

Intertek

HPFB-TGA QMS MOU FOR MEDICAL DEVICES

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Introduction

Regulatory authorities for medical devices in Canada and in Australia (Health Canada's Health Products and Food Branch (HPFB) and the Therapeutic Goods Administration (TGA) of Australia) have signed a Memorandum of Understanding (MOU) on quality systems for medical devices on June 1 2007

Introduction

Once the MOU becomes operational, MOU certificates issued to Canadian medical device manufacturers by CMDCAS-recognized registrars also recognized by the TGA will be recognized as evidence of compliance to quality system requirements in Australia

Introduction

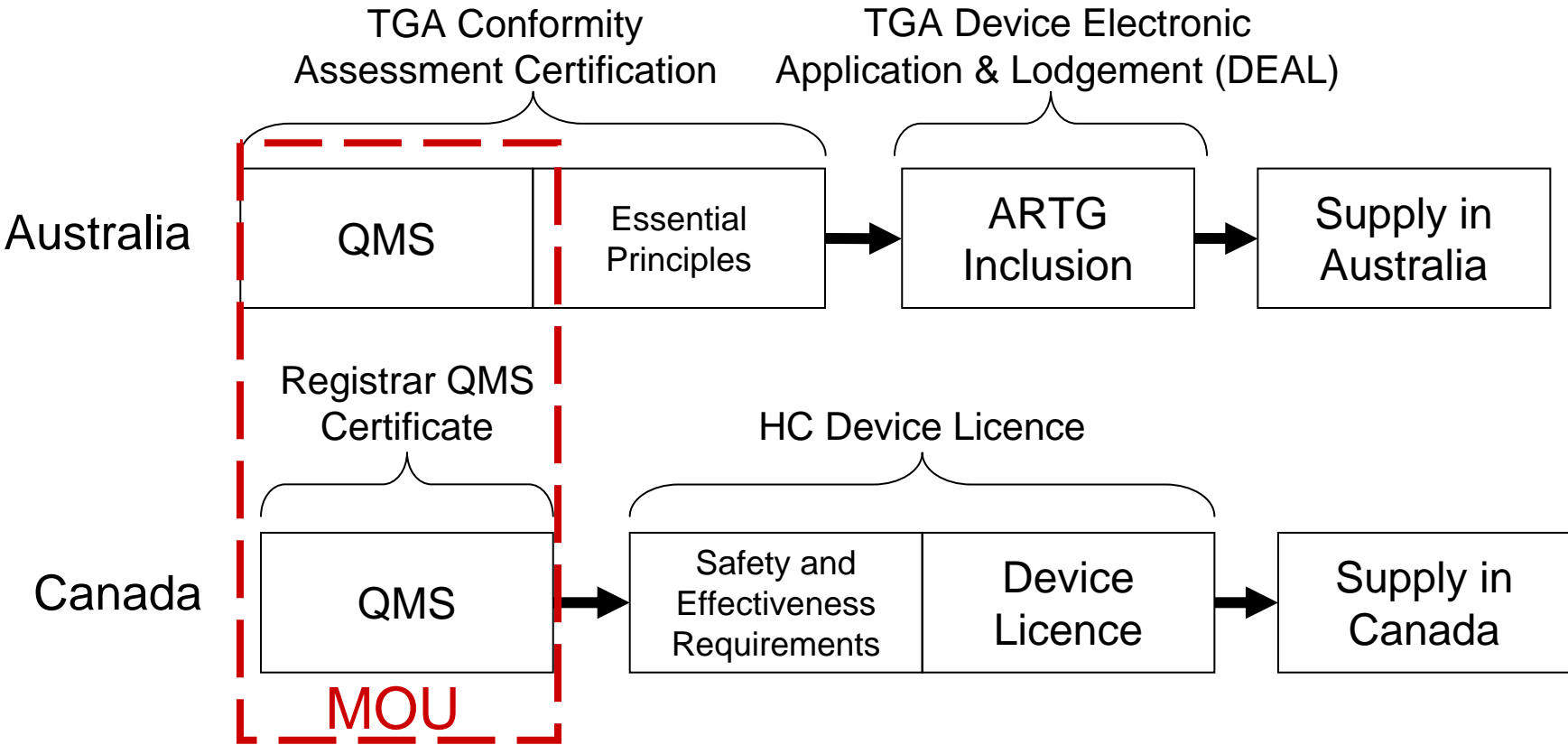
Benefits to the manufacturers:

- Reduced disruption - a single audit will cover the quality system requirements of both the Canadian and the Australian markets
- Reduced audit costs by having a local auditor

Status of the MOU

Participating registrars are currently going through the qualification process (auditor training, desk assessment of registrars, observed audit)

The scope of the MOU



The scope of the MOU

- Limited to Canadian manufacturers only
- Must fit both countries 'medical device' definition (includes combination products)
- IVDs are excluded from the MOU
- Class I (in Canada or in Australia) are excluded from the MOU
- Devices must be covered by Canadian Medical Device Licences

The scope of the MOU

- CMDCAS & MOU QMS certificate scope are tied together:
 - Same registrar
 - Same manufacturer name and address
 - Same facilities & suppliers
 - Same exclusions
 - Same kinds of medical devices (MOU scope may be subset of CMDCAS scope)
 - Same expiry date
 - CMDCAS certificate shall be maintained to have a valid MOU certificate

Implications for Canadian manufacturers

- Manufacturer must classify devices **according to Australian rules** (Therapeutic Goods (Medical Devices) Regulations 2002, Schedule 2) - Class Is, Im, Ila, I Ib, III & AIMD – classes mostly aligned with EU classes, but there are some differences in classification between Australia and the EU
- Class I Ib or higher → not permissible to exclude clause 7.3 Design and Development

Implications for Canadian manufacturers

Schedule 2 Classification rules (extract)

2.4 Non-invasive medical devices intended to have contact with injured skin

- (1) This clause applies to a non-invasive medical device that is intended by the manufacturer to be used in contact with injured skin (including a device the principal intention of which is to manage the micro-environment of a wound).
- (2) Subject to subclauses (3) and (4), the device is classified as Class IIa.
- (3) If the device is intended to be used:
 - (a) as a mechanical barrier; or
 - (b) for compression; or
 - (c) for the absorption of exudates;the device is classified as Class I.
- (4) If the device is intended to be used principally for wounds that have breached the dermis and the wounds can only heal by secondary intent, the device is classified as Class IIb.

Implications for Canadian manufacturers

- Manufacturer shall also determine GMDN preferred term for every product (Global Medical Device Nomenclature)
 - Each product requires a single GMDN code
 - GMDN codes managed by GMDN Agency (not TGA) (www.gmdnagency.com)
 - Manufacturer's responsibility to determine the code
 - Registrar to verify code exists and is appropriate
 - TGA Online services website offers limited GMDN search capability (access via Australian agent)
 - Use GMDN 'preferred terms' only

Implications for Canadian manufacturers

- Every medical device must be covered by:
 - Essential Principles compliance summary + referenced records
 - Clinical evaluation expert report + CV of author
 - Risk management report
 - Australian Declaration of Conformity
(can only be made after the TGA conformity assessment certificate is issued)

Implications for Canadian manufacturers

- Australian requirements must be incorporated into the QMS and QMS must cover supply to Australia– Intertek draft checklist available
- Manufacturer uses registrar’s MOU QMS certificate to apply for a TGA conformity assessment certificate.
Technical documentation submitted to the TGA

Essential Principles

- 14 Essential Principles - *Therapeutic Goods (Medical Devices) Regulations 2002, Schedule 1*
- Australian Essential Principles align closely with GHTF and with EU MDD Essential Requirements
- Similar to Canadian MDR Safety and Effectiveness Requirements

Essential Principles

1. Use of medical devices not to compromise health and safety
2. Design and construction of medical devices to conform with safety principles
3. Medical devices to be suitable for intended purpose
4. Long-term safety
5. Medical devices not to be adversely affected by transport or storage
6. Benefits of medical devices to outweigh any side effects
7. Chemical, physical and biological properties

Essential Principles

8. Infection and microbial contamination
9. Construction and environmental properties
10. Medical devices with a measuring function
11. Protection against radiation
12. Medical devices connected to or equipped with an energy source
13. Information to be provided with medical devices
14. Clinical evidence

Essential Principles Compliance Summary

- Essential Principles compliance summary shall be documented for every medical device
- Optional checklist available on TGA website (<http://www.tga.gov.au/devices/epcheck.htm>)
- The manufacturer may alternatively use a comparison table to document equivalence between EU ER and Au EPs
- Must address every EP including reference to specific QMS records that justify compliance
- Controlled record

Essential Principles – Clinical Evidence

- **Clinical Evidence** required for all medical devices demonstrating that the device complies with the EP, in particular EP 1, 3 and 6
- Clinical Evaluation conformity assessment procedures (Schedule 3 Part 8)
- Guidance document available on TGA website (<http://www.tga.gov.au/docs/pdf/devguid4.pdf>)

Essential Principles – Clinical Evidence

- Documented clinical evaluation of all available clinical data by competent clinical expert required whether literature review or clinical investigation is used
- CV of clinical expert must be included
- Controlled record (living document considering post-market information)

Essential Principles – Risk Management

- Risk management report required for all medical devices (EP 2 & others)
- ISO 14971:2000 (until 31 March 2010) and ISO 14971:2007 versions recognised by TGA
- Must address full product life-cycle
- Controlled record

Declaration of Conformity

- The manufacturer will be required to make a declaration of conformity which declares that the medical device complies with:
 - the applicable provisions of the essential principles;
 - the classification rules; and
 - the conformity assessment procedures;
- Guidance document on TGA website (<http://www.tga.gov.au/docs/html/devguid5.htm>)
- Templates for each of the six possible types of declarations of conformity have been included as attachments to the guidance document

MOU QMS audits

- QMS audit must be for both Canada and Australia
- ISO 13485:2003 required
- Health Canada regulatory requirements assumed as a basis
- Applicable Therapeutic Goods (Medical Devices) Regulations 2002 requirements shall also be integrated in the QMS
- Registrar follows Quality Management System Audit Tool (QMAT) - similar to Health Canada Guidance Document GD210

ISO 13485 cl. 1.2 - Application

- Audit must include processes relating to Australian customers and products
- Insufficient to only audit processes relating to Canadian customers and products
- Can be sampled
- Prioritise higher class devices (Australian classification)
- Lower class devices not to be ignored

ISO 13485 cl. 4.2.1 – Doc. requirements

- Does the documentation incorporate the technical documentation required by the TG(MD) Regulations, including:
 - Product Specifications (ISO13485 cl. 7.1 c);
 - Essential Principles compliance summary (ISO13485 cl. 7.2);
 - Risk Management records,
 - Clinical evidence TG(MD)R Schedule 3 Part 8,
 - Validation and test reports, including sterilisation validation report where applicable;
 - Labelling, IFU and advertising material?
- Registrars have no role in assessing product compliance

ISO 13485 cl. 4.2.3 & 4.2.4 - Control of documents & records

- Manufacturer to have copies or online access to Australian Regulations, TGA guidelines and technical standards to which compliance is claimed
- Technical documentation must be controlled
- If quality records are kept in e-form are the requirements for keeping of e-records defined and fulfilled?

ISO 13485 cl. 4.2.3 & 4.2.4 - Control of documents & records

- Is the device lifetime defined?
- Documents & records to be retained for at least 5 years or for the device lifetime if longer than 5 years
- Is there an agreement in place to enable Australian sponsors to provide manufacturing records to the TGA upon request for a period of at least 5 years after the supply of a device?

ISO 13485 cl. 5.6.2 - Management review input

- New or revised Australian regulatory requirements to be specific inputs to management review

ISO 13485 cl. 6.2.2 - Competence, awareness and training

- Does the manufacturer have knowledge of the Australian Regulations?
- Is training in Australian requirements considered?

ISO 13485 cl. 6.3 - Infrastructure

- Where current international standards impose requirements on infrastructure, the TGA expects the manufacturer to consider the standards
 - e.g. ISO 14644-2:2005 : Cleanrooms and associated controlled environments - Part 2: Specifications for testing and monitoring to prove continued compliance with ISO 14644-1)
- Process equipment is expected to have been qualified for use

ISO 13485 cl. 6.4 - Work environment

- For manufacture of devices labelled sterile:
 - Are the results & limits set for environmental monitoring compared to the results obtained at the time of the validation exercise?
 - Review of trends and any excursions should be checked
 - Is the Out of Specifications (OOS) procedure for environmental monitoring adequate?
 - Is pre-sterilisation bioburden monitored?
 - Are the results of bioburden monitoring compared to the ones obtained during the sterilisation validation?

ISO 13485 cl. 7.2.1 - Requirements related to the product

- Has the manufacturer determined the regulatory requirements that apply to the device?
- Do these include the Australian TG(MD)R requirements? e.g. EP, classification, GMDN code, labelling and advertising requirements, notification of substantial changes to TGA, Australian Declaration of Conformity, etc.

ISO 13485 cl. 7.2.1 - Requirements related to the product (continued)

- Devices containing medicinal substances:

Is there a QMS requirement and evidence that the manufacturer has applied the Australian Code of GMP for Medicinal Products (or equivalent) to the medicinal substance processing?

ISO 13485 cl. 7.2.1 - Requirements related to the product (continued)

- Products of animal origin:
EN 12442:2000 Animal tissues and their derivatives utilized in the manufacture of medical devices?

ISO 13485 cl. 7.2.2 - Review of requirements related to the product

- AT INITIAL AUDIT
 - Technical documentation assessed for presence and completeness (EP compliance summary, Clinical evidence - expert report, experts' CV & clinical data; product labelling, IFU)
 - It is understood that all documentation may not be complete for the initial audit. For example: Australian Declaration of Conformity (can only be made after the TGA conformity assessment certificate is issued)

ISO 13485 cl. 7.2.2 - Review of requirements related to the product (continued)

- AT SURVEILLANCE AUDIT
 - Technical documentation verified to be complete, up-to-date and to include:
 - Current Product Specifications;
 - Change control in particular any changes to products, product range, QMS;
 - Up to date Essential Principles compliance summary reflecting changes if there were any;
 - Up to date Clinical evidence and Risk Management Report;

ISO 13485 cl. 7.2.2 - Review of requirements related to the product (continued)

- AT SURVEILLANCE AUDIT
 - Technical documentation verified to be complete, up-to-date and to include:
 - Records of review of critical processes and relevant validation reports e.g. sterilisation validation report;
 - Declaration of conformity specific for Australia exists and is up to date for all products supplied to Australia?

ISO 13485 cl. 7.2.3 - Customer communication

- Is there an Australian sponsor?
- Are Australian customer complaints recorded, investigated and acted on?
- Do advisory notice procedures include Australia?
- Is there a written agreement between the manufacturer and all Australian sponsors of the product to ensure the provision of information to the TGA (eg technical docs, adverse event and recall information etc.)?

ISO 13485 cl. 7.3.1 - Design and development planning

- Has the manufacturer demonstrated how current design & development procedures apply to product in existence at the time the procedures were introduced? e.g. How do the design and development procedures ensure existing products comply with Australian requirements?
- Clause 7.3 may be excluded for class IIa or lower

ISO 13485 cl. 7.3.2 - Design and development inputs

- Australian Essential Principles and risk management outputs specified as design inputs?
- Reflected in design outputs?

ISO 13485 cl. 7.3.6 - Design and development validation

- Has the manufacturer established clinical evaluation procedures in accordance with Schedule 3 Part 8 using representative samples of normal production (finished goods)?

ISO 13485 cl. 7.3.7 - Control of design and development changes

- Is the identification of a substantial change based whether the product, once changed, continues to conform to relevant EP?
- Does the manufacturer have a procedure for notifying the TGA and registrar of the substantial change prior to implementation? (Note: If changes relate to Class III or Class AIMD devices then the procedure should require changes to the outputs of design and development to be notified to the TGA as these may require a reassessment of the design dossier)

ISO 13485 cl. 7.5.1.2.2 and 7.5.1.2.3 - Installation and servicing activities

- Installation in Australia
 - If medical devices are installed in Australia this must be covered by the requirements of clause 7.5.1.2.2, even if this activity is outsourced
- Servicing in Australia
 - If medical devices are serviced in Australia this must be covered by the requirements of clause 7.5.1.2.3, even if this activity is outsourced

ISO 13485 cl. 7.5.2.1 - Validation of processes for production and service provision

- It is expected that current standards or guidance will be used to establish and validate processes
 - e.g. Process Software verification – IEC/ISO 62304, FDA Guidance, etc.;
 - Processes to incorporate a medicinal substance into a medical device - Australian Code of GMP for Medicinal Products

ISO 13485 clause 7.5.2.2 - Particular requirements for sterile medical devices

- A Sterility Assurance Level (SAL) of 10^{-6} must be demonstrated for all terminally sterilised medical devices supplied to Australia labelled 'sterile'
- The sterilisation process validation must address this requirement
- The registrar must verify that a sterilisation process validation program is documented and implemented

ISO 13485 clause 7.5.2.2 - Particular requirements for sterile medical devices (continued)

- Where standards are used by a manufacturer to demonstrate compliance with sterilisation validation requirements, they must be current and implemented as intended and not selectively
- The audit must also ensure ongoing maintenance of the sterilisation process validation, including revalidation as specified by TGA Medical Device Standards Order No. 3 (MDSO 3)

ISO 13485 clause 7.5.2.2 - Particular requirements for sterile medical devices (continued)

- The TGA will assess the acceptability of the sterilisation process validation during the initial conformity assessment application, including the manufacturer's documented arrangements for maintenance of the validation
- The audit will address environmental monitoring and bioburden monitoring in relation to the sterilisation process validation (see also clauses 6.4 & 7.5.1.2.1)

ISO 13485 cl. 7.5.3.2.2 - Particular requirements for active implantable medical devices and implantable medical devices

- Does the manufacturer have an agreement with the Australian Sponsor (importer) to ensure that manufacturing and distribution records may be provided to the TGA on request?
- For manufacturing records, the lifetime of the device and at least 5 years; for distribution records, at least 10 years

ISO 13485 cl. 8.2.1 - Feedback

- Has the TGA required the manufacturer to conduct post-market clinical trials? If so, are these trials being performed and incorporated into the feedback system?
- The feedback and post-market surveillance systems must include Australian customers and users of the medical device and the Australian clinical environment (e.g. Australian professional guidelines)
- TGA Guidance doc. no. 11 Postmarket Activities (<http://www.tga.gov.au/docs/html/devguid11.htm>)

ISO 13485 cl. 8.5.1 - Post market vigilance

- Registrar will check that QMS addresses:
 - Australian customer complaints;
 - Reporting adverse events to the TGA (reporting criteria, timeframes and contact details);
 - Australian advisory notices and recalls;
- Uniform Recall Procedure for Therapeutic Goods (URPTG 2004) available on TGA's website at <http://www.tga.gov.au/docs/html/urptg.htm>

Standards & critical documents

- Legislative Standards Orders exist for:
 - QMS: ISO 13485:2003 (CASO1)
 - Animal origin: ISO EN 12442 standards (CASO2)
 - Risk management: ISO 14971 (MDSO2)
 - Sterility: ISO 11135, ISO 11137, etc. (MDSO3)
- Devices containing medicinal substances:
 - Australian Code of GMP for Medicinal Products

Useful links

- TGA website
(<http://www.tga.gov.au/devices/devices.htm>)
- ARTG
<https://www.tgasime.health.gov.au/SIME/ARTG/ARTGPublicWeb.nsf?OpenDatabase>

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Q & A



The Australian Device Market

- \$2 billion market (2% of world market)
- ~ 1,500 sponsors
- > 25,000 different devices
 - between 4-600,000 catalogue items
- > 85% of devices are imported
- < 10% of devices are high risk



CMDCAS / Canadian System

