Sponsor Information & Training Day

Tuesday 9 September 2014
Hyatt Hotel, Canberra
Session A2 - Medical Devices

Changes (I)
Devices that have undergone TGA Conformity Assessment

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Introduction

• You have your TGA CA certificates
• You have a current ARTG entry
• The manufacturer decides to make a change to device design and/or a manufacturing related change....
• This session will take you through which changes need to be notified to TGA
What is the legislative basis for notifying the TGA of changes?
Legislative basis – change notification

Section 41EJ subsection (3) – Therapeutic Goods Act 1989

- The manufacturer of a medical device will notify the TGA, in writing, of any plan for substantial changes to the:
  - quality management systems
  - product range
  - product design

- Guidance coming soon
So which changes are significant?
Definition of substantial change

• The TG legislation does not contain a definition for “substantial changes”
• It is not practicable to specify what types of changes are or are not “substantial”
• Recommended that manufacturers have a system for categorising changes as substantial or not.
How does a manufacturer determine what should be notified?
Certificate Fields

Conformity Assessment Certificate

Full Quality Assurance Procedures

This certificate is issued under Section 41 of the Therapeutic Goods Act 2009

Manufacturer Name: Biggs Medical Pty Ltd
Manufacturer Address: Biggs Medical
Biggs Road
Blagrove
California

Commencement Date: 22 May 2014
Certificate Expiry Date: 22 May 2016

Device Categories

Critical Suppliers

Scope of Certificate

Manufacturer Facilities

<table>
<thead>
<tr>
<th>Name and Address</th>
<th>Scope</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Biggs Medical</td>
<td>Regulatory activities</td>
</tr>
<tr>
<td>2. Biggs UK</td>
<td>Quality Management System operations including post marketing vigilance/complaint handling activities</td>
</tr>
<tr>
<td>3. Biggs USA</td>
<td>Design and development activities for Ireland</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Name and Address</th>
<th>Scope</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Synovial Fluid substitution</td>
<td></td>
</tr>
<tr>
<td>2. HA et al</td>
<td>Supply of sodium hyaluronate</td>
</tr>
</tbody>
</table>

This certificate is issued under Section 41 of the Therapeutic Goods Act 2009 by:

Delegate of the Secretary
Office of Devices Authorisation
Therapeutic Goods Administration
PO Box 150, Woden ACT 2606 Australia
Have a change assessment process

• Manufacturer may have a change assessment process to work out if a change is significant and notifiable to TGA or other regulatory authorities.
• The process may ask a series of questions such as: Does the change introduce new hazards/risks?
• Does the change alter the intended use and/or compliance with the EPs?
• Does the change affect clinical performance?
• Does the change require the device to undergo further validation?
• Does the change mean the device will be used on different users?
How can a Sponsor ensure that the TGA is notified of changes?
Manufacturer/Sponsor Quality Agreements

This an example clause for the Sponsor to determine if the change needs to be notified to TGA:

The manufacturer agrees to provide written notice the changes listed below to the Products as detailed in the scope of this agreement as soon as reasonably possible.

- Change(s) to the intent to supply any or all of the Products
- Change(s) to the part number, description or significant labelling information of the Products - Significant labelling information is considered to be change to the text information excluding formatting
- Change(s) to the intended use of the Products
- Change(s) to design of the Products or Services that affect the form, fit or function, particularly dimensional changes.
Manufacture/Sponsor Quality Agreement (continued)

- Change(s) to the material(s) used in the Products.
- Change(s) in the Australian/European regulatory certification of the Products if applicable.
- Change of manufacturing site where the Products are made
- Change(s) to Supplier/Manufacturing Quality Management System Certification
- Change(s) to Supplier ownership or contact details
- Shelf-life
Global change notification SOP

Manufacturer's Regulatory Affairs team to notify Australian sponsor of proposed changes (always notify if in doubt)

Australian sponsor reviews proposed changes

Are changes significant?

No

Get all the supporting documents and submit an application to the TGA for the proposed change

Yes

Product cannot be supplied until the changes are approved by the TGA

No Submission required
### Example Product Change Notification response from the manufacturer

**PART B – REGULATORY REQUIREMENTS**

Your response is required by (dd/mm/yyyy) 25/07/2014

1. **What country(ies) are you responding for?**
   
   [List countries here]

2. **Will change(s) to product or process require submission or registration in any countries under your responsibility?**
   - **Yes**
   - **No**
   
   *If No* (no submission or registration), include a documented rationale/reason for the decision(s): 

   *If Yes* (submission required):
   - a) Which countries require a submission or registration?
   - b) What approval time is expected (weeks/months) post filing per country (if applicable)?
   - c) Identify supportive information required per country (if any):

3. **Will change(s) to product or process require notification in any countries under your responsibility?**
   - **Yes**
   - **No**
   
   *If No* (no notification), include a documented rationale/reason for the decision(s):

   *If Yes* (notification required):
   - a) Which countries require notification?
   - b) Identify supportive information required per country (if any):

4. **Can the change be implemented immediately without restrictions (e.g. import, sale etc)?**
   - **Yes**
   - **No**
   
   *If No* (restrictions do apply),
   - a) Which countries have restrictions?
   - b) Identify the restrictions and associated timelines per country:

**Completed by:**

**Date:** (dd/mm/yyyy)

*Note:* This record must be traceable to the specific individual making the above decisions. Please scan the signed form to PDF or use an electronic signature. Attach the signed PDF file to your reply email. The geography is encouraged to maintain a copy for their records.
How do you plan for changes?
Have a plan

<table>
<thead>
<tr>
<th>ID</th>
<th>Task Name</th>
<th>Start</th>
<th>Finish</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Sponsor made aware of the proposed change of change to shelf life from X years to Y years</td>
<td>5/06/2014</td>
<td>5/06/2014</td>
</tr>
<tr>
<td>2</td>
<td>Sponsor to confirm if this is a significant change and since in this case it is, go ahead with the next steps</td>
<td>5/06/2014</td>
<td>12/06/2014</td>
</tr>
<tr>
<td>3</td>
<td>Obtain supporting documents for submission such as test reports (drug stability reports if applicable, ageing / shelf life and product performance reports etc)</td>
<td>12/06/2014</td>
<td>11/07/2014</td>
</tr>
<tr>
<td>4</td>
<td>Put in the TGA eBS application</td>
<td>11/07/2014</td>
<td>18/07/2014</td>
</tr>
<tr>
<td>5</td>
<td>TGA will issue a request for information using the S41JA format</td>
<td>18/07/2014</td>
<td>31/07/2014</td>
</tr>
<tr>
<td>6</td>
<td>Provide the TGA with the supporting documents – A cover letter explaining the change is always useful, please ensure to put in the application for “abridgement” at this point of time.</td>
<td>31/07/2014</td>
<td>2/09/2014</td>
</tr>
<tr>
<td>7</td>
<td>TGA performs initial assessment and issues invoice</td>
<td>2/09/2014</td>
<td>31/10/2014</td>
</tr>
<tr>
<td>8</td>
<td>Sponsor to pay the invoice (please note that the application will not progress until invoice is paid)</td>
<td>3/11/2014</td>
<td>10/11/2014</td>
</tr>
<tr>
<td>9</td>
<td>TGA review / approval – depending on the queries the timeline may vary</td>
<td>10/11/2014</td>
<td>10/06/2015</td>
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Timing of when to let TGA know about the change

• Please allow adequate time for the TGA to consider and complete the assessment of the proposed changes. The assessment may require an onsite inspection which will have to be incorporated into the TGA inspection schedule.

• Before products are distributed for sale in Australia
Common significant changes – what to do
How to submit a change

Change of Legal Manufacturer  HQ address

Examples of supporting documentation
• Updated CE cert
• Notified body letter
• Legal entity declaration
• Council letter
Manufacturing facility/Site change

- Communicate and submit as soon as you are aware
- Provide a plan e.g. GANNT chart, Visual Stream Map, Master Validation Plan, explanation of changes and products affected.

Examples of evidence to be provided to TGA:
- Evidence to demonstrate ongoing compliance to the EPs, Master validation plan/report (IQ/OQ/PQ), regulatory body audit report, updated certificates, validation protocols and reports for special processes e.g. Cleanroom qualification, packaging qualification, and sterilisation.
Change to design

Example changes: additional sizes, changes to material, indications and shelf-life.

• Evidence to demonstrate on going compliance to the EPs
• Updated Essential Principles Checklist
• Design Verification and Validation protocols and reports including biocompatibility if the material has change, standards applications.
• Risk analysis
• Clinical Evidence – e.g. population may have changed.
• Shelf-life: functional stability as well as sterility.
Changes to Critical Suppliers

- Evidence to demonstrate ongoing compliance to the EPs
- Explain what they are supplying e.g. Drug, tissue, sterilisation facility.
- Procedures for supplier qualification and reports
- Demonstrate compliance to ISO 13485 e.g. Supplier qualification records, audit schedule and audit reports.
- Any supplier certification e.g. ISO /GMP
- In-coming inspection procedures and records
Common Mistakes

• The applicant not being aware of changes occurring at the manufacturing site
• Not being clear on the change or the extent of a change
  – Often informed of manufacturing changes, however, several design changes have been implemented.
Considerations once the change has been assessed and approved

• What about pre-change products still in circulation, can continue to be used?
• What happens if there is another change when one change is submitted?
• What do I need to do with the new CA certs?
• Will there be another manufacturing site audit?
Thanks for listening
Questions?
Brought to you by: