Australian Government
Department of Health
Therapeutic Goods Administration

# GMP overview and an update

## on PIC/S guide to GMP for medicinal products version 14

Jenny Hantzinikolas
Director, Inspections Section | Manufacturing Quality Branch
Medical Devices & Product Quality Division
Therapeutic Goods Administration
TGA GMP Forum
12-14 May 2021

TGA Health Safety Regulation

13/05/2021

# GMP overview and update on PIC/S Guide to GMP for medicinal products version 14

- PIC/S guide to GMP version 14
- Transition plan overview
- Common deficiencies
- International collaboration
- PIC/S updates and what's on the horizon
- Conclusion

# PIC/S guide to GMP version 14

- The Pharmaceutical Inspection Co-operation Scheme (PIC/S) Guide to GMP for medicinal products Version 14 was implemented on 1 July 2020. There is a transitional plan in place with full adoption by 30 June 2021

https://www.tga.gov.au/publication/manufacturing-principles-medicinal-products

# PIC/S guide to GMP version 14

The updates to PIC/S guide to GMP version 14

- Chapters 3, 5, 8 (part 1)
- Revision of Annex 17

# PIC/S guide to GMP version 14

An assessment of all the changes was performed

**Part I Chapter 3 on Premises and Equipment:**

- General comments adding clarification in line with existing requirements and expectations.

# PIC/S guide to GMP version 14

**Part I Chapter 5 on Production:**

- Increased guidance regarding the technical and organisational controls that should be considered when developing and maintaining a control-strategy for cross-contamination, (5.21)
- Additional requirements regarding the management of suppliers requiring additional risk assessments and in some cases, on-site audits. (5.29)
- Update to PQS required in relation to raw material testing, should reduced testing be performed based on thorough supplier oversight.
- Update to PQS required in relation to outsourced raw material testing (5.36)

# PIC/S guide to GMP version 14

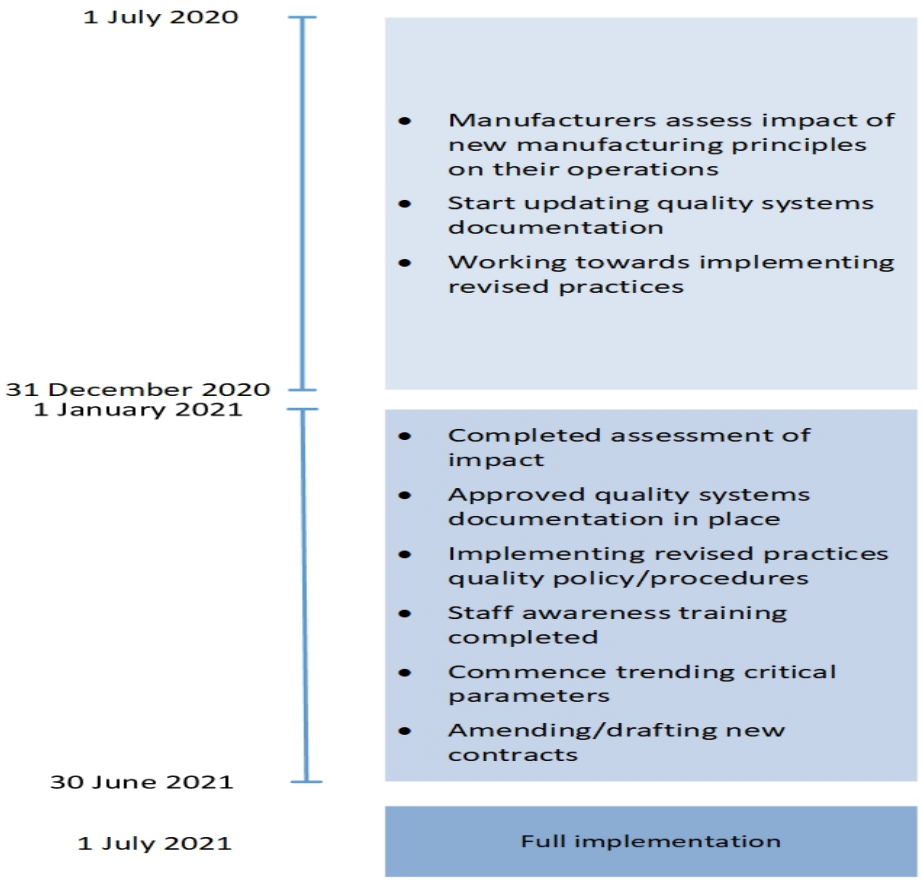
**Part I Chapter 8 on Complaints and Product Recall:**

- Minor change to align terminology in current SOPs for recalls and complaints.
- Expansion of scope in relation to defects and the possibility of product falsification (8.6)
- Minor change to ensure procedures facilitate investigation of product quality following adverse events (8.8)
- Minor change to update procedures to ensure that TGA is notified in cases where manufacturers intend to rework recalled product (8.28)
- Minor change to SOP for recalls to demonstrate the effectiveness of recalls out-of-hours (8.30)

# PIC/S guide to GMP version 14

- **Annex 17 on Real Time Release Testing and Parametric Release:**
- General comments adding clarification in line with existing requirements and expectations.

# Transition plan



# Transition plan

- The transition period from 1 July 2020 to 1 July 2021 serves to allow manufacturers to assess and plan for the changes and permit time for implementation.
- For the most significant changes, a transition plan was set up, which summarise the minimum requirements to demonstrate compliance
- Compliance with all other changes was expected from 1 July 2020 and transition arrangements do not apply.

# Common deficiencies observed

| Areas | Deficiencies |
|---|---|
| Chapter 1 | Poor investigation of deviations, quality incidents |
| Annex 11 | Inadequate electronic data security or traceability. For example:<br>❑ no unique log-ins<br>❑ using Excel to record GMP critical data without additional security or traceability<br>❑ no audit trail reviews<br>❑ poor qualification of configurable electronic systems |
| Annex 15 | Inadequate or no facility/equipment qualification and process validation (non-sterile listed and registered medicines) |

# Common deficiencies observed

| Areas | Deficiencies |
|---|---|
| Chapter 4 | Documentation (probably due to remote inspection processes relying more on documentation review)<br>❑ not up to date<br>❑ inconsistent with cross referencing to other SOPs<br>❑ missing procedures/instructions for cleaning and preventative maintenance of equipment (surprised me but often not available…only general SOPs that don't detail specific activities)<br>❑ records of sampling and testing of packaging materials – not recorded or very poor |
| Chapter 5 | Potential for cross contamination |

# Highlights - International collaboration

| | |
|---|---|
| Inspection planning | • TGA participates in international information meetings with regulatory partners to share inspection planning information for Active Pharmaceutical Ingredient manufacturing sites.<br>• TGA participates in a pilot programme for sharing inspection planning information with regulatory partners for sterile finished dosage form manufacturers |
| PIC/S working groups | • TGA is either a member of Chair of a number of PIC/S working groups<br>• Sub Committee on GM(D)P harmonisation<br>• Sub Committee on Compliance<br>• Expert Circle on Active Pharmaceutical Ingredients .<br>• Expert Circle on Blood, Tissues, Cells and ATMPs<br>• PIC/S working group on Data Integrity and Data Management.<br>• PIC/S working group on Annex 1<br>• PIC/S working group on Cross Contamination in shared facilities<br>• PIC/S working group on Annex 2<br>• PIC/S working group on Cells and Tissues |

# PIC/S mission

lead the international **development**, **implementation** and **maintenance** of harmonised GMP standards and quality systems of inspectorates in the field of medicinal products.

# PIC/S mission

Training of Inspectors is an integral and key activity of PIC/S

Annual seminars is one means for PIC/S to achieve its mission

2016 – Inspectorates of the Future

2017 – How to Inspect QC Laboratories

2018 – Management of Risk Through The Product Life-Cycle

2019 – Quality Assurance of Sterile Medicinal Products

# PIC/S updates and what's on the horizon

- The following Annexes came into force on 1 May 2021 as part of PICS guide to GMP version 15
  - PIC/S Annex 2A Manufacture of advanced therapy medicinal products for human use
  - PIC/S Annex 2B Manufacture of biological medicinal substances and products for human use

# PIC/S updates and what's on the horizon

- Areas under revision
  - Chapter 4 on documentation
  - Annex 1 - Manufacture of sterile medicinal products
  - Annex 4-  Manufacture of veterinary medicinal products other than immunological veterinary products
  - Annex 5- Manufacture of immunological veterinary products
  - Annex 11- Computerised systems

# PIC/S updates and what's on the horizon

- Areas under revision
  - Annex 13- Manufacture of investigational medicinal products
  - Annex 21- GMP for importers of medicinal products
  - Annex 16- Certification by an authorised person and batch release

# PIC/S updates and what's on the horizon

- Annex 1 is still being revised with 2nd consultation comments being reviewed. There were 2000 comments. Plan to finalise by Q3/4, 2021
- PIC/S **Annex 16** (Certification by the authorised person and batch release) to be advanced to **Step 2 - public consultation** of national stakeholders by non-EU/EEA Participating Authorities of PIC/S).

# PIC/S updates and what's on the horizon

- PIC/S Collaboration with ICH guidance documents.
- The pilot on "More Routine Engagement of ICH with PIC/S on ICH Q Guidelines that involve Inspectorates in Implementation" was successfully launched in April 2020
- The pilot cover two major ICH Q Guidelines: Q9 (Quality Risk Management) and Q12 (Pharmaceutical Product Lifecycle Management).

# PIC/S updates and what's on the horizon

- PIC/S Collaboration with ICH guidance documents.
  - PICS is an observer in the drafting of ICH Q13 on continuous manufacturing

# PIC/S updates and what's on the horizon

- Collaboration with ICMRA
  - Remote inspections experiences

# Questions?

# Thank you


Australian Government

Department of Health

Therapeutic Goods Administration