Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

Managing a Post-Market Surveillance System:

Lessons learnt from medical device adverse event report investigations

Dr Jorge Garcia
Director, Biomaterials & Engineering
Office of Laboratories and Scientific Services

Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

Did you ever think about…

- What is the purpose of the Summary Technical Evaluation Document (STED) and the manufacturers Quality Management System (QMS)?
- Who is responsible for Conformity Assessment?
- What is the role of the National Regulatory Agency?
- Why do National Regulatory Agencies want adverse event reports?

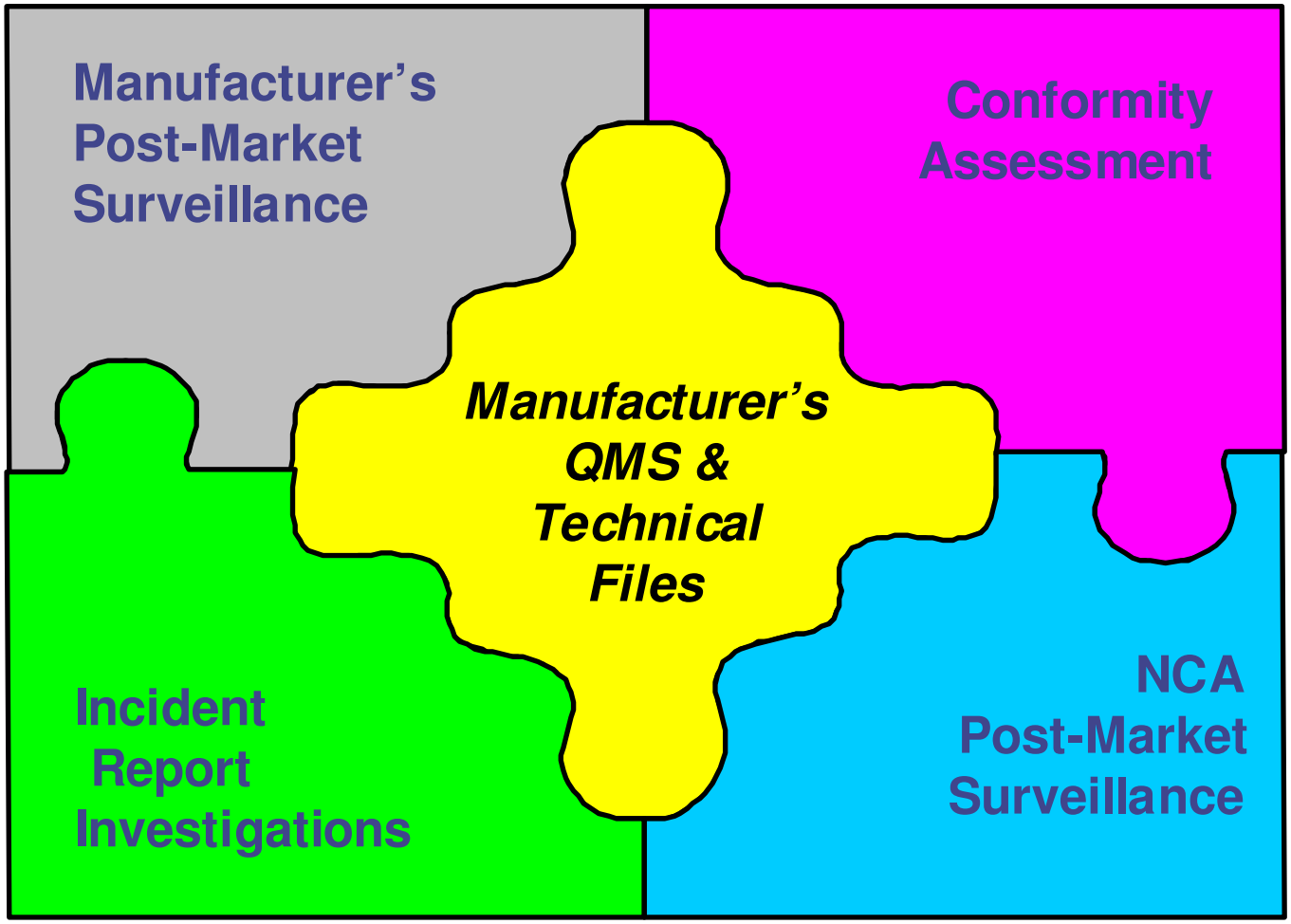
Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

Key Ideas 1, 2 & 3

- "Pre-Market" is what manufacturers do to get ready for "Post-Market".
- Conformity Assessment is the responsibility of the MANUFACTURER.
- National Regulatory Authorities MONITOR product and manufacturer compliance with the Essential Principles.

Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

Technical File and QMS



Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

Key Idea 4

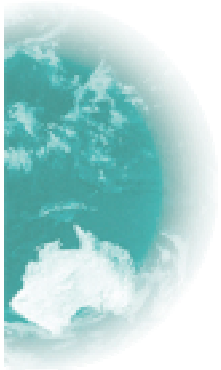
The medical device manufacturer's Quality Management System (QMS) and Technical File are key tools for Medical Device Regulation and for Medical Device Post-Market Surveillance in particular.

AHWP

Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

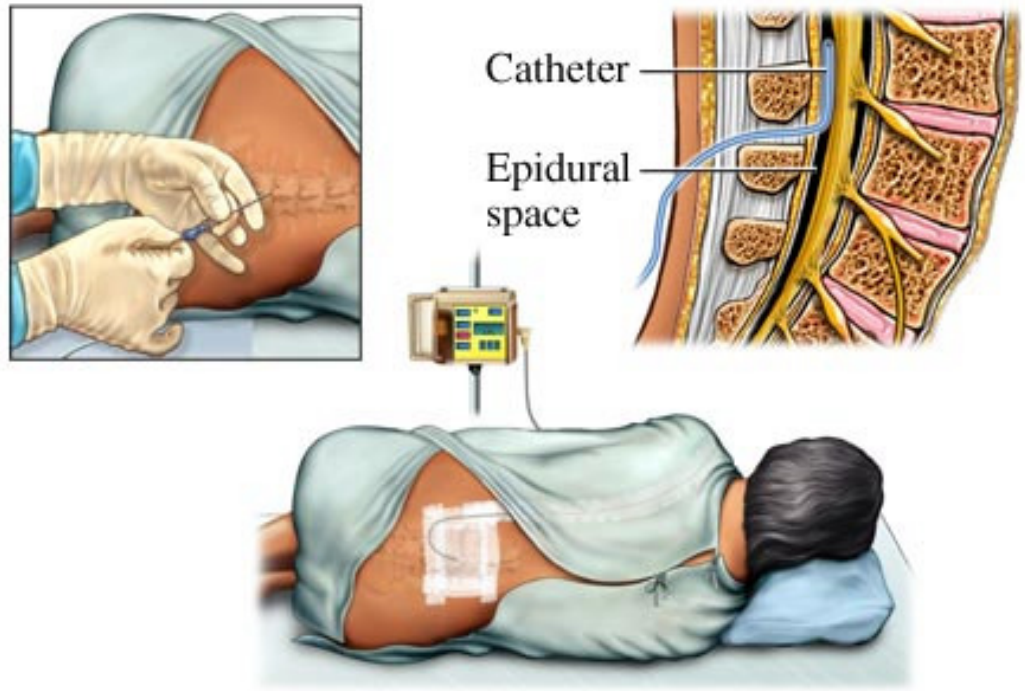
Case Study 1

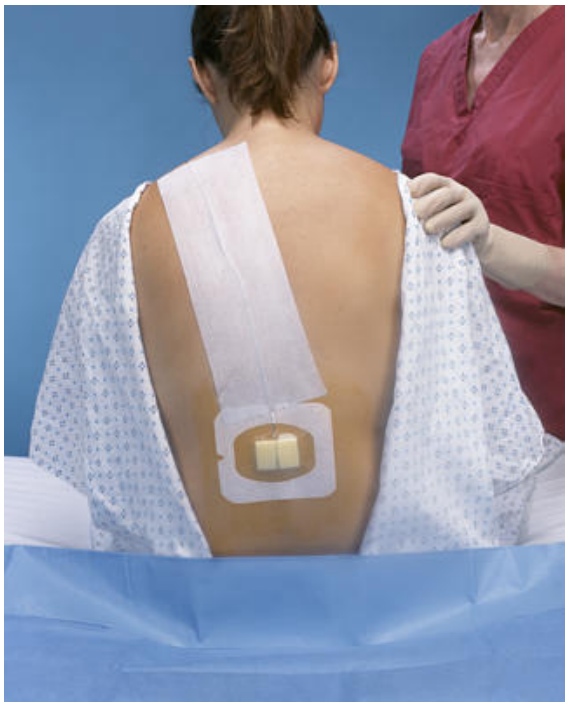
Epidural Catheters



Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

Case Study 1





Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

Case Study 1: Investigation

- Reporter: Catheter is yellow… is it safe?
- Manufacturer: The catheter was probably stored in strong heat or light by the user.
- Investigation: Tensile and bending properties OK. Accelerated light/heat testing degraded melted and turned the packaging brown – but contents OK.
- Cytotoxicity of yellowed material HIGH. Cytotoxicity of new material EVEN HIGHER.

Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

Case Study 1: Outcomes

- Leachate was the plasticiser n-butyl benzene sulphonamide. “Used for 30 years without any problems”.
- N-butyl benzene sulphonamide is a powerful neurotoxin.
- The catheter was reformulated, WORLDWIDE….
- This was the subject of Australia’s first ever “NCAR” report.

Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

Key Lessons 1 & 2

- Serendipity can be a powerful ally during an investigation, provided you keep your eyes and your mind open…
- Some problems are not easily detected by adverse event reporting alone - eg:
  - Biocompatibility issues
  - IVD performance

These types of issues require the use of complementary Postmarket strategies

Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

Case Study 2

Continuous Positive Airways Pressure (CPAP) mask and connector

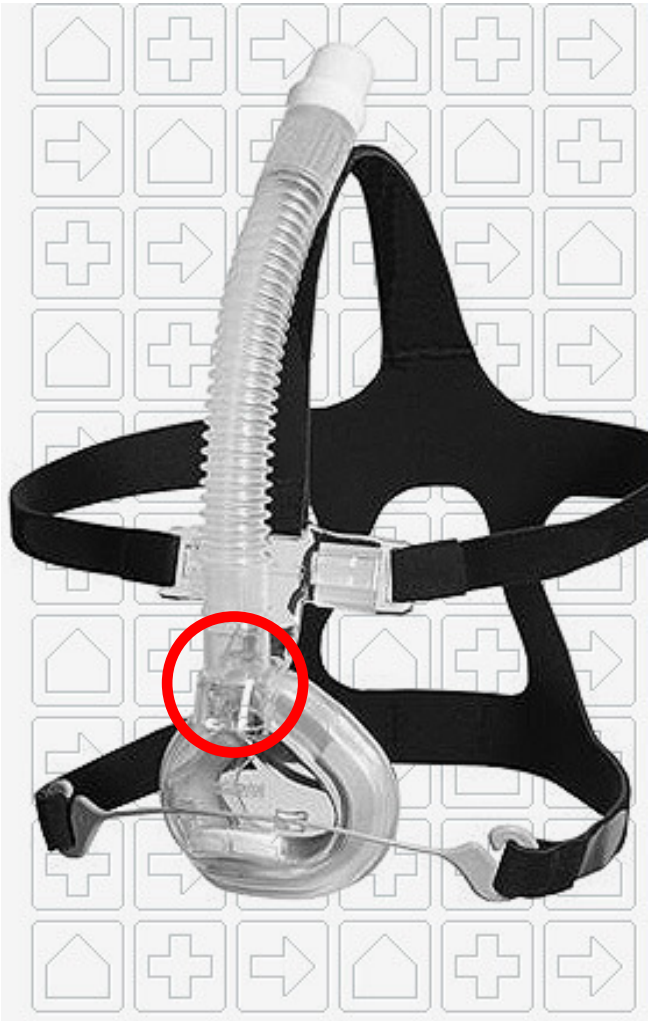
Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

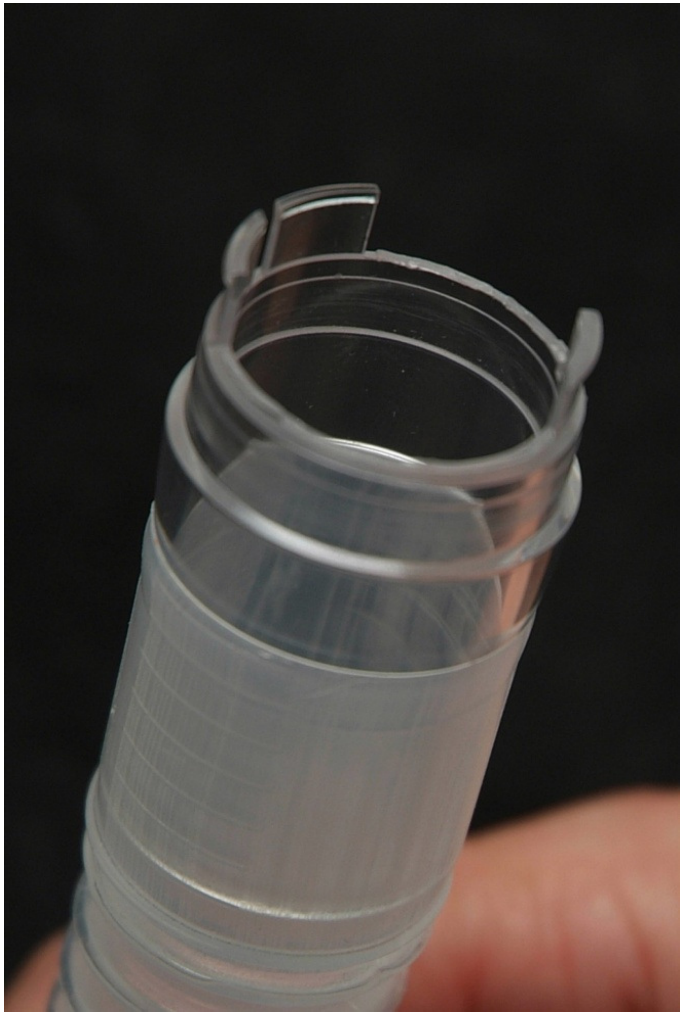
Case Study 2

- Sleep Apnoea is debilitating and possibly dangerous to the sufferer (snorer) and plain annoying to those around them.
- The condition can be treated by the use of a CPAP machine during sleep.

Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

Case Study 2





Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

Case Study 2: Investigation

- Manufacturer had received 80 reports of broken tines. On three occasions the pieces had been found in the patients mouth.
- Serious injury was possible but unlikely.
- The connector had been redesigned (no tines) but several hundred thousand units of the old design were still in use and in supplier's shelves.
- TGA "negotiated" a recall of the product.

Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

Key Lesson 3

- Even if the risk is low, easily avoided risks MUST be avoided (particularly if the device is for home use, or for use under limited clinical supervision).
- The risk taker should benefit from taking a risk. (In Case Study 2, there was no benefit to the patient that could be derived from using the connector with the faulty design)

AHWP

Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

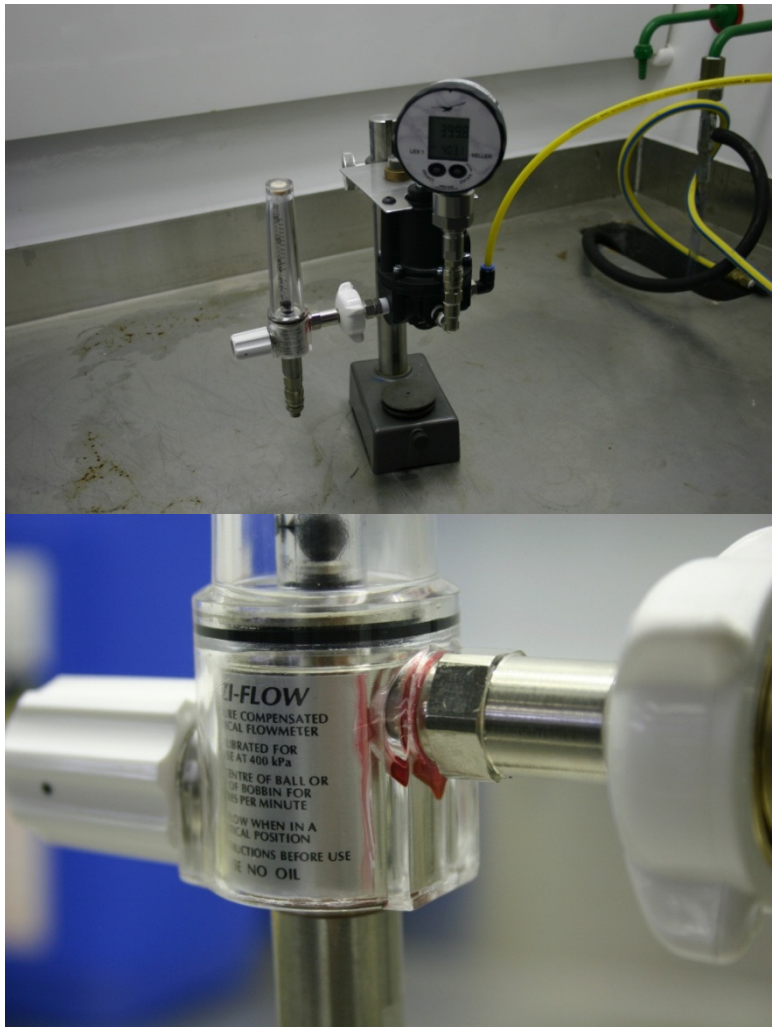
Case Study 3 (& 3.5)

Hospital flow meters
Cardiac by-pass pump

Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

Case Study 3

- Several flow meters in a hospital with cracked plastic “shrouds”.
- Company claimed that the shrouds were being wiped with cleaning agents that are incompatible with the polycarbonate.



Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

Case Study 3: Conclusions

- Application of cleaning agents did not cause any problems in the laboratory.
- The problem was caused by the combined action of an interference fit between the shroud and the gas fittings and the thread sealer Loctite®
- The manufacturer was asked to issue a safety alert – and reconsider the interference fit.

Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

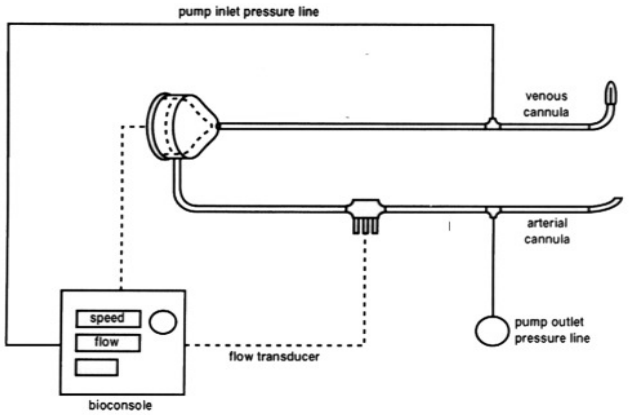
Case Study 3.5

- Cardiac Pump was once made from PMMA.
- If the pump came into contact with alcohol, it would crack and leak. The instructions for use warned against the use of alcohol wipes on the pump.
- In spite of warnings, the pump was known to have cracked on 90 occasions. On the 91 occasion a baby died of haemorrhage during a procedure.

Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

Case Study 3.5

"PROVEN RELIABILITY: Robust double-lip seal design adds sealing integrity, reduces air volume in bearing chamber and resists moisture ingress

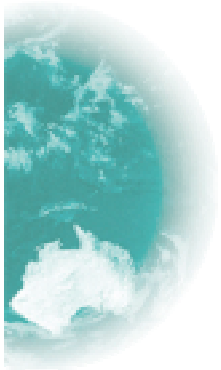


Polycarbonate outer housing and inlet/outlet ports provide increased strength and resistance to alcohol and other chemicals to minimize risk of breakage"

Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

Key Lessons 4 & 5

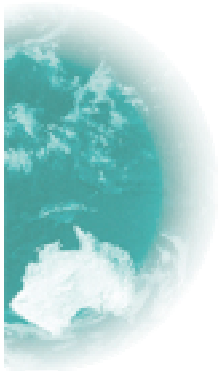
- Medical Device Events arise from complex interactions between a medical device, the user, the surroundings, the patient, and sometimes - other devices.
- There are no such things as “bad materials”. There are only good materials that are used in the wrong place & at the wrong time.



Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

Key Lesson 6

- Finding that use error contributed to the event does not exonerate the medical device.
- If the use error event happens repeatedly, then it is “foreseeable”.
- At the very least users should be made aware of common mistakes so that they are not repeated. In the majority of cases foreseeable misuse can be “designed out” and this should be the preferred risk abatement strategy.



Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

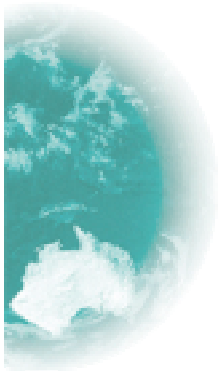
Case Study 4

Reusable orthopaedic surgical instruments

Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

Case Study 4

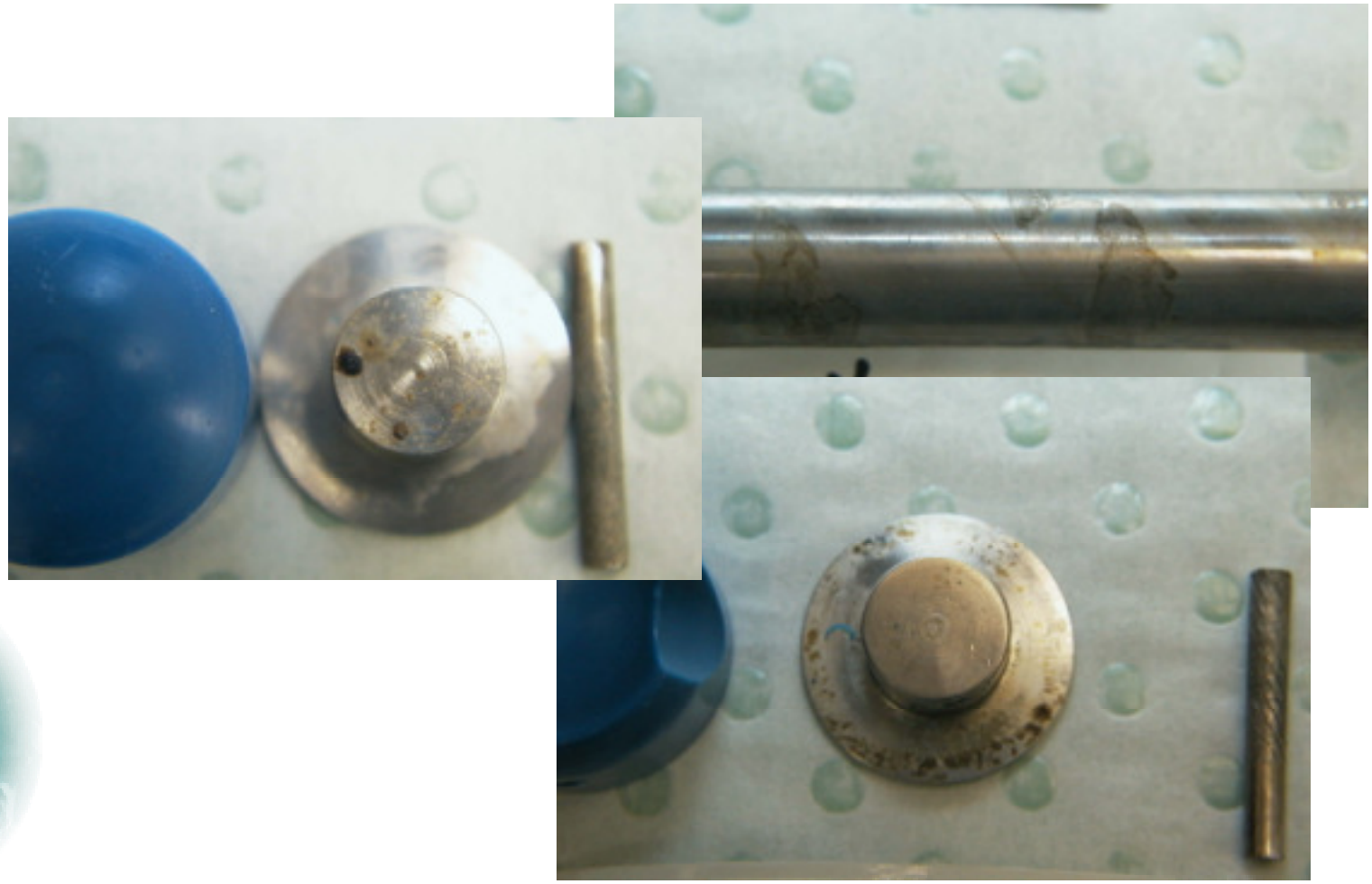
- When an orthopaedic surgical instrument was dropped on the ground, blood “oozed” out from underneath a fixed part. Fresh and dried blood was found underneath fixed parts of the instrument, including handles.



Hospital started investigation. TGA attended “the scene of the incident”. Initial inspection of the instruments on-site revealed nothing extraordinary…

Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

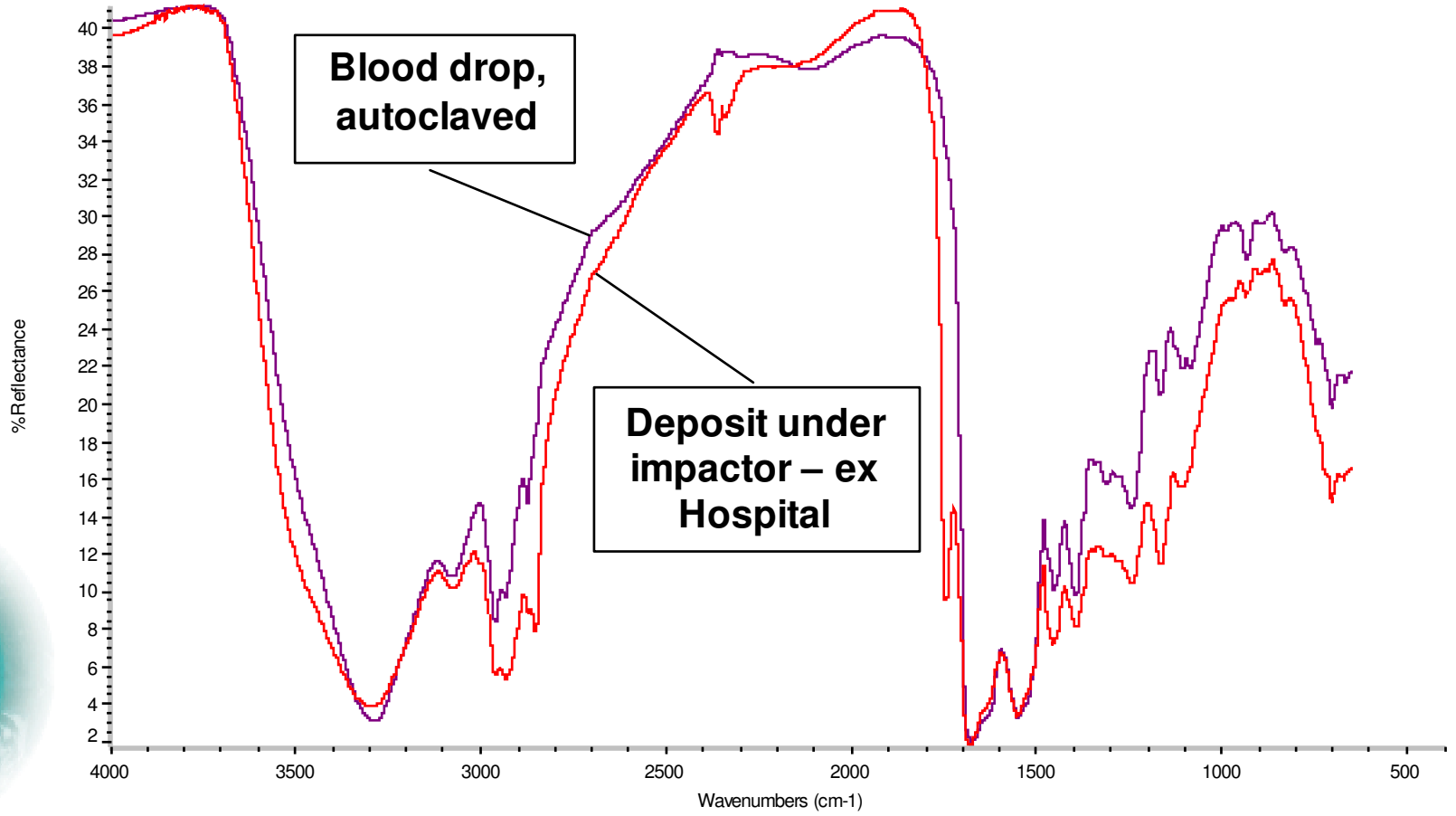
Case Study 4



Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

Case Study 4

FTIR Spectrograph of Deposit on Femoral Impactor



Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

Case Study 4: Outcomes

- Manufacturer recalled and modified the devices.
- 168 patients that had surgery using these instruments were followed up. Found 1 case of Hepatitis C.
- The TGA surveyed the market for potential problem devices.
- Report: “Reducing the Public Health Risks Associated with Reusable Medical Devices”.

Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

Key Lessons 7, 8 & 9

- Access to laboratories is very useful during investigations... but it pays to be creative.
- A picture may well paint a thousand words, but a sample paints a million pictures.
- **When conducting product surveys and testing, a product registry which incorporates the use of a comprehensive medical device nomenclature system such as the GMDN is an ESSENTIAL tool.**

Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

Key Idea 5

- A good understanding of risk assessment and risk management is an essential element for success in Adverse Event Investigations.
- Investigations can be thought of as a process of solving the risk equation by "iteration".

RISK = INCIDENCE X HAZARD

Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

Key Ideas 6 &7

- The main role of the National Regulatory Authority is to MONITOR product and manufacturer compliance.
- National Regulatory Authorities receive and investigate adverse event reports not only to ensure Performance and Safety BUT ALSO to monitor the performance, suitability of the manufacturer's QMS and its responsiveness to post market issues.

AHWP

Australian Government
Department of Health and Ageing
Therapeutic Goods Administration