TGA adoption of PIC/S Version 13

Presented by Trevor Schoerie, July 2017

National GMP & Validation Forum

Hosted by PharmOut

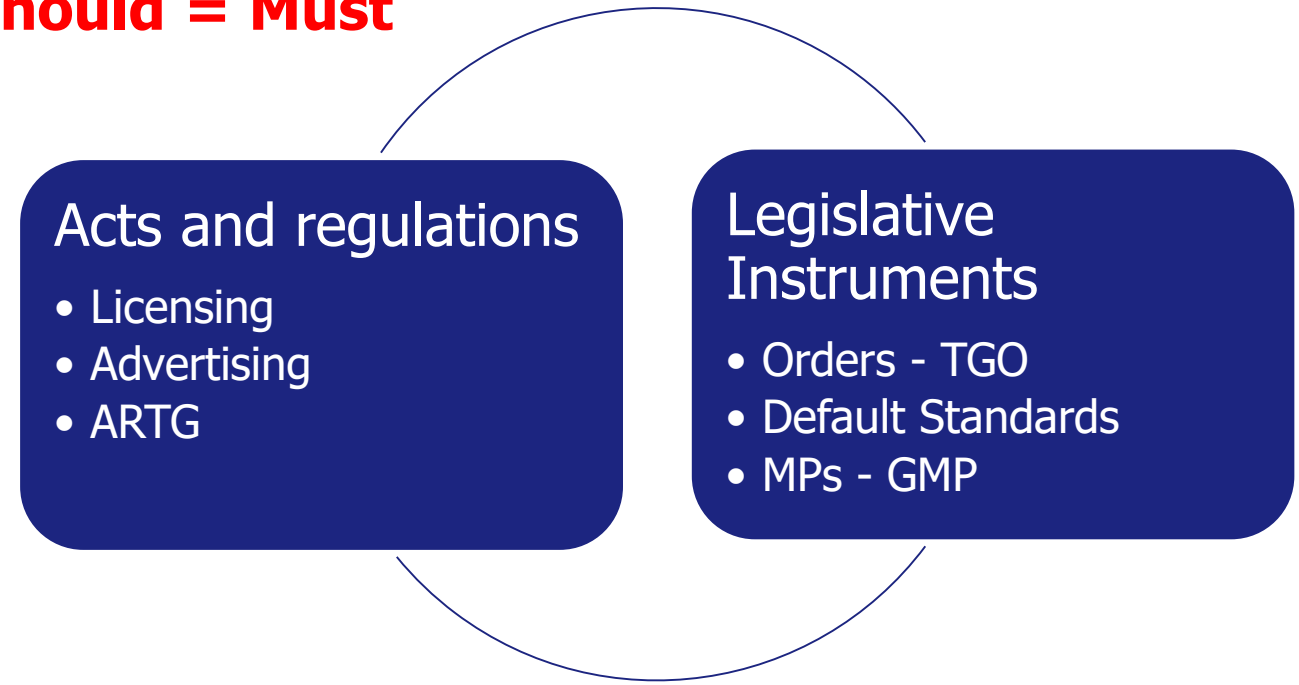
PharmOut

Australian TGA innovations

- 1974 – 4th set of GMP in the world
- Innovated the risk based inspection frequency
- Innovated the desktop audit process

The Facts – Current Situation

- Current version is **PIC/S PE 009-08** - 15th January 2009
- Manufacturing Principle (No 1 of 2009)
  - No automatic adoption
  - Excises Annex 4, 5 & 14
  - **Should = Must**



Another False Start?

Last week - 19 July 2017 - PDA – A TGA representative **will present on TGA adoption of PIC/S PE 009-13** and impending revision to Annex 1.

Neale Balwyn shared –

- Working with TIWGG – Q4 2016
- adoption end of year
- 1 year transition
- could wait for annex 1 due in Version 14 in 2018!
- Drafting Q&A
- Phased adoption strategy
- Possible road shows
- **Notification of intent to adopt V13 (early 2017)**

Several Times Announced Adoption

- Announced "rolling adoption" PIC/S Adoption - 29 May 2013
- https://www.tga.gov.au/consultation/consultation-proposal-automatic-adoption-new-versions-pics-guide-good-manufacturing-practice-medicinal-products
- Adoption of harmonized standards is **crucial to maintaining the mutual equivalence** of Australia with its Mutual Recognition Agreement (MRA) partners (the EU, Switzerland, Canada, Singapore) and partners with which a Memorandum of Understanding (MOU) is effective, such as the USA. In addition to Australia, the PIC/S GMP standard is used by the European Union and New Zealand, whereas others (Canada, USA, Singapore) have their own national GMPs that are substantially aligned with the PIC/S.

The Gap – PIC/S PE 009-08 to EU

AM

- Introduction
- Chapter 1 – Pharmaceutical Quality System*
- Chapter 2 – Personnel
- Chapter 3 - Premises & Equipment

PM

- Chapter 4 - Documentation
- Chapter 5 - Production
- Chapter 6 - Quality Control
- Chapter 7 – Outsourced Activities*
- Chapter 8 - Complaints and product recall
- Chapter 9 - Self inspection

* Chapter title changes from PE 009-8

PIC/S PE 009-08 to EU GMPs
Annexes

Annex	PE 009-8	EU	Degree of change
1	Manufacture of sterile medicinal products	Manufacture of Sterile Medicinal Products	Same
2	Manufacture of biological medicinal products for human use	Manufacture of Biological active substances and Medicinal Products for Human Use	**Major**
3	Manufacture of radiopharmaceuticals	Manufacture of Radiopharmaceuticals	**Major**
4	Manufacture of Veterinary Medicinal Products other than Immunologicals	Manufacture of Veterinary Medicinal Products other than Immunologicals	**Major**
5	Manufacture of Immunological Veterinary Medical Products	Manufacture of Immunological Veterinary Medical Products	**Major**
6	Manufacture of medicinal gases	Manufacture of Medicinal Gases	**Major**
7	Manufacture of herbal medicinal products	Manufacture of Herbal Medicinal Products	**Minor**
8	Sampling of starting and packaging materials	Sampling of Starting and Packaging Materials	**Minor**
9	Manufacture of liquids, creams and ointments	Manufacture of Liquids, Creams and Ointments	**Minor**
			Continued next page…

PIC/S PE 009-08 to EU GMPs

Annex	PICS Guide to GMP (v8)	PICS Guide to GMP (v13)	Degree of change
10	Manufacture of pressurised metered dose aerosol preparations for inhalation	Manufacture of Pressurised Metered Dose Aerosol Preparations for Inhalation	**Major**
11	Computerised systems	Computerised Systems	**Major**
12	Use of ionising radiation in the manufacture of medicinal products	Use of Ionising Radiation in the Manufacture of Medicinal Products	**Major**
13	Manufacture of investigational medicinal products	Manufacture of investigational medicinal products	**Major**
14	Manufacture of medicinal products derived from human blood or plasma	Manufacture of medicinal products derived from human blood or plasma	**Major**
15	Qualification and validation	Qualification and Validation	**Major**
16	Qualified person and batch release	Certification by a Qualified Person and Batch	N/A
17	Parametric release	Parametric Release	**Major**
19	Reference and retention samples	Reference and Retention Samples	**Minor**
20	Quality risk management	Quality risk management	Same

Must

V8 – Ch 1 Principle

- The holder of a manufacturing authorisation **must** manufacture medicinal products so as to ensure that they are fit for their intended use, comply with the requirements of the Marketing Authorisation and do not place patients at risk due to inadequate safety, quality or efficacy.

V13 – Ch 1 Principle

- The holder of a Manufacturing Authorisation **must** manufacture medicinal products so as to ensure that they are fit for their intended use, comply with the requirements of the Marketing Authorisation or ***Clinical Trial Authorisation***, as appropriate, and do not place patients at risk due to inadequate safety, quality or efficacy.

Must

V8 – Ch 1 Principle

- 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.

V13 – Ch 1 Principle

- To achieve this quality objective reliably there **must** be a comprehensively designed and correctly implemented **Pharmaceutical Quality System** incorporating Good Manufacturing Practice and Quality Risk Management.

Must

V13 New clause § 2.6

- An Authorised Person **must** ensure that each batch of medicinal products has been manufactured and checked in compliance with the laws in force in that country and in accordance with the requirements of the Marketing Authorisation

Must

V13 New clause § 2.6

- The Authorised Person(s) **must** meet the qualification requirements laid down in the national legislation, they shall be permanently and continuously at the disposal of the holder of the Manufacturing Authorisation to carry out their responsibilities;

Must

V8 §3.21

- Where quarantine status is ensured by storage in separate areas, these areas **must** be clearly marked and their access restricted to authorised personnel. Any system replacing the physical quarantine should give equivalent security.

V13 §3.21

- Where quarantine status is ensured by storage in separate areas, these areas **must** be clearly marked and their access restricted to authorised personnel. Any system replacing the physical quarantine should give equivalent security.

Must

V8 Ch 4 Principle

- Specifications, Manufacturing Formulae and instructions, procedures, and records **must** be free from errors and available in writing. The legibility of documents is of paramount importance.

V13 Ch 4 Principle

- The main objective of the system of documentation utilised **must** be to establish, control, monitor and record all activities which directly or indirectly impact on all aspects of the quality of medicinal products.

Must

V8 §4.4

- The reproduction of working documents from master documents **must** not allow any error to be introduced through the reproduction process.

V13 §4.2

The reproduction of working documents from master documents **should** not allow any error to be introduced through the reproduction process.

Must

V13 New Clause §4.10

- It should be clearly defined which record is related to each manufacturing activity and where this record is located. Secure controls **must** be in place to ensure the integrity of the record throughout the retention period and validated where appropriate.

Must

V13 New Clause §4.11

- Specific requirements apply to batch documentation which **must** be kept for one year after expiry of the batch to which it relates or at least five years after certification of the batch by the Authorised Person, whichever is the longer. For investigational medicinal products, the batch documentation **must** be kept for at least five years after the completion or formal discontinuation of the last clinical trial in which the batch was used.

Must

V8 Ch 7 Principle

Contract manufacture and analysis **must** be correctly defined, agreed and controlled in order to avoid misunderstandings which could result in a product or work of unsatisfactory quality. There **must** be a written contract between the Contract Giver and the Contract Acceptor which clearly establishes the duties of each party. The contract **must** clearly state the way in which the authorised person releasing each batch of product for sale exercises his full responsibility.

V13 Ch 7 Principle

- There **must** be a written contract between the Contract Giver and the Contract Acceptor which clearly establishes the roles and responsibilities of each party. The Pharmaceutical Quality System of the Contract Giver **must** clearly state the way that the Authorised Person certifying each batch of product for release exercises his/her full responsibility.

Must

V13 Annex 11 §3.1

- When third parties (e.g. suppliers, service providers) are used e.g. to provide, install, configure, integrate, validate, maintain (e.g. via remote access), modify or retain a computerised system or related service or for data processing, formal agreements **must** exist between the manufacturer and any third parties, and these agreements should include clear statements of the responsibilities of the third party.

Must

V13 Annex 15 §5.6

- For the site transfer of legacy products, the manufacturing process and controls **must** comply with the marketing authorisation and meet current standards for marketing authorisation for that product type. If necessary, variations to the marketing authorisation should be submitted.

Must

V8 Annex 15 §29

- The decision to carry out concurrent validation **must** be justified, documented and approved by authorised personnel.

V13 Annex 15 §5.16

- However, the decision to carry out concurrent validation **must** be justified, documented in the VMP for visibility and approved by authorised personnel.

Must – Traditional Process Validation

V8 Annex 15 §25

In theory the number of process runs carried out and observations made should be sufficient

to allow the normal extent of variation and trends to be established and to provide sufficient data for evaluation. It is generally considered acceptable that **three consecutive batches/runs** within the finally agreed parameters, would constitute a validation of the process.

V13 Annex 15 §5.19

The number of batches manufactured and the number of samples taken should be based on quality risk management principles, allow the normal range of variation and trends to be established and provide sufficient data for evaluation. **Each manufacturer must** determine and justify the number of batches necessary to demonstrate a high level of assurance that the process is capable of consistently delivering quality product.

Must – Continuous Process Validation

V8 Annex 15 §25

In theory the number of process runs carried out and observations made should be sufficient

to allow the normal extent of variation and trends to be established and to provide sufficient data for evaluation. It is generally considered acceptable that **three consecutive batches/runs** within the finally agreed parameters, would constitute a validation of the process.

V13 Annex 15 §5.24

The number of batches manufactured and the number of samples taken should be based on quality risk management principles, allow the normal range of variation and trends to be established and provide sufficient data for evaluation. **Each manufacturer must** determine and justify the number of batches necessary to demonstrate a high level of assurance that the process is capable of consistently delivering quality product.

Heat in 2017/8?

2002 to 2009 Hot Topics

- QRM
- QRM
- PQR / AQR

2009 to V13

- QRM
- Data Integrity
- § 1.4
- § 1.8
- RCA
- CAPA
- Annex 11
- Annex 15

+ Annex 1

Practically how do you close the gap

- Adobe Professional – document compare
- Impossibly large Spreadsheet with relevant gaps*
  - **Plan** – scope = gap, actions, cost, responsible
  - But MHRA have been inspecting to this standard
    - so why not learn from them?

  - Bryan Wright – ex MHRA has permission from MHRA to share their data.

***Free copy if anyone wants one?**

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