except if it is intended for monitoring of vital physiological parameters, where the nature of variations of those parameters is such that it could result in immediate danger to the patient, in which case it is classified as class IIb.

All other software is classified as class I.
EU – MDR 2017 / 745

- Clearer requirements for Software products (e.g.) in the European Medical Device Regulations (MDR 2017/745):
  - More definitions around software, for example:
    
    (19) It is necessary to clarify that software in its own right, when specifically intended by the manufacturer to be used for one or more of the medical purposes set out in the definition of a medical device, qualifies as a medical device, while software for general purposes, even when used in a healthcare setting, or software intended for life-style and well-being purposes is not a medical device. The qualification of software, either as a device or an accessory, is independent of the software's location or the type of interconnection between the software and a device.

  - Recognition that “Software” is an “active” device
  - Chapter 3, Rule 11 - Classification (IMDRF-based) for SW
  - Special Labeling (e.g. hardware, IT networks, security measures)
  - Specific Risk Management Considerations (e.g. interoperability)
  - Application of UDI for Software, including for Software changes
  - Inclusion of Software development life-cycle, information security, mobile computing platforms
Consultations & Guidance

Both Australia (TGA) and Canada (HC) have released consultation and guidance documents in 2019 specifically on SaMD.

These have not yet been implemented in the Regulations but shows the “current thinking” of the regulators.

Manufacturers of SaMDs should review guidances to facilitate transition.
US - FDA’s Software Pre-Cert Program

- FDA Pilot Program part of 21st Century Cures Act
- Currently evaluating the program – manufacturers can volunteer to participate in the Test Plan based on the selection criteria and availability.
- No pre-cert in 2019, likely in 2020
- Aim to establish a model - Focuses on a “Total product Lifecycle approach” as opposed to premarket applications
- Uses IMDRF risk categories to determine possible levels of premarket reviews
SaMDs are regulated as any other Medical Device

Rules-based device classification
- Regulatory Intervention based on Class
- Essential Requirements of S&E
- Standards as means of compliance
- Technical File construction
- Appointment of Local Representative

Product Code-based classification
- Regulatory Intervention based on Class
- Clinical experience or predication as means of compliance
- Appointment of Local Representative
IMDRF Considerations for SaMD Classification

<table>
<thead>
<tr>
<th>Type of disease or condition is:</th>
<th>Critical</th>
<th>Serious</th>
<th>Non-Serious</th>
</tr>
</thead>
<tbody>
<tr>
<td>o Life-threatening state of health, including incurable states;</td>
<td>o Moderate in progression, often curable;</td>
<td>o Slow with predictable progression of disease state (may include minor chronic illnesses or states);</td>
<td></td>
</tr>
<tr>
<td>o Requires major therapeutic interventions;</td>
<td>o Does not require major therapeutic interventions;</td>
<td>o May not be curable; can be managed effectively;</td>
<td></td>
</tr>
<tr>
<td>o Sometimes time critical, depending on the progression of the disease or condition that could affect the user's ability to reflect on the output information.</td>
<td>o Intervention is normally not expected to be time critical in order to avoid death, long-term disability or other serious deterioration of health, whereby providing the user an ability to detect erroneous recommendations.</td>
<td>o Requires only minor therapeutic interventions;</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>o Interventions are normally non-invasive in nature, providing the user the ability to detect erroneous recommendations.</td>
<td></td>
</tr>
</tbody>
</table>

| Intended target population is: | Fragile with respect to the disease or condition (e.g., pediatrics, high risk population, etc.). | NOT fragile with respect to the disease or condition. | Individuals who may not always be patients. |
| Intended to be used by: | Specialized trained users. | Either specialized trained users or lay users. | Either specialized trained users or lay users. |
Interpretation of Essential Principles for SaMDs

**Safety and Efficacy requirements for the device within “GHTF frameworks”**

**EP 1** The Device must be safe!
- Risk:benefit ratio of SaMD = risk of inaccurate or incorrect output of the SaMD upon clinical management of a patient.

**EP 2** Design reflects latest knowledge
- **Standards**

Risk mitigation strategy
- minimise risk by design
- Verify/validate
- document any residual risk
EP 3 Performance to manufacturer’s specification

EP 4 Long term safety and performance

EP 5 Safety and performance not affected by transport and storage

EP 6 Benefits outweigh undesirable effects

EP 7 Chemical physical and biological properties

EP 8 Sterilisation

EP 9 Construction and “environmental” properties

EP 10 Devices with a measuring function

EP 11 Radiation Protection

EP 12 Powered devices (electrical safety, EMC etc.)

EP 13 Labelling and claims

ER 14 Clinical Studies

Example provided based on Australian Regulations
Possible Use of Standards

Use standards as a means of compliance to the EPs

EP 1 Not compromise health and safety
- ISO 14971 Risk Management
  - (IEC 80002-1 Risk Management to medical device software)

EP 2 Conform with safety principles
- ISO 62366-1 Usability Engineering
- IEC 62304 Software development

EP 12 Powered devices (electrical safety, EMC etc.)
- IEC 62304 Software development

EP 13 Product Information
- EN 980 Symbols
- EN 1041 Information
- ISO 15523 Symbols

EP 14 Clinical Studies
- ISO 14155 Clinical Trials

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- QMS for SaMD
Quality Management System (QMS)

QMS Design Processes need to be established prior to commencing any Product Development

- Establish QMS Control Processes
  - ISO13485, IEC 62304, MDSAP, 21 CFR 820 etc.
- Design Planning & Product Development
- QMS Certifications & Product Registrations
- Release to Market
- Post-Market Surveillance
QMS Characteristics for SaMDs

- Common QMS standards & regulations must be used for SaMD but with certain “interpretations”:
  - ISO 13485
  - US FDA 21 CFR 820
  - MDSAP etc

- Due to safety & nature of SaMDs, almost entirely relying on good design (i.e. not production), SaMDs QMSs should focus on:
  - Planning (including Lifecycle management)
  - Organisational Structure (Leadership, competence and training)
  - Design Controls
  - Verification and Validation (including SOUP)
  - Procurement and Supplier Controls (including OTS)
  - Pre-Market Processes
  - Post-Market (e.g. complaints, adverse events, maintenance, recalls)
IEC 62304 – A Software Lifecycle Process Standard

- Integrate IEC 62304 within Design and Development
- Applies to all types of Medical Device Software (incl. SaMDs)
- Focuses on lifecycle planning and defines documentation requirements based on software Class.
  - A: no injury possible
  - B: non-serious injury possible
  - C: death or serious injury
- Maps to ISO 13485 & risk management (ISO 14971)

### Table C.1 – Relationship to ISO 13485:2003

<table>
<thead>
<tr>
<th>IEC 62304 clause</th>
<th>Related clause of ISO 13485:2003</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.1 Software development planning</td>
<td>7.3.1 Design and development planning</td>
</tr>
<tr>
<td>5.2 Software requirements analysis</td>
<td>7.3.2 Design and development inputs</td>
</tr>
<tr>
<td>5.3 Software ARCHITECTURAL design</td>
<td></td>
</tr>
<tr>
<td>5.4 Software detailed design</td>
<td></td>
</tr>
<tr>
<td>5.5 SOFTWARE UNIT implementation and verification</td>
<td></td>
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<tr>
<td>5.6 Software integration and integration testing</td>
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<tr>
<td>5.7 SOFTWARE SYSTEM testing</td>
<td>7.3.3 Design and development outputs</td>
</tr>
<tr>
<td></td>
<td>7.3.4 Design and development review</td>
</tr>
<tr>
<td>5.8 Software release</td>
<td>7.3.5 Design and development verification</td>
</tr>
<tr>
<td></td>
<td>7.3.6 Design and development validation</td>
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</table>
Life-Cycle Considerations

Design Planning
- Software Development Planning
- Risk Management Planning
- Regulatory & Clinical Strategy

Design Inputs
- User Requirements
- Hazards Analysis
- Essential Principles
- HIPAA / GDPR
- Cybersecurity
- Usability (IEC 62366)/ Human Factor
- Mobile App Guidance

Design Outputs
- Architectural Design
- Detailed Design & Implementation
- Software Integration
- Configuration Management
- Software Build

QMS (ISO 13485, 21 CFR 820)
Risk Management (ISO 14971)
Software Development (IEC 62304, ISO 15288 & ISO 12207*, FDA Software Guidance, SOUP)

* Not specific to SaMD but relevant Lifecycle management references
Life-Cycle Considerations

**Design Verification**
- Unit Verification
- Integration Testing
- System Verification
- Problem Resolution
- Change Management

**Design Transfer**
- Software Build
- Configuration Management
- Installation Qualification

**Design Validation**
- Clinical Evaluation
- Usability Testing & UAT

**Deployment**
- Post Market Surveillance
- Software Maintenance

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**QMS** (ISO 13485, 21 CFR 820)

**Risk Management** (ISO 14971)

**Software Development** (IEC 62304, ISO 15288 & ISO 12207*, FDA Software Guidance, SOUP)

*Not specific to SaMD but relevant Lifecycle management references*
Life-Cycle Considerations – Post-Market

**Issue Management**
- Adverse Event Monitoring
- Complaints & Recalls
- Problem Resolution

**Information Security**
- Monitor Vulnerabilities & Threats
- Monitor 3rd Party Software
- Patching & Updates

**Software Maintenance**
- User Requirements Changes and Enhancements
- 3rd Party software changes
- Configuration Changes (Platform & OS Changes)

**Quality Assurance**
- Customer Feedback
- Performance Metrics
- Quality Metrics

- Risk Assessment
- Clinical Impact
- Regulatory Impact
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Context of SaMD Clinical Evaluation

Intended Use, Claims, Indications

SaMD inputs
- Patient data
  (lab results, imaging data, medical device data, physiological status, symptoms, etc)

SaMD Algorithm
- Algorithm, inference engine, Equations, Analysis engine, Model based logic, etc
- Reference Data Knowledge Base, Rules Criteria

SaMD outputs
- SaMD defined outputs (inform, drive, diagnose, treat)

Clinical Evaluation

Treat or Diagnose
- Drive Clinical Management
- Inform Clinical Management

Significance of Information in the clinical decision affects the depth of clinical evidence
Type of clinical evidence for SaMD

<table>
<thead>
<tr>
<th>Clinical Evaluation</th>
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</thead>
<tbody>
<tr>
<td>1 Valid Clinical Association</td>
</tr>
<tr>
<td>Is there a valid clinical association between your SaMD output and your SaMD’s targeted clinical condition?</td>
</tr>
<tr>
<td>2 Analytical Validation</td>
</tr>
<tr>
<td>Does your SaMD correctly process input data to generate accurate, reliable, and precise output data?</td>
</tr>
<tr>
<td>3 Clinical Validation</td>
</tr>
<tr>
<td>Does use of your SaMD’s accurate, reliable, and precise output data achieve your intended purpose in your target population in the context of clinical care?</td>
</tr>
</tbody>
</table>

- Published literature review and appraisal
- Predicate comparison
- Additional data analysis / Clinical trial?
- V&V (e.g. testing)
- Clinical Trial (sensitivity, specificity, confidence intervals)
- Usability Evaluations
Clinical Evidence – Lifecycle considerations

- Leverage capability of SaMD to collect post-market experience data (consider Cybersecurity)

- Risk categorization can change overtime, however:
  - Activate/deactivate features
  - Re-align intended uses and claims
Key Take Aways & Conclusions

- Apply medical device definition to stand-alone software based on Intended Use.
- Adoption of SaMD in the regulatory framework is progressing but harmonisation is not complete.
- Key guidance (IMDRF) and standards provide help with interpretation
- QMS controls and lifecycle management are essential (e.g. ISO 13485 and IEC 62304). Implement Design QMS processes early in software development life-cycle.
- Continual post-market monitoring and responding to changes is required (cybersecurity, platform changes, changes to third party software etc.)
- Depth and Type of Clinical Evidence should be based on the significance of information provided by the SaMD.
Time for Q&A...

Think of something later? Ask us by email...
help@brandwoodckc.com