Checklist guidance to supporting data required for adding or changing sterilisation suppliers for TGA conformity assessment applications

This short guidance document provides a checklist of information required by the TGA for medical device conformity assessment applications that involve changes or additions to sterilisation suppliers or facilities.

With recent announcements by FDA related to closures of ethylene oxide (EtO) facilities, the TGA expects a rise in the number of applications in changing existing sterilisation suppliers for medical devices. Sterilisation suppliers are considered critical suppliers and are listed on TGA issued conformity assessment certificates (Schedule 3, Part 1 certificates). Therefore, any changes to suppliers of sterilisation services or to sterilisation processes are also considered as substantial changes and require TGA conformity assessment prior to implementation.

TGA will focus on reviewing the changes described rather than a full conformity assessment for these applications. Please note that as sterilisation validation is site, cycle and chamber specific, the risk in terms of sterility assurance is the same regardless of whether the sterilisation site is for a new product or a proposed additional site is for an existing already approved product.

When assessing a sterilisation process at a new supplier of sterilisation services or assessing changes to an approved sterilisation process the TGA reviews the information on three key areas- the Quality management systems (QMS) and controls, review of sterilisation process at the site, and the verification on any products or UPIs (unique product identifiers) that have undergone the sterilisation process.

How you can help

While some of these changes require expedited processing, the TGA has noted some common issues with the quality, accuracy and completeness of supporting data submitted to the TGA for conformity assessment applications that result in significant delays in processing.

Applicants should ensure that the supporting data packages submitted to the TGA contains the full suite of expected information outlined in the checklist below, and to provide justification where the information is considered not applicable or otherwise not available.

Submitting clear and complete data packages allows TGA to process the requested changes quickly and efficiently.

Some of the noted inadequacies with submitted data from similar applications include the following:

- Poor characterisation of product families (e.g assessment of suitability of a product to belong to a specified sterilisation group) and poor characterisation of master product

- Insufficient justification for the inclusion of a new or modified product into a previously validated product family. Incorrect and inadequate product adoption procedures for inclusion of product into an existing product family sterilised in a specified cycle at a site.

- Incorrect and inadequate characterisation of Process Challenge Devices (PCDs).

- Inadequate definition of loads in validation studies with regard to load composition, dunnage and density determination.

- Inadequate information regarding process monitoring and control, particularly in relation to parametric release.

Required data:

Quality Management System

The device manufacturer needs to provide documents and records to demonstrate control over the supplier.

The following information should be submitted:

- For changes to sterilisation facilities/ processes, submit information related to change control records (ISO 13485:2016 Ch 4.1.4).

- Provide description of how purchasing requirements are fulfilled for new sterilisation suppliers (ISO 13485 clauses 7.4.1, 7.4.2 and 7.4.3 and Schedule 3, Part 1.4 and 4.4 of the Regulations).

- Updated risk management review conducted in accordance with ISO 14971, including but not limited to, whether the changes have introduced any new risks or increased the existing risks' level, whether the risks identified have been controlled to an acceptable level, and highlighting any updates that cover the proposed changes in the application.

Review of sterilisation site processes

The applicant must provide evidence to demonstrate that the conditions and processes at the supplier of sterilisation services have been validated and recorded, including evidence that regular dose audits (where applicable) are undertaken:

- Sterilisation validation information (ISO 13485 clause 7.5.5-7 and Schedule 3, Part 1.4 and 4.4 of the Regulations) including

    - Protocols/procedures for the validated process including frequency of re-validation
    - The procedures for monitoring and controlling the process parameters of a validated process should be fully described.
    - Validation report generated using final products or 'dummy' product packaged in the sterile barrier systems/packaging system; or

justification why revalidation on new products packaged in same sterile barrier system; or revalidation at new sites, is not necessary.
    - Sterility testing of the product and integrity testing on primary packaging system at the end of shelf life, if applicable, or justification why such testing is not required by the change.

Validation of the sterilisation process applied to the product

The TGA would typically review validation reports to ensure that the sterilisation methods and processes applied satisfy the sterilisation requirements for the product.

For terminally sterilised products, the applicant is expected to provide documented information showing that the process has been physically and microbiologically validated to demonstrate that the process will achieve a Sterility Assurance Level (SAL) of 10^{-6} or less in routinely processed products, with reference to appropriate standards. Information required includes:

- The method of sterilisation used and the parameters of the process (validation and routine)
- A clear statement as to the standards being applied and/or details of any alternative sterilisation validation method used, if not specified in an internationally recognised standard
- The pre-sterilisation bioburden limit, the bioburden testing method and the bioburden test method validation
- A report describing the initial validation of the process and information/reports on revalidations carried out, if applicable
- Method of batch release e.g. Biological Indicator (BI) release, parametric release, dosimetric release
- Ethylene Oxide (EtO) sterilisation residue reports, where applicable.

For aseptically processed products, the TGA requires the following information:

- Bioburden information including pre-sterilisation bioburden limits and for extended processing times, evidence to show that microbiological quality before filtration and sterility after filtration is not compromised.
- Parameters of sterilisation processes applied to the containers and closures and evidence to show that these processes have been physically and microbiologically validated to a SAL of 10^{-6} or less
- Details of filter integrity testing and information to show that the sterilising filter has been validated for bacterial retention in the presence of the product.
- Statements of maximum permitted processing times during manufacture (holding, storage and filling times).

- Media fill studies to validate the aseptic manufacturing process. Media fill studies should be conducted under worst case conditions including maximum processing and filling times and should include simulation of all aseptic manufacturing processes.

For products that are intended for multi-dose use, the TGA requires:

- Information on antimicrobial preservative efficacy data at the beginning and end of the closed shelf life.

- Information on microbiological challenge testing/simulated use testing to support the open shelf life (in-use period).

Tips on completeness and quality of data

Please ensure that any reports uploaded are digitised and digitally searchable. Handwritten records should be clearly legible.

Reports and records should be up to date and covers the proposed changes.

For records that are originally in a language other than English, an accurate English translation of the documents must be provided.

Ensure records are systematically and logically named, and that any associated attachments referenced by each record have been included.

Applications that are incomplete or contains inadequate data to allow a certificate to be issued will be lapsed in accordance to provisions in section 41EG of the *Therapeutic Goods Act 1989*.

Questions

If you have questions, you can reach out to the medical devices info unit on 1800 141 144 or devices@tga.gov.au.