Australian Government
Department of Health
Therapeutic Goods Administration

Good Manufacturing Practices for Complementary Medicines

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Complementary Medicines Australia - 2015 Quality Learning Seminar

3 June 2015

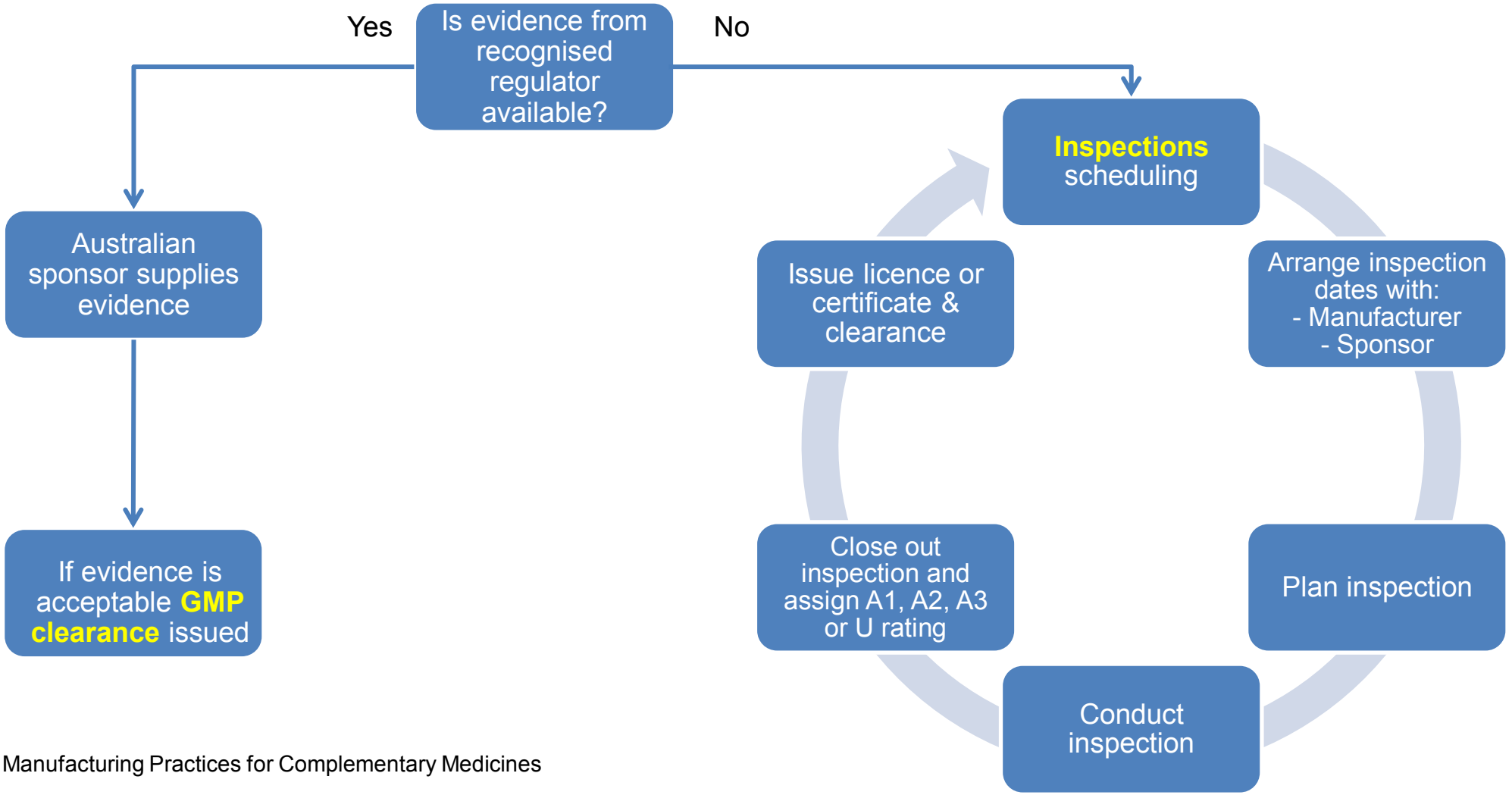
TGA Health Safety Regulation

Overview

- GMP clearance application process
- TGA compliance risk framework
- Major deficiencies commonly identified
- Manufacturing quality challenges
- TGA industry working group

Manufacturing Quality Branch
GMP clearance application process

High level TGA manufacturer assessment process



TGA compliance risk framework

TGA's approach to compliance

Help and support	Inform and advise	Correct behaviour	Enforce
• Make ongoing compliance easy	• Help to become and stay compliant	• Deter by detection	

TGA compliance risk framework

Regulated entity – attitude to compliance

Voluntary compliance	Accidental non-compliance	Opportunistic non-compliance	Intentional non-compliance
• Effective compliance systems • Management is compliance orientated	• Ineffective and/or developing compliance systems • Management compliance orientated but lacks capability	• Resistance to compliance • Limited poor compliance systems • Management not compliance orientated	• Deliberate non-compliance • No compliance systems • Criminal intent

Current MQB reinspection frequency based on risk

Inspection frequency matrix - medicines				
	Re-inspection period in months			
Risk category	Compliance rating			
	Acceptable			Unacceptable
	A1	A2	A3	
High	24	18	12	Determined by Review Panel
Medium	30	20	12	
Low	36	24	12	

Current MQB reinspection frequency based on risk

Compliance levels	
A1 = Good	Few deficiencies of a relatively minor nature
A2 = Satisfactory	Few major deficiencies (x<6) and /or a large number of minor deficiencies and no critical.
A3 = Basic	A large number of major (5<x<11) and/or a large number of minor deficiencies and no critical.
Not rated = unacceptable	One or more critical and/or a large number of major deficiencies.

Inspection frequency matrix - medicines				
	Re-inspection period in months			
Risk category	Compliance rating			
	Acceptable			Unacceptable
	A1	A2	A3	
High	24	18	12	Determined by Review Panel
Medium	30	20	12	
Low	36	24	12	

Current MQB reinspection frequency based on risk

Product/process risk classifications	
Medium risk	• Non-sterile medicines, including herbal, unless specified as high risk
Low risk	• Minerals, vitamins, fish oils and other supplements • Sunscreens • Single step – labelling/packaging; analysis/testing; release for supply and storage

Inspection frequency matrix - medicines				
	Re-inspection period in months			
Risk category	Compliance rating			
	Acceptable			Unacceptable
	A1	A2	A3	
High	24	18	12	Determined by Review Panel
Medium	30	20	12	
Low	36	24	12	

MQB reinspection frequency under consideration

Product/process risk classifications	
Medium risk	• **Registered** non-sterile medicines, **including registered herbal**
Low risk	• **All listed medicines, including listed herbal** • Sunscreens • Single step – labelling/packaging; analysis/testing; release for supply and storage

Inspection frequency matrix - medicines				
	Re-inspection period in months			
Risk category	Compliance rating			
	Acceptable			Unacceptable
	A1	A2	A3	
High	36	24	12	Determined by Review Panel
Medium	42	30	18	
Low	48	36	24	

Major deficiencies commonly identified by TGA

- Quality management system (QMS)
- Personnel
- Premises and equipment
- Documentation
- Production
- Quality Control
- Storage

Major deficiencies commonly identified by TGA

- Quality management system (QMS)
  - Unsatisfactory deviation management , such as inadequate investigation and record keeping
  - Inadequate resourcing of quality management functions including product release
  - All product quality reviews not conducted and/or not all elements covered

Major deficiencies commonly identified by TGA

- Personnel
  - Inadequate training and skills assessment
  - Practices do not reflect documented procedures

Major deficiencies commonly identified by TGA

- Documentation
  - Inadequate manufacturing instructions
  - Inadequate records keeping – including batch records

Major deficiencies commonly identified by TGA

- Production
  - Processes not validated or inadequately validated
  - Revalidation not conducted routinely
  - Inadequate change control management
  - Inadequate design of facilities, equipment and procedural measures for the prevention of contamination and cross-contamination
  - Reprocessing/rework inadequately controlled

Major deficiencies commonly identified by TGA

- Quality Control
  - Test methods not validated or verified and/or validation incomplete
  - Testing inadequate
  - Records of testing incomplete and/or ineffective review arrangements

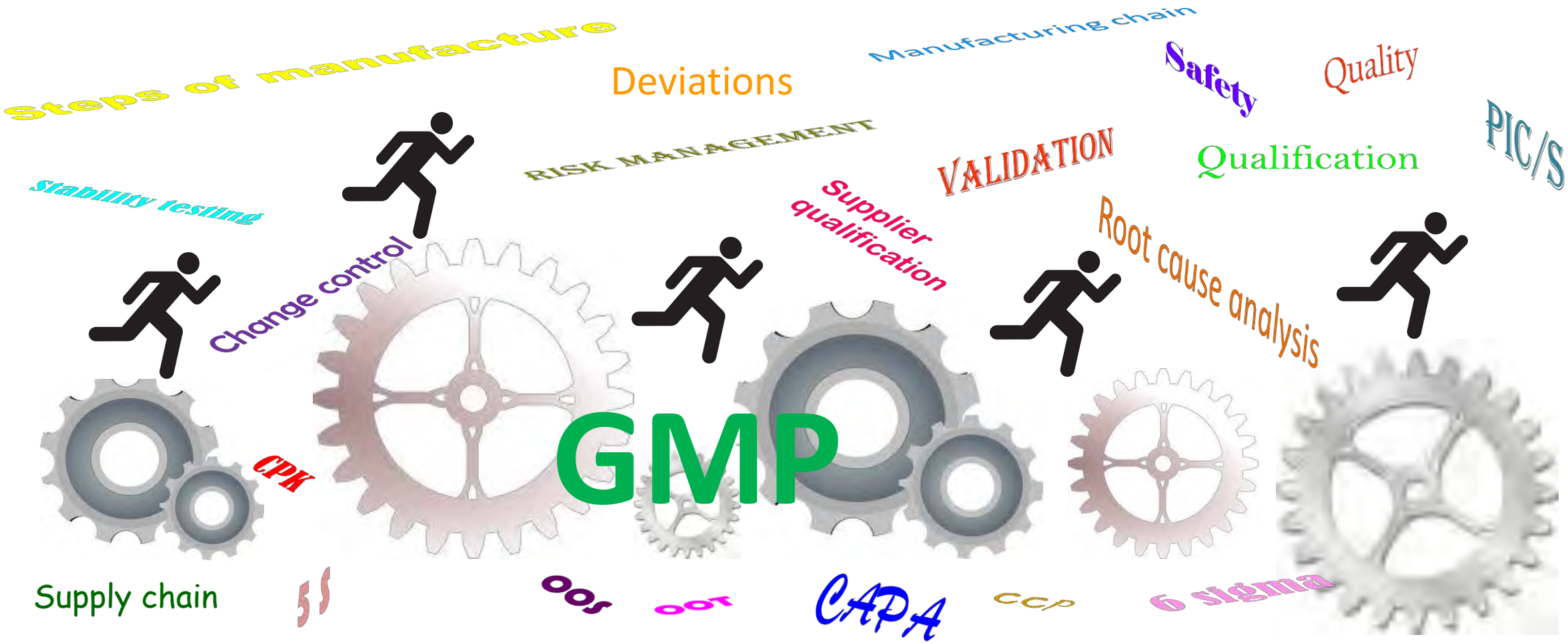
Major deficiencies commonly identified by TGA

- Storage
  - Inadequate controls and monitoring of storage conditions
  - Storage conditions not always as per label requirements

Manufacturing quality challenges

- Control of the supply chain
- Complex formulations
- Complex manufacturing chains

Manufacturing quality challenges



TGA – Industry Working Group on GMP

- Membership:
  - Accord
  - Active Pharmaceutical Ingredient Manufacturer's Association of Australia
  - Australia New Zealand Industrial Gas Association
  - Australian Self Medication Industry
  - Complementary Medicines Australia
  - Generic Medicines Industry Australia
  - Medicines Australia
- To prioritise and discuss issues of a regulatory and technical nature arising from current regulation and propose solutions
- Establish and oversight Technical Working Groups to develop:
  - new, or review existing, guidelines
  - comments on draft PIC/S guidelines for tabling by TGA at PIC/S meetings
  - guidance documents

TGA – Industry Working Group on GMP

- Technical guidance documents
- Guidance on release for supply
  - Part 1 published TGA website version 2.0 January 2015
    - Clarifies general requirements and responsibilities for undertaking release for supply (RFS) and release for further processing (RFFP)
  - Part 2 close to publication
    - Includes specific examples of the manufacturing process chain and how RFS and RFFP work in the specific examples cited

TGA – Industry Working Group on GMP

- Guidance on release for supply – Part 2
  - The specific examples included to-date include the following:
    - Release for supply from a secondary packaging site
    - Re-release of a product after minor further steps of manufacture
    - Stability conducted by a separate licensed manufacturer
    - Full product manufacture at one site followed by secondary packaging at another site and returned to the original manufacturer for release for supply
    - Bulk packaging from 2 manufacturing sites
  - Part 2 will be a live document that can have more relevant useful examples added as needed

References

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