Global Medical Device Regulatory Overview

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Why postmarket .................
Some statistics

Patient treatments to enable detection of adverse events

<table>
<thead>
<tr>
<th>Expected number of adverse incidents</th>
<th>1 event</th>
<th>2 events</th>
<th>3 events</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 in 100</td>
<td>300</td>
<td>480</td>
<td>650</td>
</tr>
<tr>
<td>1 in 200</td>
<td>600</td>
<td>960</td>
<td>1,300</td>
</tr>
<tr>
<td>1 in 1,100</td>
<td>3,000</td>
<td>4,800</td>
<td>6,500</td>
</tr>
<tr>
<td>1 in 2,000</td>
<td>6,000</td>
<td>9,600</td>
<td>13,000</td>
</tr>
<tr>
<td>1 in 10,000</td>
<td>30,000</td>
<td>48,000</td>
<td>65,000</td>
</tr>
</tbody>
</table>

Source: Safety requirements for the first use of drugs and diagnostic agents in man; WHO, Geneva, 1983

Medical devices and Medicines – the differences

Medical Device

- Physical object, complex assembly and construction, generally based on mechanical, electrical and materials engineering.
- Act through interaction with the body
- Duration and nature of exposure varies widely
- Typically durable, available for study after use
- Focus on biocompatibility of materials

Medicine

- Pure molecule – base on pharmacology and chemistry, but now incorporating biotechnology, genetic engineering, etc
- Typical systemic effect
- Short half life in the body
- Consumed by use
- Focus on local systemic effect and toxicity
### Medical devices and Medicines – the differences

<table>
<thead>
<tr>
<th><strong>Medical Device</strong></th>
<th><strong>Medicine</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Generally not subject to ethnic differences</td>
<td>May be subject to ethnic differences</td>
</tr>
<tr>
<td>Relatively limited populations of exposure</td>
<td>Large populations of exposure</td>
</tr>
<tr>
<td>Wide range – bandages to MRI Scanners........</td>
<td>Tend to differ only in molecular structure, active site and mode of application</td>
</tr>
<tr>
<td>Diverse technologies, presentations and modes of action</td>
<td>Usually only tablets, ointments, solutions of aerosols</td>
</tr>
<tr>
<td>Typically require significant user interaction</td>
<td>Little user interaction....other than ingestion, application, etc</td>
</tr>
</tbody>
</table>

Medical Device Industry – over 80% are small to medium enterprises
Intellectual property – continuous innovation and iterative improvements based on new science, technologies and materials
Short lives patents because of continual improvement and innovation
Short product life cycle and investment recovery period (typically 18 – 24 months)
Few ‘generic’ devices

Medical
Large, multi-national companies dominate
Extensive R & D of new molecules, many years for new medicine to enter the marketing pipeline
Strong patent protection to maintain market exclusivity
Long product life cycle and long investment recovery (15 year patent protection with possible extensions)
Significant ‘generics’ industry after patent expiry
## Medical devices and Medicines – the differences

**Medical Device**
- Invented and designed, often with input from clinical users
- Designed to perform a specific function
- Regulatory approval on the basis of safety and performance
- Constantly evolving design and process changes occur throughout product life

**Medical**
- Discovered in lab based research processes
- Development by discovery and trial
- Regulatory approval on the basis of safety and efficacy
- Stable formulation

**Medical Device**
- Incremental improvement and innovation brings newer products with added functions and clinical value
- Performance often validated through bench studies ...many also subject to clinical trial
- Often manufactured by manual operation
- Quality Management systems (QMS)

**Medical**
- Usually large step innovation
- Validated through clinical studies
- Highly mechanised manufacture
- Good Manufacturing Practice (GMP)
## Medical devices and Medicines – the differences

### Medical Device

**Use and postmarket** -

- Most intended for professional use
- Device malfunction or failure
- User error (professional or patient)
- Adverse events most often localised in nature

### Medicine

- Prescribed by professional, used by patient
  - Risk of patient choosing to stop use
- Medicine adverse reaction or interaction
- Incorrect medicine or dosage prescribed
- Adverse events may be widespread

### Medical Device

**Manufacturer support** -

- Sales channels vary based on the device......wholesalers generally not involved
- Large investments in manufacturing, distribution and user training/education
- Technical training and support, service and repair

### Medicine

- Typically supplied through (lengthy ?) wholesale chain
- Large investments in manufacturing, distribution, training and clinical support
- No service or maintenance
Medical devices and Medicines – the differences

Medical Device

Remedial action -
Upgrades through -
• field engineering modifications
• Software updates
• Amended indications for use

Recalls -
• Cease use
• Explant !!

Medicine

Adjustments to dosage or application indications

Recalls -
• Cease use

Conclusion

Significant differences in products, technologies, life cycles, marketing and industry structures

Medical devices are different !!

While each can learn from the other, different regulatory schemes for postmarket programs are required

Adverse event programs for medical devices need to take into account many factors

Remedial/upgrades of medical devices are possible in many instances

Recall of implanted medical devices presents a ‘unique’ challenge
### Global Model

**What is a medical device**

**What is needed to ensure**

Safety and performance

How to meet the Essential Principles

What is needed to ensure

The safety of the product

What level of Conformity Assessment is appropriate

Supporting Documentation

Regulatory Assessment

Market entry

- Quality System
- Design Control Process
- Full Technical Evidence

### Pre-market Technical Requirements

<table>
<thead>
<tr>
<th>Definitions</th>
<th>Essential Principles of Safety &amp; Performance</th>
<th>Use of Standards (or other means)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Evidence Requirements</td>
<td>Clinical Evaluation (as appropriate)</td>
<td>Labelling (including Instructions for use)</td>
</tr>
<tr>
<td>Use of Standards (or other means)</td>
<td>Risk based classification Rules – Four classes</td>
<td>Summary Technical File</td>
</tr>
<tr>
<td>Clinical Evidence Requirements</td>
<td>Conformity Assessment</td>
<td>Entry on a Register</td>
</tr>
</tbody>
</table>

### Establishment of a Regulatory Framework

- Premarket Assessment
- Postmarket Monitoring
- Postmarket Monitoring

- Register
- Register
- Register

- Quality System
- Design Control Process
- Full Technical Evidence

- Audit procedures and protocols

- Post Market Vigilance and Reporting Procedures

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*ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators*

*March 27 - 28, 2014, San Francisco, California*
Questions for ‘Postmarket’ ……..

- Long term safety
- After the bench verification, testing and clinical trial
  - use in the broader population
- Unusual pattern of adverse events which may not lead to product recall
- Interaction with the clinical environment (e.g. other medical devices)
- Change of use setting
  - Eg. Moving from the hospital to the home setting
- New risks
  - Off label use
  - User error
- Market experience…...’what will the new model look like ……..’

What is ‘postmarket’ ……..

- Many think of ‘postmarket’ as adverse event reporting……..
- ……… but it is so much more !!!
‘Postmarket’ is ..........

- Adverse incident reporting
  - Manufacturers and Authorised Representatives
  - Clinical users
  - General public

- Adverse event investigations
  - Manufacturer
  - Regulator

‘Postmarket’ is also ..........

- Audits
  - On-going QMS audits of the manufacturer
  - Technical File Audits
  - Product group reviews
  - Authorised Representative / Distributor reviews/audits (eg - GDP, record keeping, storage conditions....)
  - Clinical trials ( ?? Pre or post market activity)

- Pro-active Vigilance systems/epidemiological studies
  - Manufacturer and Authorised Representatives
  - Regulator
‘Postmarket’ is also

- **Advertising controls**
  - Vary between jurisdictions
    - Restrictions on advertising to some audiences
    - Content pre-approval
    - Complaint handling

- **Formal recall processes**
  - Responsibility / Accountability
  - Product withdrawal/remediation

- **Enforcement**
  - Authorised Representatives
  - Manufacturer

- **Inter-agency information exchange**
  - NCAR program

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**Life Cycle with regulatory aspects included**

**Audit practice**

**Quality Management Systems & Risk Management**

- Concept
- Product Realisation
- Placing on Market
- End of Product Life
- Product Use
- Disposal

Design inputs Leading to new product
Improvements and corrective actions
Life Cycle with applied processes

Compliance Audit - by Conformity Assessment Body or the Manufacturer
Quality Management Systems & Risk Management by the manufacturer

Premarket Classification & Conformity Assessment
- Essential Principles
- Use of Standards
- Design inputs
- Design control
- Design -
  - Verification
  - Validation
- Clinical Evidence
- Summary Technical Documentation
- Declaration of Conformity

Placing on the market
- Registration
- Entities
- Listing
- Products

Postmarket Surveillance/Vigilance
- Adverse event reporting
- Complaint management
- Maintenance & Service
- Corrective and preventive actions
- Postmarket Clinical Follow-up

Postmarket – Sources of information

Field Safety Notice
- Classification
- Definition

Field safety corrective action

Corrective and Preventive Action

Quality Management System

Risk Management ISO 14971
- Detectability
- Probability
- Severity
- Risk/benefit
- Trend
- Review of labelling & Product Info

Adverse event Reporting
- Locally, to the Regulatory Authority

NCAR Exchange Program
- Exchange criteria
- Application to join
- Handling of reports

AE Reporting during clinical investigation

Information collection
- Media
- Regulatory Auth.
- Patients/Consumers
- Healthcare Institutions
- Manufacturer's QMS
- Lab testing

(Inc. complaints & dissatisfaction reports)
**Postmarket – Risk Management**

- Manufacturer’s must use adverse event reporting as part of the Risk Management Process – ISO 14971 – covering the total life cycle of the device

- ‘Closing the loop’

- Things to consider
  - Was the Adverse event considered in the original risk analysis at the design/development stage?
  - Is the occurrence and severity as predicted?
  - ?? caused by off label use – was this considered in original risk analysis?
  - Have the steps taken to reduce the risk been adequate?

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**Postmarket – even before marketing approval**

- Clinical trials
  - Adverse event reports recorded, analysed and reported
  - Observed side effects, not considered in the risk analysis
    - Singular event
    - Recognised patterns
  - Should the trial be allowed to continue ........pause, or stopped !!

- Even clinical trial adverse events provide information about the marketed device performance and history
Postmarket - other information sources

- Not just adverse event reports
- What about -
  - Customer complaints
  - Journal articles
  - Repair requests
  - Regulatory Authority product surveys or product testing
  - Independent lab studies or customer trials
  - Manufacturer's QMS product testing
  - Attention in the media!!

Postmarket – (CAPA)

- CAPA - Corrective and Preventive Action
- Adverse event data using in the QMS and manufacturing process -
  - Was the adverse event due to a design or production issue
  - ?? Any other products use the same design, production or manufacturing process
  - ?? Changes in product design, manufacture, labelling or training
  - Knowledge used in development of future products
Postmarket – NCAR Exchange program

- Established by GHTF Study Group 2

- NCAR – National Competent Authority Report
  - Information exchange between Regulator’s
    - Two levels
      - Confidential information
      - Adverse event; or
      - Observation of trend, etc in relation to device or device type
    - Public information
      - Recalls/Hazard Alerts
      - Product Notifications, Field engineering changes, etc

Postmarket – Adverse event reports

- Adverse event reports
- Customer Complaints
- Information from the Regulatory Authority
  - Consumer adverse event reports/complaints
  - Adverse event trend analysis
  - QMS Audit findings
  - Outcomes of product surveys or laboratory testing
  - NCAR Reports
Postmarket – Adverse event reports

Extensive guidance available on adverse event reports

- Who should report
- Who to report to
- What to report
- When to report
  - What not to report….exemptions
- Investigation
  - Regulatory Authority
  - Manufacturer
- Outcomes
  - Product recall
  - Field modification
  - Product advisory

Postmarket

Early step in the introduction of regulation

- Introduction of adverse event reporting systems

Examples of countries with active postmarket programs -

- Australia
- Brazil
- Canada
- China
- South Africa
- New Zealand
- Singapore
- Saudi Arabia
- United States
- European Union
- Japan
- Hong Kong
- Malaysia
- Taiwan
- Korea
- India
**Adverse events – what to report**

An event needs to meet three basic reporting criteria –

- An adverse event has occurred;
- The medical device is associated with the adverse event;
- The event lead, or might have lead (often called ‘near miss events) to death or serious injury; or
- Might lead to death or serious injury if it were to occur again

**Adverse events – What to report**

**Death or serious injury**

- ‘Serious public health threat’
  - Any event type, which results in imminent risk of death, serious injury or serious illness that requires prompt remedial action........GHTF

- ‘Unanticipated death or serious injury’
  - ......considered unanticipated if the conditionleading to the event was not considered in the risk analysis performed during the design or development phase .....GHTF

- ‘serious injury’ not defined by GHTF
  - Serious deterioration in the state of health, of a patient, a user of the device, or another person .......Australia
**Information to be provided in the report**

- Authorised Representative/manufacturer details – name, contact, address etc
- Device identification – name, model, serial #, batch #, etc
- Any associated devices
- Details of the incident – reporter, date, patient ID, narrative
- Outcome of the event – patient or user outcome
- Contact point for further information
- Disposition of the device in question – preferably immediately quarantined
- Authorised Representative/Manufacturer initial comments
- Intended action ............ If any
- Is the Authorised Representative/Manufacturer aware of similar events
  - Details

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**Adverse events – who should report**

- **Mandatory reporting**
  - Manufacturers
  - Authorised representatives
  - Distributors (??)
- **Voluntary reporting ............ to the Regulatory Authority and**
  - Authorised Representative/manufacturer
  - Clinical users
  - General public
- **Sentinel reporting**
  - FDA initiative utilising selected clinical users and institutions
### Adverse events – when to report

- **Immediate adverse event report**
  - Unanticipated death or serious injury
  - Serious threat to public health ..................
  - 10 days
- **All other adverse events** ..................
  - 30 days
- **If in doubt** ..................
  - Report
- **Australia**
  - Serious threat to public health .............48 hours

### Adverse events – what not to report

- **Exemptions**
  - Exemption from reporting at all; or
  - Changed to periodic or summary reporting
  - .....however any upward change to observed trending of incidents must be reported immediately
**Adverse events – what not to report**

**Exemptions**

- Deficiency in a device found by user prior to patient use
  - eg - damaged sterile packaging discovered before use, and product labelled do not used if packaging damaged

- Adverse event caused by patient conditions
  - eg - patient died after dialysis treatment...patient had end stage renal failure

- Used after expiration of labelled shelf life or service life
  - eg - pacemaker ceased pacing .... But ERI and EOL indicators had both been activated in accordance with correct device operation

- Malfunction protection systems operated correctly
  - Infusion pump alarms because of ‘air-in-line’ detected, and ceases pumping

**Exemptions**

- Negligible likelihood of occurrence of death or serious injury
  - eg - Manufacturer or Authorised Representative contact details incorrect on packaging ........likelyhood of serious injury determined as negligible

- Expected and foreseeable side effects
  - eg - undesirable skin reaction to nickel in spectacle frames .....previously known and documented in product information

- Adverse event described in an already published advisory notice
  - Eg - advisory notice issued in relation to coronary stent migrating because of inadequate inflation of balloon.......further reports of of stent migration provided to RA in summary reports
**Lines of Communication**

- Biomedical Engineering
- Purchasing Dept.
- Supplier or Manufacturer
- Clinicians
- Quality/Risk Manager (Hospital Administration)
- Regulators
- Patient's Lawyer
- Legal Counsel
- Insurer

**Real Life.......

- Purchasing Dept.
- Clinicians
- Biomedical Engineering
- Supplier or Manufacturer
- Regulators
- Quality/Risk Manager (Hospital Administration)
- Patient's Lawyer
- Legal Counsel
- Insurer
The IRIS process ...... Australia

The investigation process

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**Result of Investigations**

![Bar Chart: Result of Investigations](image1)

**Source of Reports**

![Bar Chart: Source of Reports](image2)
Type of Reports Received

Postmarket product monitoring

- Regulator activity
  - Sampling product from the market
  - Testing for compliance to
    - Regulatory requirements
    - Labelling
    - Product Performance
      - Standards
- Generally focus on high volume consumer products
  - Condoms
  - Bandages and dressings
  - Contact lens care solutions
- But also
  - Professional use products with poor performance or high failure rates
    - Gloves
    - Urinary catheters
Enforcement

- Field Safety Corrective Action
- Recall
  - Recall product from the market
  - Recall for product correction
  - Hazard Alert
- Non-recall advisory
  - Eg unanticipated interaction between two devices when used together
- Financial penalties

Postmarket – Advertising controls

- Global model is silent on advertising controls
- Definitions
  - What is an advertisement
- Allowable target audience for an advertisement
  - Clinical user
  - General public
- Truth in Advertising
  - Allowable claims
- Enforcement
Australia’s Vigilance and Market Monitoring Systems

Postmarket - Device Registers

- Recent tool in the postmarket package
- Take time to build up reliable data
- Early ‘signals’ about poor performance
- Analysis of data is complex, and multi-dimensional
- Best example to date
  - National Joint Replacement Register
Postmarket – Device Registries

- Monitors on-going performance of higher risk implantable medical devices
  - Heart valves
  - Pacemakers
  - Breast implants
  - Orthopaedic implants
  - High risk materials ... eg animal origin

- Extremely useful for new and innovative technologies
  - Combination products
  - Materials/devices with genetically modified organisms or recombinants

National Joint Replacement Register

- Operated by the Australian Orthopaedic Association
  - 1998 - Commonwealth Gov't agreed to fund establishment
  - 1999 - Commenced operation in South Australia
  - 2002 - Commenced national data collection
  - 2007 - Expanded to
    - Shoulder,
    - elbow,
    - wrist,
    - ankle and
    - spinal disc
  - 2008 - Data now inclusive enough to share with TGA for regulatory consideration
  - 2009 - Funding tenuous until Commonwealth agreed to fund the operation through cost recovery from industry
  - 2011 - recorded 665,000 Hip and knee procedures up to July
**Algorithm used to identify any prosthesis (or combination) not performing to the level of all others of the same type/class**

- The revision rate per 100 component years exceeds **twice** that of the group, **and**
- The poisson probability of observing that number of revisions given the rate of the group, is **0.05**, **and**
- There are at least 10 primary procedures for that component, **or**
- The proportion revised is at least 75% and there have been at least two revisions recorded

**Data Validation**

- Registry receives 96% of data from hospitals
- Registry data are checked against Government data using a sequential multi-level matching process
- This process enables the Registry to subsequently collect the remaining 4%
‘There is considerable evidence that the Australian Registry has produced major beneficial change in Arthroplasty practice in Australia’

Overall Change in number of revisions

- Proportion of hip procedures that are revisions has declined from 13.0% in 2003 to 11.2% in 2009.

- Proportion of knee procedures that are revisions has declined from a peak of 8.8% in 2004 to 7.9% in 2009.

- These declines are accounted for by significant reductions in early revision rates specifically related to changing practices as a consequence of Registry data.
Change in number of revisions in 2009

- Equates to **600 less hip revision procedures** and **378 less knee revision procedures** in 2009 compared to what would have been the case if the proportion had not declined.

- This has resulted in a significant cost saving to the health care sector.

Annual Report Published October each year

- 2010 Annual Report
  - Analysis of 547,607 primary and revision hip and knee procedures recorded by the Registry up to the 31st December 2009
  - Increase of 74,641 procedures compared to 2009 Annual Report
Typical NJRR Data available to the Regulator

Femoral Component Total Hip Investigation

Revision Rates

<table>
<thead>
<tr>
<th>Component</th>
<th>Revised</th>
<th>Total</th>
<th>'Component' Years</th>
<th>Revisions per 100 'Component' Years</th>
<th>Exact 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Other/Total</td>
<td>3127</td>
<td>124822</td>
<td>388063</td>
<td>0.8</td>
<td>(0.78, 0.85)</td>
</tr>
<tr>
<td>DUR</td>
<td>18</td>
<td>162</td>
<td>398</td>
<td>4.5</td>
<td>(2.68, 7.15)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>3145</td>
<td>12644</td>
<td>398461</td>
<td>0.8</td>
<td>(0.79, 0.86)</td>
</tr>
</tbody>
</table>

Cumulative % Revision

<table>
<thead>
<tr>
<th>CPR</th>
<th>1 Yr</th>
<th>2 Yrs</th>
<th>3 Yrs</th>
<th>5 Yrs</th>
<th>7 Yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Other/Total</td>
<td>1.5 (1.4, 1.6)</td>
<td>2.1 (2.0, 2.2)</td>
<td>2.5 (2.4, 2.6)</td>
<td>3.4 (3.2, 3.5)</td>
<td>4.1 (3.9, 4.4)</td>
</tr>
<tr>
<td>DUR</td>
<td>6.2 (3.5, 10.9)</td>
<td>9.4 (5.9, 14.9)</td>
<td>12.2 (7.5, 19.7)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

** DUR – Device under Review

Type of revision performed by primary failure

<table>
<thead>
<tr>
<th>Type of Revision</th>
<th>Other/Total</th>
<th>DUR</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>%</td>
<td>N</td>
<td>%</td>
</tr>
<tr>
<td>Femoral/Component Only</td>
<td>903</td>
<td>28.9</td>
<td>10</td>
</tr>
<tr>
<td>Acetabular Component Only</td>
<td>771</td>
<td>24.7</td>
<td>2</td>
</tr>
<tr>
<td>Head/Insert</td>
<td>615</td>
<td>19.7</td>
<td>2</td>
</tr>
<tr>
<td>Femoral and Acetabular (THR)</td>
<td>336</td>
<td>10.7</td>
<td>.</td>
</tr>
<tr>
<td>Head Only</td>
<td>204</td>
<td>6.5</td>
<td>3</td>
</tr>
<tr>
<td>Cement Spacer</td>
<td>129</td>
<td>4.1</td>
<td>1</td>
</tr>
<tr>
<td>Cable/Other Minor Components</td>
<td>65</td>
<td>2.1</td>
<td>.</td>
</tr>
<tr>
<td>Inset only</td>
<td>60</td>
<td>1.9</td>
<td>.</td>
</tr>
<tr>
<td>Removal Prostheses</td>
<td>31</td>
<td>3.0</td>
<td>.</td>
</tr>
<tr>
<td>Reimplant of Components</td>
<td>8</td>
<td>0.3</td>
<td>.</td>
</tr>
<tr>
<td>Cement Only</td>
<td>3</td>
<td>0.1</td>
<td>.</td>
</tr>
<tr>
<td>Bipolar head and Femoral Component</td>
<td>1</td>
<td>0.0</td>
<td>.</td>
</tr>
<tr>
<td>Cable and Cement</td>
<td>1</td>
<td>0.0</td>
<td>.</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>3127</td>
<td>100.0</td>
<td>18</td>
</tr>
</tbody>
</table>

** DUR – Device under Review

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### Revision Diagnosis by Days to Revision for Other Total

<table>
<thead>
<tr>
<th>Revision Diagnosis</th>
<th>1. &lt;2wks</th>
<th>2. 2wks-3mths</th>
<th>3. 3mths-1yr</th>
<th>4. 1yr-3yrs</th>
<th>5. &gt;=3yrs</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>% Row%</td>
<td>N</td>
<td>% Row%</td>
<td>N</td>
<td>% Row%</td>
</tr>
<tr>
<td>Other</td>
<td>36</td>
<td>11.2</td>
<td>26</td>
<td>3.1</td>
<td>31</td>
<td>13.7</td>
</tr>
<tr>
<td>Dislocation of Prosthesis</td>
<td>130</td>
<td>40.4</td>
<td>365</td>
<td>43.0</td>
<td>219</td>
<td>25.7</td>
</tr>
<tr>
<td>Implant Breakage</td>
<td>95</td>
<td>29.5</td>
<td>170</td>
<td>20.0</td>
<td>33.2</td>
<td>13.8</td>
</tr>
<tr>
<td>Acetabular</td>
<td>2</td>
<td>0.6</td>
<td>6</td>
<td>0.8</td>
<td>4</td>
<td>0.8</td>
</tr>
<tr>
<td>Implant Breakage Head</td>
<td>.</td>
<td>.</td>
<td>.</td>
<td>.</td>
<td>3</td>
<td>0.4</td>
</tr>
<tr>
<td>Implant Breakage Stem</td>
<td>.</td>
<td>.</td>
<td>2</td>
<td>0.2</td>
<td>11.8</td>
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</tr>
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<td>Infection</td>
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<td>31.1</td>
<td>15.7</td>
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<tr>
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<td>119</td>
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<td>Pain</td>
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<td>1</td>
<td>0.1</td>
<td>5.9</td>
<td>1</td>
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<td>Total</td>
<td>322</td>
<td>100</td>
<td>948</td>
<td>25.1</td>
<td>732</td>
<td>21.7</td>
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### Revision Diagnosis by Days to Revision for DUR

<table>
<thead>
<tr>
<th>Revision Diagnosis</th>
<th>1. &lt;2wks</th>
<th>2. 2wks-3mths</th>
<th>3. 3mths-1yr</th>
<th>4. 1yr-3yrs</th>
<th>5. &gt;=3yrs</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>% Row%</td>
<td>N</td>
<td>% Row%</td>
<td>N</td>
<td>% Row%</td>
</tr>
<tr>
<td>Dislocation of Prosthesis</td>
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<td>2</td>
<td>50.0</td>
<td>1</td>
<td>16.7</td>
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<tr>
<td>Fracture</td>
<td>1</td>
<td>50.0</td>
<td>2</td>
<td>50.0</td>
<td>1</td>
<td>16.7</td>
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<tr>
<td>Infection</td>
<td>.</td>
<td>.</td>
<td>.</td>
<td>.</td>
<td>1</td>
<td>16.7</td>
</tr>
<tr>
<td>Other</td>
<td>1</td>
<td>50.0</td>
<td>2</td>
<td>50.0</td>
<td>1</td>
<td>16.7</td>
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<td>50.0</td>
<td>3</td>
<td>50.0</td>
</tr>
<tr>
<td>Pain</td>
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<td>.</td>
<td>.</td>
<td>1</td>
<td>16.7</td>
</tr>
<tr>
<td>Total</td>
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</table>

### Revision rate by hospital

<table>
<thead>
<tr>
<th>Hospital</th>
<th>Number Revised</th>
<th>Total Number</th>
<th>Observed Component Years</th>
<th>Revisions per 100 Observed Component Years</th>
<th>Exact 95% CI</th>
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</thead>
<tbody>
<tr>
<td>Hospital 001</td>
<td>0</td>
<td>1</td>
<td>4</td>
<td>0.0 (0.00, 101.8)</td>
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</tr>
<tr>
<td>Hospital 002</td>
<td>1</td>
<td>3</td>
<td>9</td>
<td>10.9 (0.28, 60.68)</td>
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</tr>
<tr>
<td>Hospital 003</td>
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<td>1</td>
<td>2</td>
<td>0.0 (0.00, 229.8)</td>
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</tr>
<tr>
<td>Hospital 004</td>
<td>0</td>
<td>2</td>
<td>6</td>
<td>0.0 (0.00, 66.73)</td>
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</tr>
<tr>
<td>Hospital 005</td>
<td>1</td>
<td>8</td>
<td>24</td>
<td>4.1 (0.10, 22.85)</td>
<td></td>
</tr>
<tr>
<td>Hospital 006</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>14.3 (0.00, 428.4)</td>
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</tr>
<tr>
<td>Hospital 007</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>14.3 (0.00, 500)</td>
<td></td>
</tr>
<tr>
<td>Hospital 008</td>
<td>0</td>
<td>3</td>
<td>4</td>
<td>25.2 (0.00, 140.4)</td>
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</tr>
<tr>
<td>Hospital 009</td>
<td>0</td>
<td>1</td>
<td>10</td>
<td>1043.6 (26.42, 5814)</td>
<td></td>
</tr>
<tr>
<td>Hospital 010</td>
<td>2</td>
<td>69</td>
<td>138</td>
<td>5.3 (0.00, 19.19)</td>
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</tr>
</tbody>
</table>

### Revision rate by State

<table>
<thead>
<tr>
<th>Component</th>
<th>State</th>
<th>Number Revised</th>
<th>Total Number</th>
<th>Observed Component Years</th>
<th>Revisions per 100 Observed Component Years</th>
<th>Exact 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Other</td>
<td>ACT/NT</td>
<td>7</td>
<td>7</td>
<td>1.0</td>
<td>(0.77, 1.20)</td>
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</tr>
<tr>
<td>Other</td>
<td>NSW</td>
<td>284</td>
<td>103742</td>
<td>12740</td>
<td>0.8 (0.76, 0.88)</td>
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</tr>
<tr>
<td>Other</td>
<td>VIC</td>
<td>555</td>
<td>63907</td>
<td>1.0</td>
<td>(0.78, 0.92)</td>
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</tr>
<tr>
<td>Other</td>
<td>SA</td>
<td>286</td>
<td>47566</td>
<td>0.6</td>
<td>(0.53, 0.67)</td>
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<td>Other</td>
<td>WA</td>
<td>107</td>
<td>14645</td>
<td>0.7</td>
<td>(0.59, 0.67)</td>
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<tr>
<td>Other</td>
<td>QLD</td>
<td>855</td>
<td>100474</td>
<td>0.8</td>
<td>(0.76, 0.87)</td>
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<tr>
<td>Other</td>
<td>TAS</td>
<td>424</td>
<td>46382</td>
<td>0.9 (0.83, 1.01)</td>
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<td></td>
</tr>
<tr>
<td>DUR</td>
<td>ACT/NT</td>
<td>5</td>
<td>90</td>
<td>191</td>
<td>2.6 (0.85, 6.10)</td>
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</tr>
<tr>
<td>DUR</td>
<td>NSW</td>
<td>2</td>
<td>22</td>
<td>40</td>
<td>0.49 (0.46, 17.88)</td>
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</tr>
<tr>
<td>DUR</td>
<td>WA</td>
<td>7</td>
<td>59</td>
<td>95</td>
<td>7.3 (2.95, 15.13)</td>
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</tr>
<tr>
<td>DUR</td>
<td>QLD</td>
<td>4</td>
<td>29</td>
<td>71</td>
<td>5.6 (1.33, 14.48)</td>
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</tbody>
</table>

| Total     | ACT/NT| 3145           | 123204       | 30814                    | 0.8 (0.78, 0.84)                         |              |
Revision rates by year of implant

<table>
<thead>
<tr>
<th>Component/Procedure Year</th>
<th>Revision</th>
<th>Total</th>
<th>%</th>
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<tbody>
<tr>
<td>1999</td>
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<td>379</td>
<td>0.3</td>
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<tr>
<td>2000</td>
<td>151</td>
<td>3699</td>
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<td>2001</td>
<td>421</td>
<td>11228</td>
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<tr>
<td>2002</td>
<td>505</td>
<td>15827</td>
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<td>2003</td>
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<tr>
<td>2004</td>
<td>528</td>
<td>18092</td>
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<td>2005</td>
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<td>18869</td>
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<td>19524</td>
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<tr>
<td>2007</td>
<td>199</td>
<td>20143</td>
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</tr>
<tr>
<td>2004</td>
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<td>43.4</td>
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<td>2006</td>
<td>1</td>
<td>56</td>
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</tr>
<tr>
<td>2007</td>
<td>0</td>
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</tr>
<tr>
<td>Subtotal</td>
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<tr>
<td>Total</td>
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<td>125004</td>
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Implants of DUR by year

<table>
<thead>
<tr>
<th>Year of Implant</th>
<th>2004</th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
</tr>
</thead>
<tbody>
<tr>
<td>DUR</td>
<td>41</td>
<td>79</td>
<td>56</td>
<td>6</td>
</tr>
</tbody>
</table>
Resulting Action by the Regulator

Data reviewed by Expert Panel

Recommendations –
- Continue to monitor
- ‘Show cause’ to manufacturer regarding removal from market

Manufacturer encouraged to provide further/different evidence of product performance

Dialog with Manufacturer

Regulatory decision is made
- Manufacturer has formal right of appeal

So......what have we learned .........
Conclusions ..........

- Effective postmarket programs are essential to ensure ongoing safety of medical devices
- Postmarket monitoring is **not** just Adverse Event Reporting
- Postmarket monitoring is a critical element of a manufacturer’s QMS
- Lessons learned from Postmarket monitoring are taken forward into new products leading to improved safety and performance

Questions .................