



Australian Government  
Department of Health and Ageing  
Therapeutic Goods Administration

# Risk Management – TGA Perspective

Tony Gould  
Chief Auditor

Office of Manufacturing Quality





# Topics

- Introduction
- Risk management in the PIC/S GMP Guide
- An example of the application of risk management
- Conclusion





# Introduction

- Risk management is not new – we do it informally all the time
- Military Standard 1629 dated 1974 regarding formal risk management
- Risk management has been used in the medical device, food, telecommunications, aerospace and car industries for many years





# Introduction

- Risk management has also been part of the pharma industry for many years, e.g.:
  - GMP requirements are designed to address risk. For example, the specific GMP requirements for sterile products are designed to mitigate the risk of sterility failure
  - In some cases, GMP specifies a risk based approach. For example, "a risk assessment approach should be used to determine the scope and extent of validation required" (Annex 15, Principle)
  - Specifications in pharmacopoeial monographs include tests for known potential contaminants





# Introduction

- Greater use of risk management tools in the future
- Organisations use risk principles in many other areas, e.g. finance, occupational safety.
- From a GMP point of view, we are only concerned with risks associated with quality, safety and efficacy – quality risk management





# QRM - the dangers

- There is a desired outcome and risk management is used to justify it
- Invalid assumptions – suit the desired outcome
- Cost reduction (increased profits) may be the real reason that many risk assessments are done
  - Cost reduction should be a secondary outcome of QRM
- Variable tolerance of risk
- Subjectivity





# QRM –auditors point of view

## Auditors will:

- Be prepared so that the process is understood
- Have sufficient knowledge to understand what has been done and challenge assumptions, omissions etc
- Be clear about when QRM is not appropriate
- Be flexible and accept the outcome of a scientifically sound QRM exercise
- If done properly there should be increased assurance of quality (and possibly cost savings)





# Quality Risk Management in the PIC/S GMP Guide, Jan 09

- Soon to be a Manufacturing Principle with 12 month transition period





# New in Chapter 1

## Principle

- “The basic concepts of Quality Assurance, Good Manufacturing Practice, Quality Control and **Quality Risk Management** are inter-related”
- “To achieve the quality objective reliably there must be a comprehensively designed and correctly implemented system of Quality Assurance Incorporating Good Manufacturing Practice, and thus Quality Control and **Quality Risk Management**”





# New in Chapter 1

## **QUALITY RISK MANAGEMENT**

1.5 Quality risk management is a systematic process for the assessment, control, communication and review of risks to the quality of the medicinal product. It can be applied both proactively and retrospectively.





# New in Chapter 1

## 1.6 The quality risk management system should ensure that:

- the evaluation of the risk to quality is based on scientific knowledge, experience with the process and ultimately links to the protection of the patient;
- the level of effort, formality and documentation of the quality risk management process is commensurate with the level of risk.





# Annex 20

- The new GMP Annex 20 corresponds to ICH Q9 guideline on Quality Risk Management
- It is voluntary
- It provides guidance on a systematic approach to quality risk management facilitating compliance with GMP and other quality requirements.





# Annex 20

- Quality risk management becomes an integral part of a manufacturer's QS
- Annex 20 itself is not intended to create new regulatory expectations
- It provides an inventory of internationally acknowledged risk management methods and tools together with a list of potential applications at the discretion of manufacturers.





# Annex 20

- QRM supports a scientific and practical approach to decision-making
- It provides documented, transparent and reproducible methods
- The degree of rigor and formality of QRM should reflect available knowledge and be commensurate with the complexity and/ or criticality of the issue to be addressed.





# QRM tools

- Basic risk management facilitation methods (flowcharts, check sheets etc.);
- Failure Mode Effects Analysis (FMEA);
- Failure Mode, Effects and Criticality Analysis (FMECA);
- Fault Tree Analysis (FTA);
- Hazard Analysis and Critical Control Points (HACCP);
- Hazard Operability Analysis (HAZOP);
- Preliminary Hazard Analysis (PHA);
- Risk ranking and filtering;
- Supporting statistical tools.





# Potential applications for QRM

- Annex 20 includes an Appendix to identify potential uses of QRM
- Examples for illustrative purposes only

A real example:

- **Risk Approach to GMP Audits**





## Audit scheduling - context

- Wide range of product types:
  - Rx, OTC, complementary medicines, APIs
  - sterile/non-sterile
  - specific risks, eg highly potent, highly sensitising
  - potential for quality defects across all types
  - potential to cause harm varies according to type





# Audit scheduling - context

- Different types of manufacturer:
  - size, number of sites
  - range of products
  - number of employees
  - steps of manufacture
  - complexity; eg automation
  - GMP knowledge
  - location
  - varying levels of GMP compliance





# Audit scheduling - context

- Other knowledge:
  - compliance history
  - recalls
  - complaints
  - changes, eg key personnel
  - internal information, eg from dossier evaluation
  - external intelligence
  - results of TGA testing





# Audit scheduling - context

- What we can control:
  - audit frequency
  - audit duration
  - size of audit team, including specialists
  - audit notice; announced vs unannounced (local only)
  - the audit plan; time spent on each activity
  - licence/certification issue





## Audit Scheduling – Risk Approach

- The TGA risk based model assumes a relationship between GMP compliance and potential for product defect or failure:
  - **Consequences** of product defect or failure depends on type of product
  - **Probability** of product defect or failure depends on level of GMP compliance
  - The TGA's assurance of compliance diminishes with time since last audit





## Audit Scheduling – Risk Approach

- Manufacturers are profiled according to
  - type of products manufactured or type of manufacture
  - level of compliance after each audit
- This is used to determine **routine** re-audit frequency





## Audit Scheduling – Risk Approach

- Unacceptable GMP compliance:
  - risk assessment done (modified FMEA)
    - [FB4.10.a - Manufacturer Risk Assessment.doc](#) [FB4.10.a - Manufacturer Risk Assessment.doc](#)
    - [Risk consequence, likelihood and matrix.doc](#) [Risk consequence, likelihood and matrix.doc](#)
  - audit report and risk assessment considered by an internal, independent Review Panel
  - decision on a case by case basis





# Ongoing risk management

- The routine re-audit frequency may be modified at any time in response to post-audit information, eg:
  - recalls
  - complaints
  - internal information, eg dossier evaluation
  - external intelligence
  - results of TGA testing
  - Changes to manufacturer – e.g. key staff, relocation





# Ongoing risk management

- Possible action in response to post-audit information:
  - bring forward next routine audit
  - conduct a “special” (non-routine) audit - usually unannounced
  - request specific information/documentation from the manufacturer
  - include specialist in next audit team
  - etc...





# Finally

- Quality risk management is a process that supports science-based and practical decisions when integrated into quality systems (Annex 20)
- Used properly it will support GMP and increase assurance of quality
- PIC/S has established an Expert Circle on QRM – further guidance will be available





Australian Government  
Department of Health and Ageing  
Therapeutic Goods Administration

Thank you for listening!

