Increasing Post-Market Vigilance Requirements for Medical Devices

Pam Carter
Director
Devices Vigilance and Monitoring, Medical Devices Branch
Medical Devices and Product Quality Division, TGA
2017 ARCS Annual Conference

August 2017
Presentation Overview

- TGA’s role
- Definitions
  - Vigilance
  - Surveillance
- Australian regulation of medical devices
  - Legislative authority
  - Risk base approach to regulation
- Vigilance
- Surveillance
- Increasing post-market burden
TGA’s Role

The Therapeutic Goods Administration (TGA) safeguards and enhances the health of the Australian community through the effective and timely administration of the Therapeutic Goods Act 1989.

- We undertake our role by:
  - applying scientific and clinical expertise to all of our decisions
  - assessing the suitability of therapeutic goods for supply in and export from Australia
  - monitoring (through audits) that manufacturers of therapeutic goods are achieving acceptable standards of manufacturing quality
  - monitoring the quality, safety and performance (efficacy) of therapeutic goods on the market, including through laboratory testing where appropriate
  - undertaking regulatory actions that are proportionate to the potential risk arising from the non-compliance or safety risk
  - working collaboratively with consumers, health professionals, industry, technical and scientific specialists and our international regulatory counterparts
  - Informing consumers and health professionals of issues.
**Definitions**

- **Vigilance** is derived from the Latin “vigilare” - to stay awake or to care for.
  - Active monitoring/investigation of adverse events and complaints.
  - Fundamental principle is to reduce the change of the same types of adverse incident being repeated in different places\(^1\).

- **Surveillance** is defined as the systematic ongoing:
  - Collection;
  - Collation; and
  - Analysis of data for public health purposes.

- And, the timely dissemination of public health information for assessment and public health response as necessary\(^2\).

---

2. History of Vigilance and Surveillance, [http://www.notifylibrary.org/content/3-history-vigilance-and-surveillance](http://www.notifylibrary.org/content/3-history-vigilance-and-surveillance)
The TGA has authority to...

- Ask questions of sponsors and manufacturers. There are penalties for providing false and misleading information and not providing all information in the time frame specified.
- Seize products and inspect premises.
- Cancel/suspend products from supply:
  - Immediate if there is a potential risk of death or serious injury.
  - Failure to respond to a letter requiring information.
  - Not reporting an adverse event.
  - Safety or performance is unacceptable.
- Mandate a recall of a therapeutic product.
Risk-based approach to regulation

• Regulators work on risk-benefit assessment of products at a population level
• The benefit of using the device should be greater than the possible adverse events
• Higher levels of risk may be acceptable for a product used to treat a sudden deterioration in health, but not for a minor injuries
Regulating throughout the lifecycle

The TGA’s role is to continually monitor and evaluate the safety and performance of therapeutic goods that are available on the market and to ensure that devices continue to be ‘free from unacceptable risk’.

At all times it is the supplier and manufacturer that must demonstrate compliance with the Essential Principles of Safety and Performance. The TGA’s role is to monitor that they are fulfilling this responsibility.
# TGA's approach to compliance

## TGA's approach to compliance

<table>
<thead>
<tr>
<th>Help and support</th>
<th>Inform and advise</th>
<th>Correct behaviour</th>
<th>Enforce</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Make ongoing compliance easy</td>
<td>• Help to become and stay compliant</td>
<td>• Deter by detection</td>
<td></td>
</tr>
</tbody>
</table>

## Regulated entity - attitude to compliance

<table>
<thead>
<tr>
<th>Voluntary compliance</th>
<th>Accidental non-compliance</th>
<th>Opportunistic non-compliance</th>
<th>Intentional non-compliance</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Effective compliance systems</td>
<td>• Ineffective and/or developing compliance systems</td>
<td>• Resistance to compliance</td>
<td>• Deliberate non-compliance</td>
</tr>
<tr>
<td>• Management is compliance oriented</td>
<td>• Management compliance oriented but lacks capability</td>
<td>• Limited or poor compliance systems</td>
<td>• No compliance systems</td>
</tr>
<tr>
<td>‘Committed to doing the right thing’</td>
<td>‘Trying to do the right thing but don't always succeed’</td>
<td>‘Don't want to comply but will if made to’</td>
<td>‘Decision to be non-compliant’</td>
</tr>
</tbody>
</table>
Adverse Event Reporting - Vigilance

• Who? What? When? and How?
• IRIS Insite
• Case studies
IRIS – (Medical Device) Incident Report Investigation Scheme

“A scheme intended to help maintain the standard of devices used in health care through voluntary cooperation between users, government and industry through the investigation of adverse events and incidents”
What is an adverse event/incident?

An event that resulted in, or could have resulted in (had effective intervention not taken place) serious injury, illness or death to patient, healthcare worker or other person.

A medical device adverse event is an event associated (caused or partially attributable) with the use (or misuse) of a medical device.

Faults that may affect the quality, timeliness and cost-effectiveness such as, problems with getting the device to operate, repeated repairs, device design and difficulty of use.
What is a serious injury?

Serious injury (also known as serious deterioration in state of health) is:

• A life threatening illness or injury
• A permanent impairment of a body function (The term “permanent” means irreversible impairment or damage to a body structure of function. The term excludes minor impairment or damage).
• Permanent damage to a body structure
• A condition necessitating medical or surgical intervention to prevent permanent impairment of a body function or permanent damage to a body structure

(In this context, medical intervention is not in itself a serious injury. It is the reason that motivated the medical intervention that should be used to assess whether an event should be reported)
Sponsor – mandatory obligations

Why Report

- Sponsors must report the details of events associated with their device(s) that have resulted, or could have resulted, in serious injury or death
  - These are conditions of inclusion set out in the Therapeutic Goods (Medical Devices) Regulations (2002)
  - Consumers and Health Professionals are encouraged to report to the TGA and/or the sponsor

When to report

- Within **two days** of becoming aware of an issue of serious public health threat or concern that will require prompt action to reduce the hazard
- Within **ten days** of becoming aware of a death or serious injury
- Within **thirty days** of becoming aware of an event that might have led to serious injury or death
Exemption rules

Eight exemption rules

• found by the user prior to its use
• caused solely by patient conditions
• Service life of the medical device
• Protection against a fault functioned correctly
• Remote likelihood of occurrence of death or serious injury
• Expected and foreseeable side effects that are documented in manufacturer’s Instructions for Use or labelling
• Adverse events described in an advisory notice
• Reporting exemptions granted by the TGA

None of which apply if;
- Identified by the TGA as an issue that requires close monitoring
- A change in trend (usually an increase in frequency) or pattern is identified
- Adverse events associated with user error
Medical Device Adverse Events

The preferred method of reporting is online

Go to TGA website www.tga.gov.au and follow links to eBs or go directly to the eBs portal if in favourites. Enter user name and password. Select “New Report” or an existing report.

Enter information into the web based form

Device Incident Report (DIR) number will be available immediately after submitting the report.

Save or print your report.
What happens to the report?

- Reports are entered into the IRIS database and risk assessed
- Reports assessed as urgent are addressed immediately
- Focus is on unusual problems, potentially serious problems, or problems that have high levels of incidences
- Many reports are not investigated, however they are utilised for trending and monitoring purposes
- Reports are treated as confidential and the reporter and sponsor are informed of the outcome of the investigation
- Most reports are placed onto the Database of Adverse Event Notifications (DAEN)
Investigation

- Investigation
- Information from the sponsor
- Patient/user feedback
- Testing
- Research
- TGA regulatory information
- Other regulators information, i.e. FDA
Potential outcomes of investigation

- Safety alert
- Hazard alert
- Recall
- Articles in TGA publications (Medical Devices Safety Update)
- Product and labelling improvements (e.g. updating Instructions for Use)
- Increasing post-market surveillance
- Imposing limitations on the device’s use
- Investigating manufacturing sites
- Suspending or cancelling the product’s entry on the Australian Register of Therapeutic Goods
- Referral to other TGA sections for other regulatory actions
Post-Market Reviews

• Post-market monitoring
  - why, who, when, and what

• Quality Management System
  - Clinical evaluation report
  - Literature search
  - Risk management documentation
  - Instructions for Use
  - Technical documentation

• Case Studies
Post-market review – Why and Who

• Why are post-market reviews conducted (not an exhaustive list):
  − Trends from IRIS
  − Recurrent advertising breaches
  − Unresolved/repeated recalls
  − Information from other regulatory agencies
  − ARTG anomalies

• Who or what is reviewed:
  − Sponsor
  − Manufacturer
  − Ingredient
  − Product
  − Kind of device

• When:
  − Any point in the product’s life-cycle.
Post-market review process

What - Calling in and reviewing:

- Essential Principles checklist
- Post-market data incl. supply, adverse events and complaints
- Labels
- IFU
- Current clinical evidence report
- Risk management documentation

- Declaration of conformity & manufacturer’s certification
- Technical documentation
- Ingredients and formulations of medicated/formulated devices
- Advertising material
- CAPAs
- Samples

Dependent on the issue under review
Post-market review: Evidence

Clinical Evidence Report

Post-market vigilance

Risk assessment

Risk mitigations
Post-market reviews: What

Validation of evidence for relevant Essential Principles (EPs) and conformity assessment, dependent upon scope/issue being reviewed. For example:

- EP checklist
- Conformity report against relevant technical standards
- ISO 13485 certification for manufacturer
- Test reports demonstrating design and development changes; verification and validation
- Sterilisation process records
- Useability studies
- Adverse event monitoring (ISO 13485:2016, 8.2.2)
Post-market review outcomes

- Closure of review
  - Not in scope
  - Sufficient and satisfactory evidence provided
- Amendment to Instructions for Use
  - With or without recall action
  - Recall of devices or safety notice

- Additional conditions of inclusion (s41 FP)
- Suspension (s41 GA & GF)
- Cancellation (s41 GK, GL, GM, & GN)
- Referral to:
  - Advertising Compliance (s42 DL), or
  - Regulatory Compliance

Uniform Recall Procedure for Therapeutic Goods
### Number of Reviews

<table>
<thead>
<tr>
<th>Financial Year</th>
<th>No. ARTG entries under review carried forward</th>
<th>No. new ARTG reviews commenced</th>
<th>No. ARTG reviews completed</th>
<th>Cancelled by Sponsor</th>
<th>Cancelled by TGA</th>
</tr>
</thead>
<tbody>
<tr>
<td>2015-2016</td>
<td>104</td>
<td>87</td>
<td>86</td>
<td>22</td>
<td>3</td>
</tr>
<tr>
<td>2016-2017</td>
<td>105</td>
<td>396</td>
<td>239</td>
<td>20</td>
<td>30</td>
</tr>
</tbody>
</table>

### Reason for TGA Cancellation

<table>
<thead>
<tr>
<th>Reason for TGA Cancellation</th>
<th># 2015-16</th>
<th># 2016-17</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non compliance with automatic conditions of inclusion</td>
<td>3</td>
<td>28</td>
</tr>
<tr>
<td>Non compliance with additional conditions of inclusion</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>

Post-Market Vigilance Requirements for Medical Devices
Case study #1 – heart valve

Signal:

• adverse events relating to leaflet breakage
  • IRIS investigation
• same problem reported for another manufacturer’s heart valve
  • TGA checks available data
  • reports for other heart valves
  • recall for heart valve

Review of all similar heart valves to determine if isolated issue or systemic
Case study #1 – heart valve

• **Information requested**
  – Clinical evidence
  – Technical documentation
  – Risk assessment documents
  – IFUs
  – Post-market data

• **When was it sent**
  – Following a reminder s41JA letter
  – Emails stretched across a week or more

• **What was sent**
  – Multiple emails with lots of journal articles
  – IFUs
  – EP checklist
  – Risk assessment

So, what happened next?
What happened next?

Case study #1 – heart valve

• Proposal to Cancel (s41GN(2))
  – Failure to provide information after a s41JA letter (s41GN(1)(c)); and
  – Failure to comply with the Conditions of Inclusion (s41GN(1)(b))
    ▪ sufficient information is provided that shows compliance with the Essential Principles; and
  – The safety and performance of the device is unacceptable (s41GN(1)(d))
What happened next?
Case study #1 – heart valve

- Information was supplied which showed that this device was performing within specification
- However, the manufacturer had a new improved valve that had an even lower rate of problem
- Negotiation with the sponsor to cancel the device and submit an application for the better valve
- The sponsor cancelled the ARTG entry
Annual Reporting

- **Sponsors** are required to submit three annual reports to the TGA following a new inclusion of a high risk medical devices

- The devices subject to annual reporting are as follows:
  - AIMD
  - Class III
  - Implantable Class IIb
  - Class 4 IVDs

- The sponsor is required to provide, number of devices supplied, complaint and adverse event data

- To ensure that high risk devices new to the Australian market are continuing to meet the essential principles for safety and performance.

- To ensure that the sponsor and manufacturer’s post-market surveillance system is functioning sufficiently to detect any issues as early as possible.
• Increasing post-market burden
Further Information

- *Therapeutic Goods Act 1989*
- Therapeutic Goods (Medical Devices) Regulations 2002
- Therapeutic Goods Regulations 1990
- Australian regulatory guidelines for medical devices (ARGMD) – Under Review
- Database of Adverse Event Notifications (DAEN)
- Medical device reporting form
- Medical device adverse event reporting information