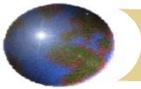


# *Global Medical Device Regulatory Overview*

Michael Flood  
Locus Consulting Pty Ltd  
Australia

*ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California*



# *Why postmarket .....*

*ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California*



## *Some statistics*

### Patient treatments to enable detection of adverse events

Expected number of adverse incidents	1 event	2 events	3 events
1 in 100	300	480	650
1 in 200	600	960	1,300
1 in 1,100	3,000	4,800	6,500
1 in 2,000	6,000	9,600	13,000
1 in 10,000	30,000	48,000	65,000

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

*ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California*

3



## *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

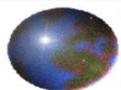
Typical systemic effect

Short half life in the body

Consumed by use

Focus on local systemic effect and toxicity

*ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California*



## *Medical devices and Medicines – the differences*

### **Medical Device**

Generally not subject to ethnic differences

Relatively limited populations of exposure

Wide range – bandages to MRI Scanners.....

Diverse technologies, presentations and modes of action

Typically require significant user interaction

### **Medicine**

May be subject to ethnic differences

Large populations of exposure

Tend to differ only in molecular structure, active site and mode of application

Usually only tablets, ointments, solutions of aerosols

Little user interaction....other than ingestion, application, etc

*ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California*



## *Medical devices and Medicines – the differences*

### **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

### **Medicine**

Large, multi-national companies dominate

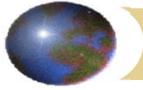
Extensive R & D of new molecules, many years for new medicine to enter the marketing pipeline

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

*ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California*



## *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

### **Medicine**

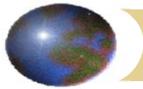
Discovered in lab based research processes

Development by discovery and trial

Regulatory approval on the basis of safety and efficacy

Stable formulation

*ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California*



## *Medical devices and Medicines – the differences*

### **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)

### **Medicine**

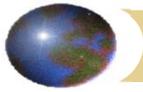
Usually large step innovation

Validated through clinical studies

Highly mechanised manufacture

Good Manufacturing Practice (GMP)

*ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California*



## Medical devices and Medicines – the differences

### Medical Device

### Medicine

#### Use and postmarket –

Most intended for professional use

Prescribed by professional, used by patient

- Risk of patient choosing to stop use

Device malfunction or failure

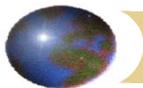
Medicine adverse reaction or interaction

User error (professional or patient)

Incorrect medicine or dosage prescribed

Adverse events most often localised in nature

Adverse events may be widespread



## Medical devices and Medicines – the differences

### Medical Device

### Medicine

#### Manufacturer support –

Sales channels vary based on the device.....wholesalers generally not involved

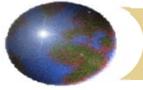
Typically supplied through (lengthy ?) wholesale chain

Large investments in manufacturing, distribution and user training/education

Large investments in manufacturing, distribution, training and clinical support

Technical training and support, service and repair

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 !!

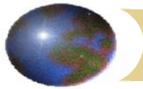
### Medicine

Adjustments to dosage or application indications

Cease use

*ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California*

11

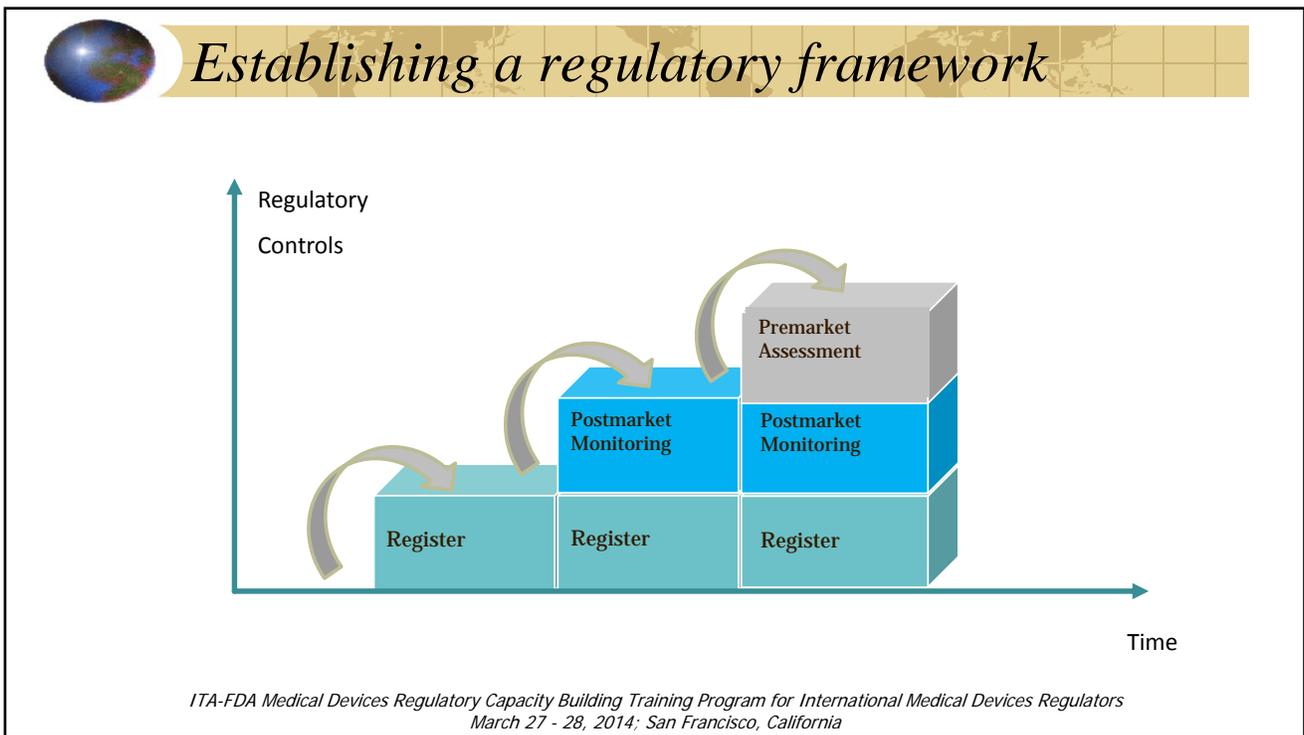
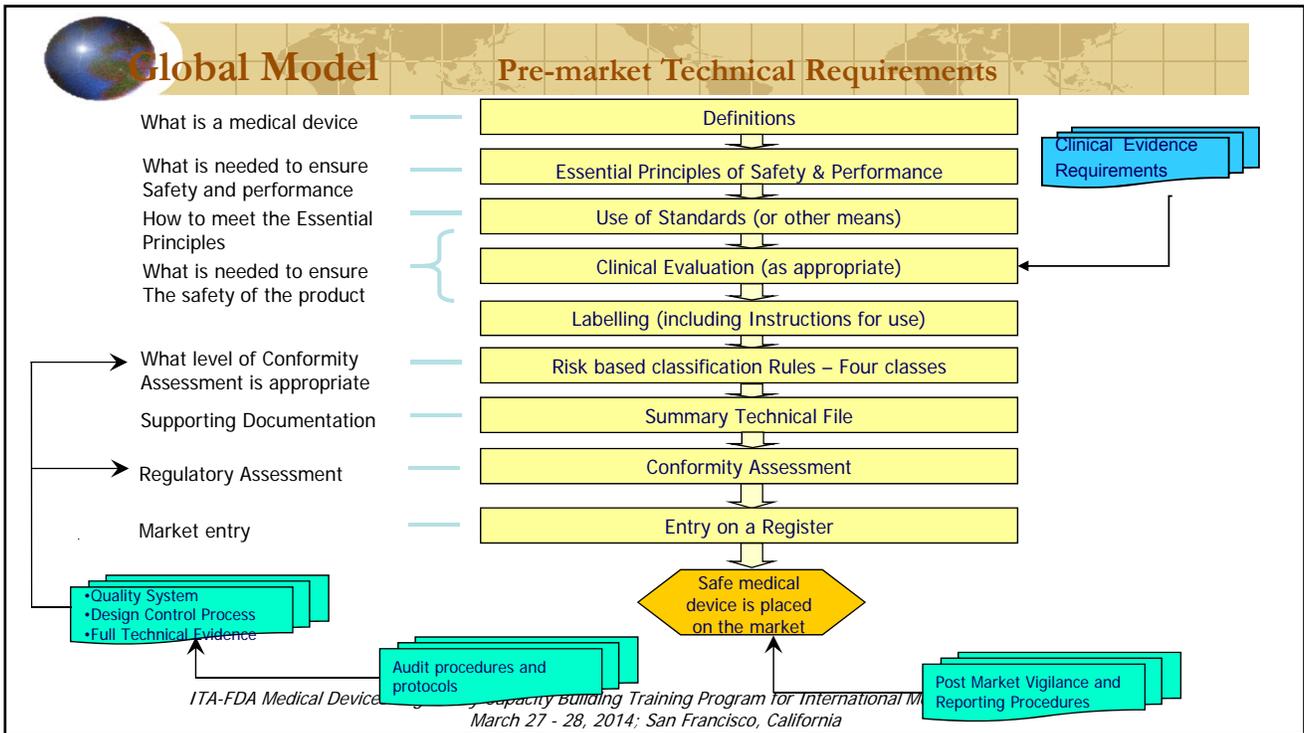


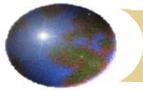
## Conclusion

- ✦ 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

*ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California*

12

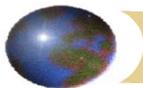




## Questions for 'Postmarket' .....

- ✦ 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 (eg. 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 .....

*ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California*

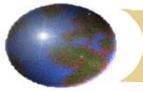


## What is 'postmarket' .....

- ✦ Many think of 'postmarket' as adverse event reporting.....
- ✦ ..... but it is so much more !!!



*ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California*

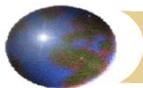


## 'Postmarket' is .....

- ✦ Adverse incident reporting
  - ❖ Manufacturers and Authorised Representatives
  - ❖ Clinical users
  - ❖ General public
  
- ✦ Adverse event investigations
  - ❖ Manufacturer
  - ❖ Regulator

*ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California*

17



## '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

*ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California*

18



## '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

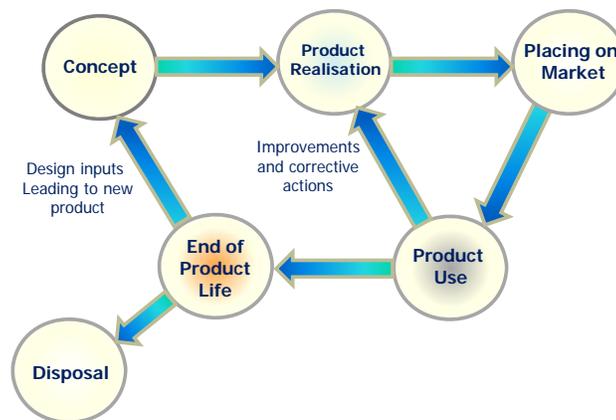
*ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California*



## Life Cycle with regulatory aspects included

### Auditing practice

#### Quality Management Systems & Risk Management



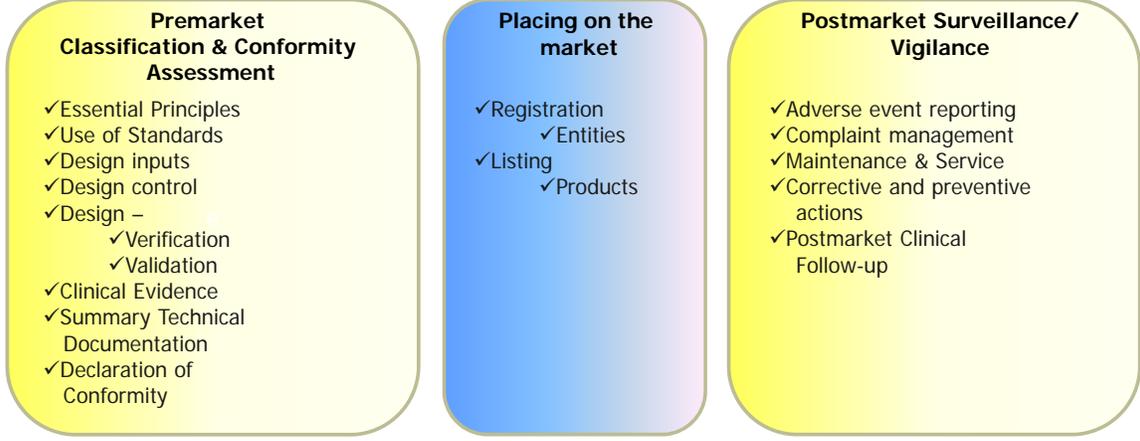
*March 27 - 28, 2014; San Francisco, California*



# Life Cycle with applied processes

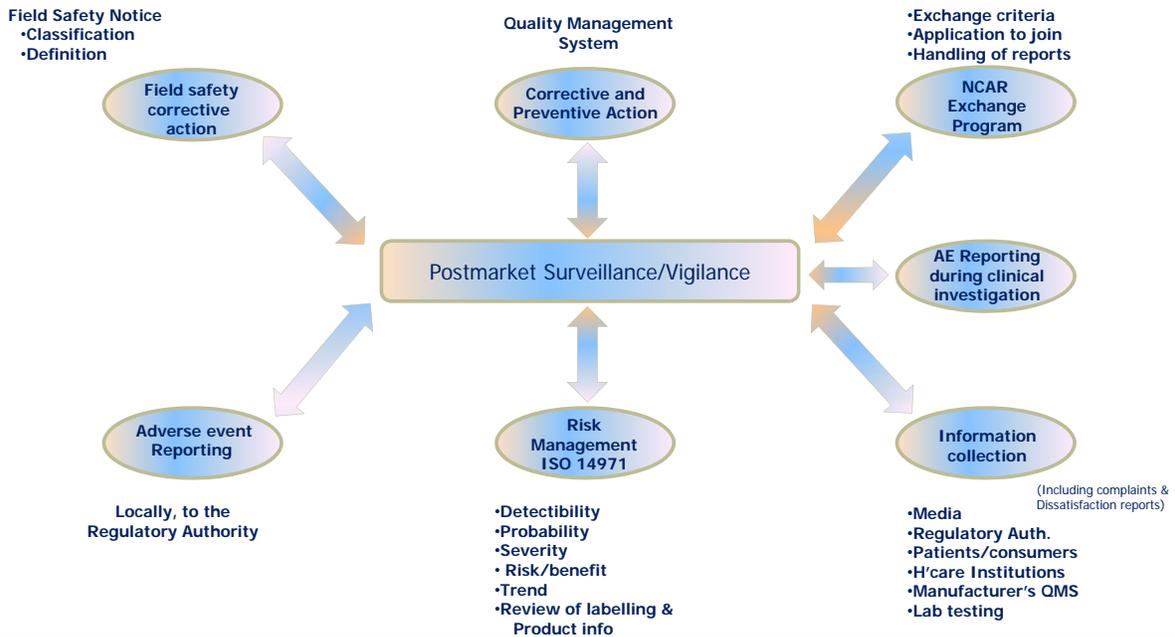
## Compliance Audit – by Conformity Assessment Body or the Manufacturer

### Quality Management Systems & Risk Management by the manufacturer



March 27 - 28, 2014; San Francisco, California

## Postmarket – Sources of information





## *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 consider 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



## *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 !!

*ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California*

25

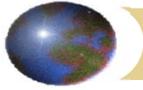


## *Postmarket – (CAPA)*

- ✦ 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

*ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California*

26

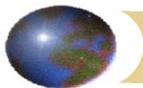


## *Postmarket – NCAR Exchange program*

- ✦ 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

*ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California*

27



## *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

*ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California*

28



## 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

*ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California*

29



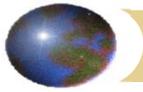
## Postmarket

- ✦ Early step in the introduction of regulation
  - ❖ Introduction of adverse event reporting systems
  - ❖ Examples of countries with active postmarket programs -
 

<input type="checkbox"/> Australia	<input type="checkbox"/> United States
<input type="checkbox"/> Brazil	<input type="checkbox"/> European Union
<input type="checkbox"/> Canada	<input type="checkbox"/> Japan
<input type="checkbox"/> China	<input type="checkbox"/> Hong Kong
<input type="checkbox"/> South Africa	<input type="checkbox"/> Malaysia
<input type="checkbox"/> New Zealand	<input type="checkbox"/> Taiwan
<input type="checkbox"/> Singapore	<input type="checkbox"/> Korea
<input type="checkbox"/> Saudi Arabia	<input type="checkbox"/> India

*ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California*

30

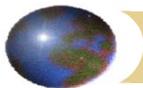


## Adverse events – what to report

- ✦ 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

*ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California*

31



## 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 condition leading 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*

*ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California*

32



## *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

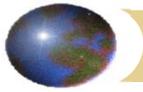
*ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California*



## *Adverse events – who should report*

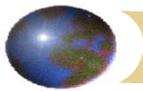
- ✦ **Mandatory reporting**
  - ❑ Manufacturers
  - ❑ Authorised representatives
  - ❑ Distributors (??)
- ✦ **Voluntary reporting** ..... to the Regulatory Authority and Authorised Representative/manufacturer
  - ❑ Clinical users
  - ❑ General public
- ✦ **Sentinel reporting**
  - ❑ FDA initiative utilising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

*ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California*



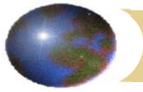
## Adverse events – when to report

- ✦ 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



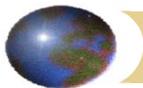
## *Adverse events – what not to report*

### ✦ 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

*ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California*

37



## *Adverse events – what not to report*

### ✦ Exemptions

- ❏ Negligible likelihood of occurrence of death or serious injury
  - eg – Manufacturer or Authorised Representative contact details incorrect on packaging .....likelihood 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

*ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California*

38



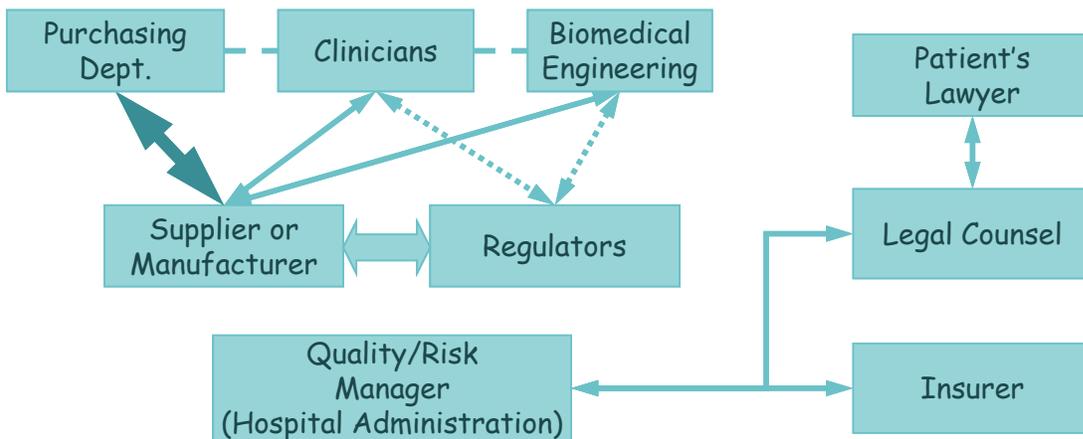
## Lines of Communication



ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
 March 27 - 28, 2014; San Francisco, California

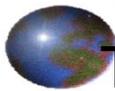
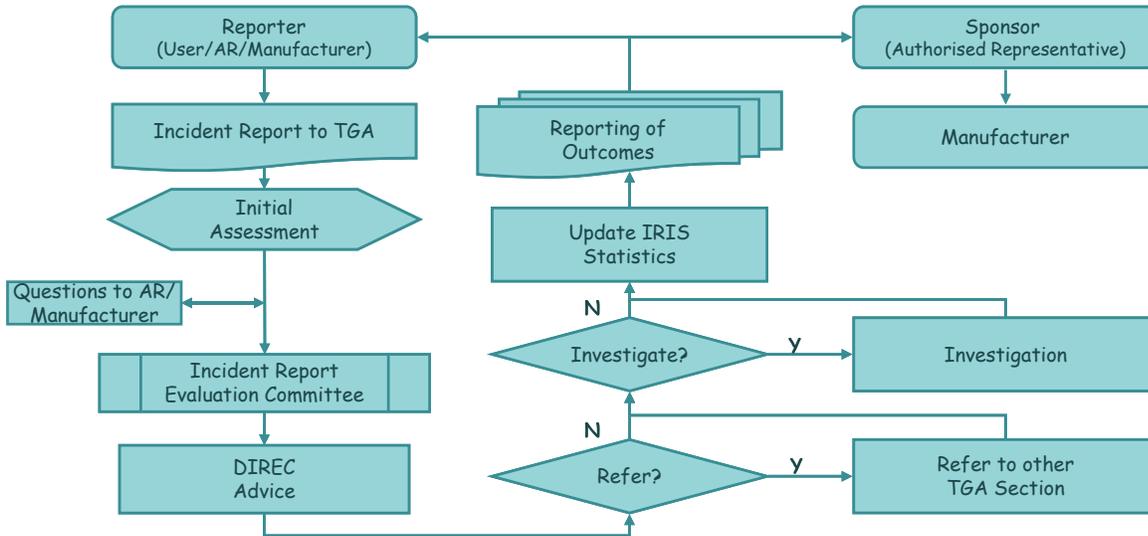


## Real Life.....

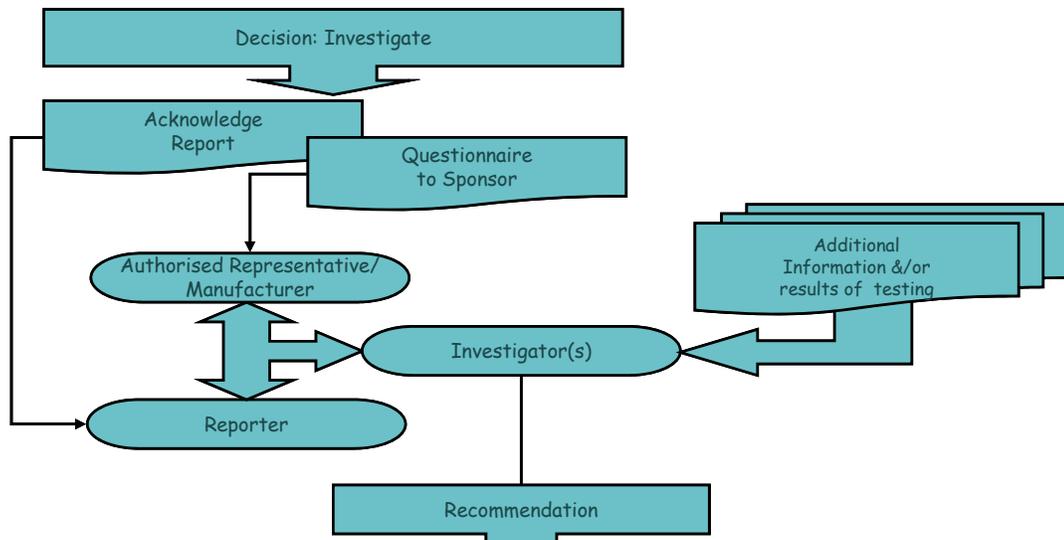


ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
 March 27 - 28, 2014; San Francisco, California

## The IRIS process ..... Australia



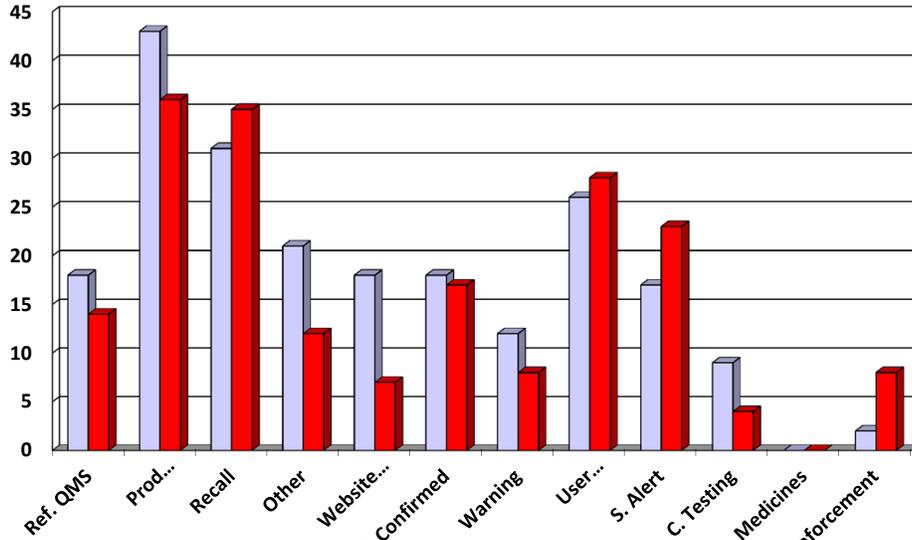
## The investigation process



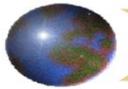
ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
 March 27 - 28, 2014; San Francisco, California



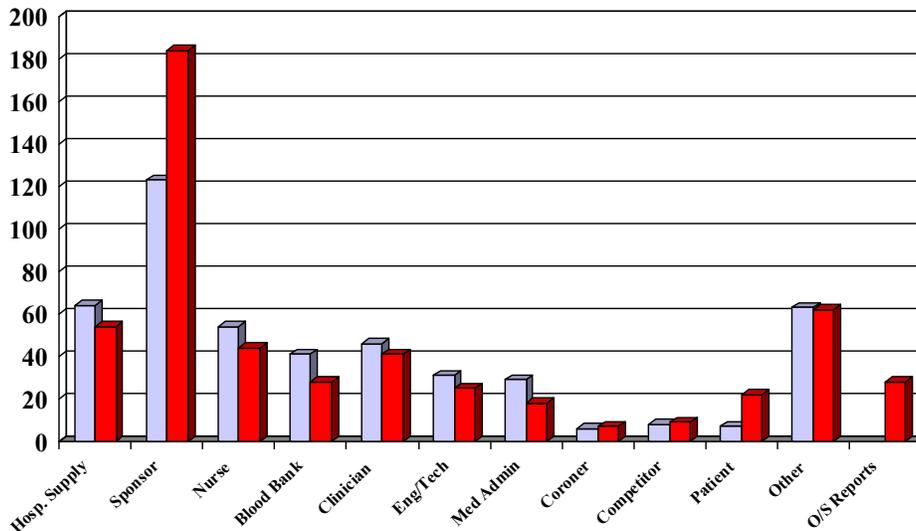
## Result of Investigations



ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California



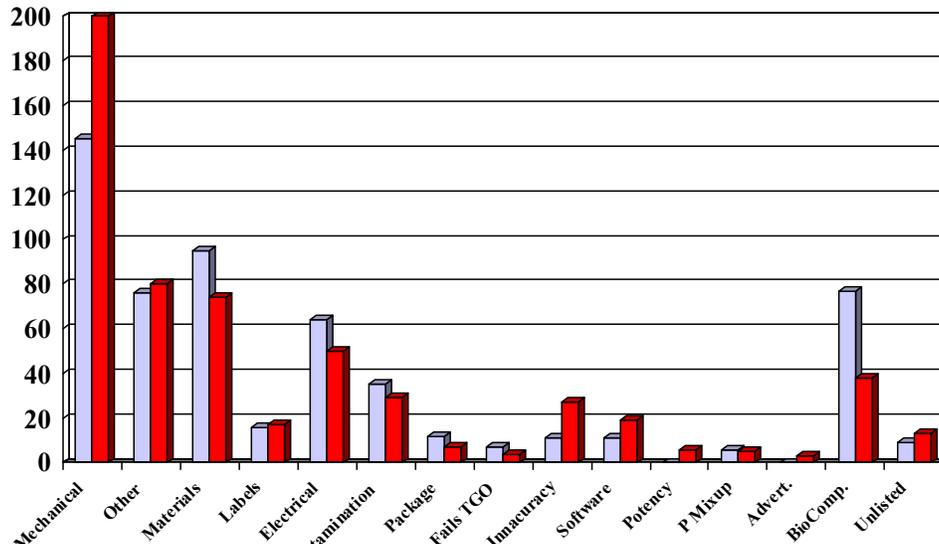
## Source of Reports



ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California



## Type of Reports Received



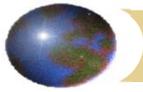
ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California



## 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

ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California

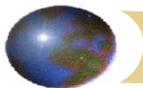


## *Enforcement*

- ✦ 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

*ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California*

47



## *Postmarket – Advertising controls*

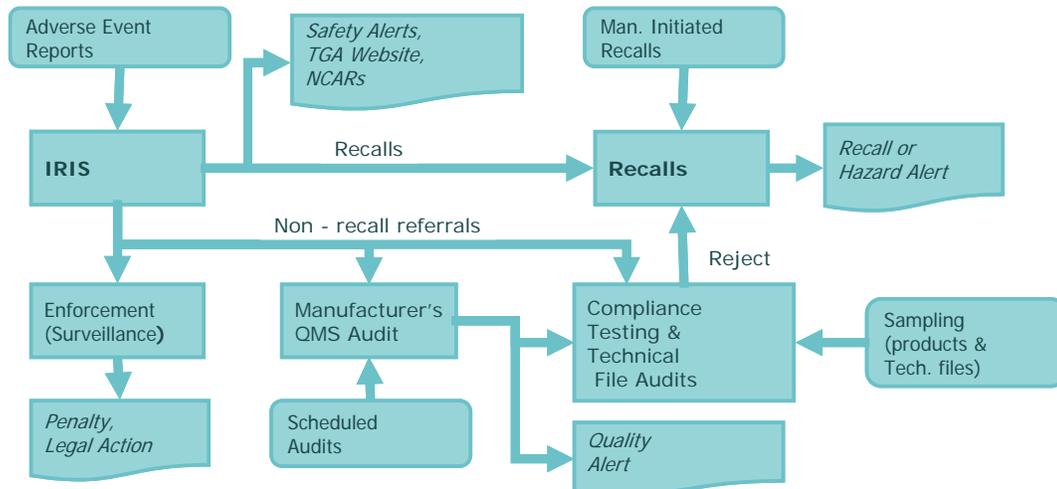
- ✦ Global model is silent on advertising controls
- ✦ Definitions
  - ❑ What is an advertisement
- ✦ Allowable target audience for an advertisement
  - ❑ Clinical user
  - ❑ General public
- ✦ Truth in Advertising
  - ❑ Allowable claims
- ✦ Enforcement

*ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California*

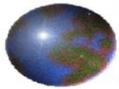
48



## Australia's Vigilance and Market Monitoring Systems



ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California



## 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

ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California



## 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

*ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California*

51



## 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

*ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California*



## National Joint Replacement Register

- ✦ 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

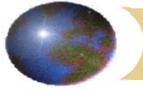
*ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California*



## Data Validation

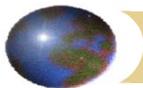
- ✦ Registry receives 96% of data from hospitals
- ✦ Registry data are checked against Government data using a sequential multi-level matching process
- ✦ This process enables the Registry to subsequently collect the remaining 4%

*ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California*



***‘There is considerable evidence that the Australian Registry has produced major beneficial change in Arthroplasty practice in Australia’***

*ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California*



## *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

*ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California*



## *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

*ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California*



## *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 31<sup>st</sup> December 2009
  - ❖ Increase of 74,641 procedures compared to 2009 Annual Report

*ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California*



## Typical NJRR Data available to the Regulator

### Femoral Component Total Hip Investigation

#### Revision Rates

Component	Number Revised	Total Number	Observed 'Component' Years	Revisions per 100 Observed 'Component' Years	Exact 95% CI
Other Total	3127	124822	388063	0.8	(0.78, 0.83)
<b>DUR</b>	18	182	398	4.5	(2.68, 7.15)
<b>Total</b>	<b>3145</b>	<b>125004</b>	<b>388461</b>	<b>0.8</b>	<b>(0.78, 0.84)</b>

#### Cumulative % Revision

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

\*\* **DUR** – Device under Review

*ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California*



### Type of revision performed by primary failure

Type of Revision	Component				Total N
	Other Total		<b>DUR</b>		
	N	%	N	%	
Femoral Component Only	903	28.9	10	55.6	913
Acetabular Component Only	771	24.7	2	11.1	773
Head/Insert	615	19.7	2	11.1	617
Femoral and Acetabular (THR)	336	10.7	.	.	336
Head Only	204	6.5	3	16.7	207
Cement Spacer	129	4.1	1	5.6	130
Cable/Other Minor Components	65	2.1	.	.	65
Insert only	60	1.9	.	.	60
Removal Prosthesis	31	1.0	.	.	31
Reinsertion of Components	8	0.3	.	.	8
Cement Only	3	0.1	.	.	3
Bipolar head and Femoral Component	1	0.0	.	.	1
Cable and Cement	1	0.0	.	.	1
<b>Total</b>	<b>3127</b>	<b>100.0</b>	<b>18</b>	<b>100.0</b>	<b>3145</b>

\*\* **DUR** – Device under Review

*ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California*

### Revision diagnosis by days to revision for **Other** Total

Revision Diagnosis	1. <2wks			2. 2wks-3mths			3. 3mths-1yr			4. 1yr-3yrs			5. >=3yrs			Total		
	N	%	Row%	N	%	Row%	N	%	Row%	N	%	Row%	N	%	Row%	N	%	Row%
Other	36	11.2	18.9	26	3.1	13.7	40	5.5	21.1	65	6.8	34.2	23	4.4	12.1	190	5.6	100
Dislocation of Prosthesis	130	40.4	12.2	365	43.0	34.2	219	29.9	20.5	244	25.7	22.9	109	20.7	10.2	1067	31.6	100
Fracture	95	29.5	18.6	170	20.0	33.2	101	13.8	19.7	81	8.5	15.8	65	12.3	12.7	512	15.2	100
Implant Breakage																		
Acetabular	2	0.6	4.3	2	0.2	4.3	11	1.5	23.4	16	1.7	34.0	16	3.0	34.0	47	1.4	100
Implant Breakage Head	.	.	.	.	.	.	3	0.4	20.0	8	0.8	53.3	4	0.8	26.7	15	0.4	100
Implant Breakage Stem	.	.	.	2	0.2	11.8	2	0.3	11.8	4	0.4	23.5	9	1.7	52.9	17	0.5	100
Infection	5	1.6	1.0	156	18.4	31.1	115	15.7	22.9	168	17.7	33.5	58	11.0	11.6	502	14.9	100
Loosening	51	15.8	5.8	119	14.0	13.5	214	29.2	24.2	300	31.6	34.0	199	37.8	22.5	883	26.1	100
Lysis	.	.	.	4	0.5	7.0	7	1.0	12.3	17	1.8	29.8	29	5.5	50.9	57	1.7	100
Pain	3	0.9	4.2	3	0.4	4.2	15	2.0	20.8	40	4.2	55.6	11	2.1	15.3	72	2.1	100
Wear Acetabulum	.	.	.	1	0.1	5.9	5	0.7	29.4	7	0.7	41.2	4	0.8	23.5	17	0.5	100
<b>Total</b>	<b>322</b>	<b>100</b>	<b>9.5</b>	<b>848</b>	<b>100</b>	<b>25.1</b>	<b>732</b>	<b>100</b>	<b>21.7</b>	<b>950</b>	<b>100</b>	<b>28.1</b>	<b>527</b>	<b>100</b>	<b>15.6</b>	<b>3379</b>	<b>100</b>	<b>100</b>

### Revision diagnosis by days to revision for **DUR**

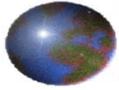
Revision Diagnosis	1. <2wks			2. 2wks-3mths			3. 3mths-1yr			4. 1yr-3yrs			Total		
	N	%	Row%	N	%	Row%	N	%	Row%	N	%	Row%	N	%	Row%
Dislocation of Prosthesis	1	50.0	25.0	2	50.0	50.0	1	16.7	25.0	.	.	.	4	21.1	100
Fracture	1	50.0	50.0	.	.	.	.	.	.	1	14.3	50.0	2	10.5	100
Infection	.	.	.	.	.	.	1	16.7	100	.	.	.	1	5.3	100
Other	.	.	.	.	.	.	.	.	.	1	14.3	100	1	5.3	100
Loosening	.	.	.	2	50.0	20.0	3	50.0	30.0	5	71.4	50.0	10	52.6	100
Pain	.	.	.	.	.	.	1	16.7	100	.	.	.	1	5.3	100
<b>Total</b>	<b>2</b>	<b>100</b>	<b>10.5</b>	<b>4</b>	<b>100</b>	<b>21.1</b>	<b>6</b>	<b>100</b>	<b>31.6</b>	<b>7</b>	<b>100</b>	<b>36.8</b>	<b>19</b>	<b>100</b>	<b>100</b>

Hospital	Number Revised	Total Number	Observed 'Component' Years	Revisions per 100 Observed 'Component' Years	Exact 95% CI
Hospital 001	0	1	4	0.0	(0.00, 103.8)
Hospital 002	1	3	9	10.9	(0.28, 60.68)
Hospital 003	0	1	2	0.0	(0.00, 219.8)
Hospital 004	0	2	6	0.0	(0.00, 66.73)
Hospital 005	1	8	24	4.1	(0.10, 22.85)
Hospital 006	0	1	1	0.0	(0.00, 418.4)
Hospital 007	0	1	0	0.0	(0.00, 7091)
Hospital 008	0	3	4	25.2	(0.64, 140.4)
Hospital 009	0	1	0	1043.6	(26.42, 5814)
Hospital 010	2	69	138	5.3	(0.64, 19.18)
Hospital 011	0	1			
Hospital 012	0	1			
Hospital 013	0	2			
Hospital 014	0	3			
Hospital 015	2	20			
Hospital 016	3	5			
Hospital 017	0	4			
Hospital 018	0	11			
Hospital 019	0	1			
Hospital 020	0	2			
Hospital 021	1	11			
Hospital 022	0	9			
Hospital 023	4	17			
Hospital 024	0	1			
Hospital 025	0	1			
Hospital 026	0	1			
Hospital 027	0	2			
<b>Total</b>	<b>18</b>	<b>182</b>	<b>398</b>	<b>4.5</b>	<b>(2.68, 7.15)</b>

### Revision rate by hospital

### Revision rate by State

Component	State	Number Revised	Total Number	Observed 'Component' Years	Revisions per 100 Observed 'Component' Years	Exact 95% CI
Other Total	ACT/NT	79	2789	8174	1.0	(0.77, 1.20)
Other Total	NSW	841	36282	102740	0.8	(0.76, 0.88)
Other Total	VIC	535	19962	63007	0.8	(0.78, 0.92)
Other Total	SA	286	13283	47766	0.6	(0.53, 0.67)
Other Total	WA	107	4587	14945	0.7	(0.59, 0.87)
Other Total	QLD	855	33705	105047	0.8	(0.76, 0.87)
Other Total	TAS	424	14214	46382	0.9	(0.83, 1.01)
<b>DUR</b>	ACT/NT	5	90	191	2.6	(0.85, 6.10)
	NSW					
	VIC					
<b>DUR</b>	SA	2	22	40	4.9	(0.60, 17.86)
<b>DUR</b>	WA	7	41	95	7.3	(2.95, 15.13)
<b>DUR</b>	QLD	4	29	71	5.6	(1.53, 14.40)
<b>Total</b>	TAS	3145	125004	388461	0.8	(0.78, 0.84)



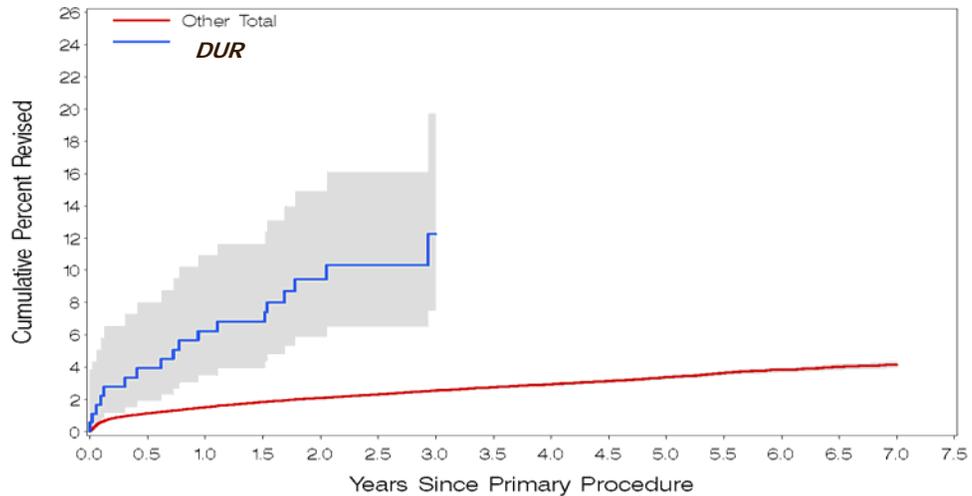
### Revision rates by year of implant

Component by Procedure Year	Revision	Total	%
1999	13	379	0.3
2000	151	3699	3.0
2001	421	11228	9.0
2002	505	15827	12.7
2003	570	17061	13.7
2004	528	18092	14.5
2005	400	18869	15.1
2006	340	19524	15.6
2007	199	20143	16.1
Subtotal	3127	124822	100.0
2004	5	41	22.5
2005	12	79	43.4
2006	1	56	30.8
2007	0	6	3.3
Subtotal	18	182	100.0
<b>DUR</b>			
Total	3145	125004	100.0

### Implants of *DUR* by year

Year of Implant	2004	2005	2006	2007
<b>DUR</b>	41	79	56	6

\*\* *DUR* – Device under Review *ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators*  
 March 27 - 28, 2014; San Francisco, California



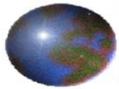
*ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators*  
 March 27 - 28, 2014; San Francisco, California



## *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
    - anufacturer has formal right of appeal

*ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California*



## **So.....what have we learned .....**

*ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California*



## 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

*ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California*



## Questions .....



*ITA-FDA Medical Devices Regulatory Capacity Building Training Program for International Medical Devices Regulators  
March 27 - 28, 2014; San Francisco, California*