

Establishing the Essential Principles of Quality Systems/GMP for Blood/Plasma Collection

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Introduction

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Introduction

- ▶ What do we mean by “Essential Principle”?
 - Absolutely necessary proposition that serves the foundation for a system of behaviour
- ▶ Essential principles form the basis for what we do and how we do it

Essential Principles for Blood

- ▶ The “Essential Principles” for blood & plasma collection should be based on:
 1. Do no harm to the donor
 2. Do no harm to the staff
 3. Do no harm to the patient
 4. Remembering that blood is a THERAPEUTIC PRODUCT
- ▶ In other words, we must work in a way that removes or reduces all risks that might cause harm

Essential Principles for Blood

Risks to Donors:

- ▶ Donor's health affected by removal of blood volume
- ▶ Unsafe environment
- ▶ Poor collection process
- ▶ No post-donation rest & rehydration to make up lost volume before leaving Centre



Essential Principles for Blood

Risks to Staff:

- ▶ Infectious donor
- ▶ Unsafe environment
- ▶ Personal protective equipment not provided or used
- ▶ Lack of infection control practices
- ▶ Unsafe collection process (needle sticks)
- ▶ Unsafe waste management



Essential Principles for Blood

Risks to Patients:

- ▶ Insufficient supply
- ▶ Infectious or contaminated components
- ▶ Blood grouping or antibody screening errors
- ▶ Poor quality components that are not efficacious



Essential Principles for Blood

Therapeutic Goods:

- ▶ Blood & blood components are transfused into patients who need them

- ▶ They are used therapeutically



- ▶ Therefore their manufacture needs to be very strictly controlled (like medicines)



Essential Principles for Blood

- ▶ So what must we do to reduce risk & ensure safety & quality?
 1. Establish a Quality System (QS)
 2. Implement Good Manufacturing Practice (GMP)
 3. Select & follow a Blood Standard

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Quality System (QS)

- ▶ Also called “quality management system (QMS)”
- ▶ Provides a quality framework, for example:
 - Personnel & training
 - Documentation & records
 - Management of facilities, buildings, equipment & materials
 - Monitoring systems eg QC, internal audits, CAPA
- ▶ Builds a quality approach into all systems & processes

Quality System (QS)

- ▶ Where do we find principles/requirements for a QS?
 - International Standards eg *ISO 9001:2015 Quality management systems - Requirements*
- OR**
- *Codes of Good Manufacturing Practice* include requirements for a QS
- ▶ There are also documents that provide QS principles/requirements for specific activities, eg:
 - *ISO 15189:2012 Medical laboratories - Requirements for quality and competence*

Essential Principles for Blood

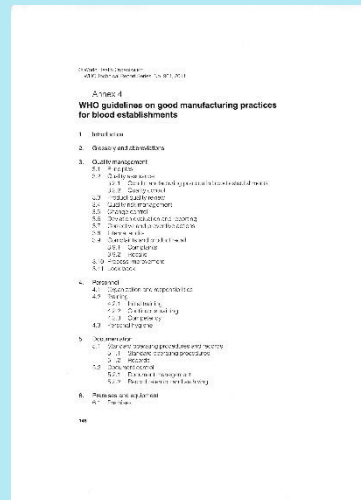
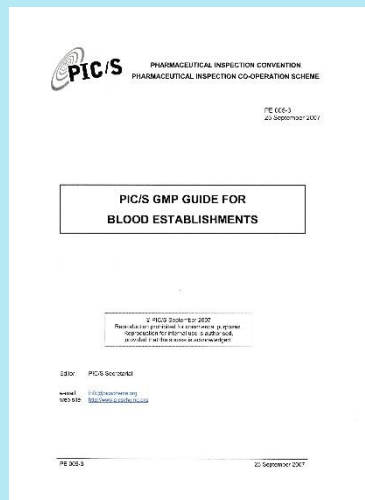
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Good Manufacturing Practice (GMP)

- ▶ Based on manufacturing principles or **requirements** for manufacturing **therapeutic goods** (regulated in many countries)
- ▶ Main objective of GMP is **risk reduction** by **controlling manufacture** within a **quality management framework**
- ▶ Also includes requirements for QS

Good Manufacturing Practice (GMP)

- ▶ Where do we find principles/requirements for GMP?
 - Documents called *Codes of Good Manufacturing Practice*
- ▶ There are Codes of GMP written specifically for Blood & other biological products



► Most **Codes of GMP** for Blood have the following contents:

- Quality Management
- Personnel & Training
- Buildings & Facilities
- Documentation & Records
- Equipment
- Control of Materials
- Donor Selection / Donation
- TTI Screening
- ABO Rh(D) Testing
- Process Control
- Storage, Packaging and Transport

• Quality Management

- ▶ Documented Quality System & Quality Policy
- ▶ Nominated Quality Manager independent from “production” function
- ▶ Change control system
- ▶ Qualification & Validation system
- ▶ Monitoring systems:
 1. Internal Audit program (risk based)
 2. Customer Feedback
 3. Management Review / Product Review (including Quality Control)
 4. Corrective Action/Preventative Action (CAPA)

• Personnel & Training



Staff need to know WHAT their jobs are:

- ▶ Clear staff roles & responsibilities eg job descriptions, organisational charts
- ▶ Key roles required under GMP eg Quality Manager, Manufacturing Manager

Staff need to know HOW to do their jobs properly:

- ▶ All staff must be trained & assessed for competency in their roles
- ▶ Training should be ongoing

• Documentation



Good documentation reduces staff errors

- ▶ Quality/GMP documentation provides:
 - quality objectives, direction & commitment (policies)
 - clear, unambiguous procedures to follow (SOPs)
 - evidence or records of outcomes or activities (forms)
 - the basis for training programs
- ▶ Must be **document controlled** – current, regular review & update

• Records

There must be evidence of activities & outcomes to prove that standards have been met

- ▶ Records provide **evidence & traceability**
- ▶ Records may be:
 - paper or electronic
 - photographic
 - provided by an **external source**
- ▶ Storage must maintain integrity for required period



• Buildings & Facilities

- ▶ Should be located, designed, constructed, used & maintained to make sure:
 - Product is protected
 - Risk of error is minimised (through safe work flows)
 - Cleaning & maintenance can be performed properly

- ▶ Need to ensure:
 - Orientation eg Processing separate from Collection & Testing
 - Security
 - Environmental control & emergency power
 - Sealed surfaces (no cracks etc in floors, walls & ceilings)
 - Pest control & adequate cleaning

• Equipment & Material

CRITICAL equipment & material must be shown to be reliable before & during use

- ▶ **Equipment & material management** processes make sure that equipment & materials are:
 - Properly **evaluated against specifications**
 - Correctly **installed & checked** before use (Qualified & validated)
 - **Monitored** once in use – controls, QC, checks
 - **Cleaned, maintained, calibrated & serviced** regularly (Equipment)
 - **Handled & stored** as required by the manufacturer (Material)
 - **Defects reported** (Material)
 - Staff **trained & SOPs** written before use

• Donor Selection

This is the first step in assuring safety of blood supply

- ▶ Selecting a “safe” donor includes:
 - Good identification procedures (donor & previous history)
 - Donor questionnaire completed by donor:
 - standard questions
 - filled out in private
 - filled out at time of donation
 - Donor’s health & risk factors assessed by trained staff in confidential area, using documented acceptance criteria

• Donation / Collection

- ▶ Donor identity checked against paperwork
- ▶ Selection & inspection of blood collection pack
- ▶ Handling of pack (clean surfaces)
- ▶ Venepuncture **CCP** – prevent contamination
- ▶ Collection technique:
 - Labelling of bags & samples at bedside
 - Mixing, weighing & timing donation (correct vol & time)
 - Seal & strip tubing as quickly as possible (clotting)
 - Collect & mix samples as quickly as possible

• Processing

- ▶ Components only manufactured from whole blood & apheresis donations that have been:
 - collected properly from eligible donors
 - collected within required timeframes
 - transported in controlled & validated conditions
- ▶ All work areas cleaned & free of other materials or paperwork before processing
- ▶ Validated processes, materials, equipment
- ▶ Closed systems & heat sealers

• Donation Screening

- ▶ Donation screening must ensure each donation is correctly grouped & screened for infectious agents
- ▶ All donations must be tested **every time** for:
 - ABO & Rh(D) blood groups
 - Transfusion Transmitted Infections (TTI)
 - Clinically significant antibodies (if required by cGMP)
- ▶ Components should not be released for transfusion until all tests have been completed & are acceptable (CCP)

• Storage, Packing & Transport

▶ Focus on:

- Security & identification of components
 - segregation of quarantined components from released components (untested & tested)
 - released components clearly labelled
- ## ▶ Storage facilities properly maintained at correct temperature
- ## ▶ Components maintained at appropriate temperatures during transport

• Quality Control

- ▶ Monitors all manufacturing processes against requirements to ensure they are “in control”
- ▶ Representative sampling & testing program for all:
 - component types
 - manufacturing sites
 - manufacturing methods
 - different equipment & types of materials
 - modes of transport
- ▶ Results compared to specifications, failed components discarded

ISO vs GMP?

- ▶ Many countries implemented ISO 9001 before GMP
- ▶ Some countries are still focussing on ISO 9001 implementation first, even after learning about GMP
- ▶ They are not gaining the benefit of improved component quality & safety that GMP brings
- ▶ Some countries are also focussing on implementing ISO 15189 because of the importance given to TTIs
- ▶ This approach results in little attention given to the processing activities

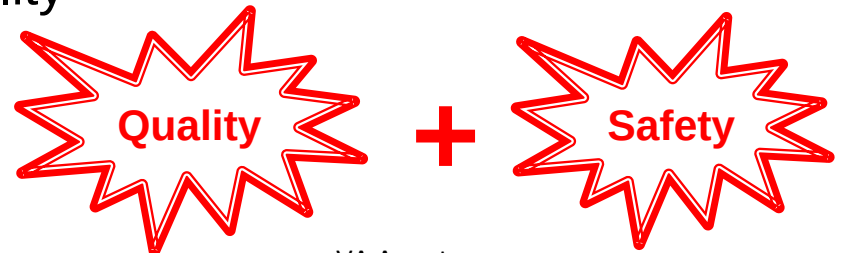
ISO 9001 vs GMP?

- ▶ Both cover the same principles for the Quality System.
- ▶ ISO QS:
 - more detailed
 - emphasises meeting customer needs & continuous improvement
- ▶ GMP QS:
 - Has a stronger focus on:
 - **SAFETY**
 - **traceability**
 - **change control**
 - **qualification & validation**

ISO 9001 vs GMP?



- ▶ ISO does NOT cover any principles for manufacturing therapeutic goods
- ▶ GMP DOES cover the principles for manufacturing therapeutic goods & is focussed on:
 - Preventing errors
 - Preventing contamination/cross contamination
 - Reliability of staff, processes, premises, equipment, materials (qualification, validation, change control)
 - Good documentation = traceability
- ▶ GMP is MORE than ISO



ISO 15189 vs ISO 9001 vs GMP?

- ▶ ISO 9001 & GMP are applicable to the whole of business & all activities
- ▶ ISO 15189 is limited to diagnostic medical testing laboratories (note: Blood Services run screening not diagnostic laboratories)

► Most **Codes of GMP** for Blood have the following contents:

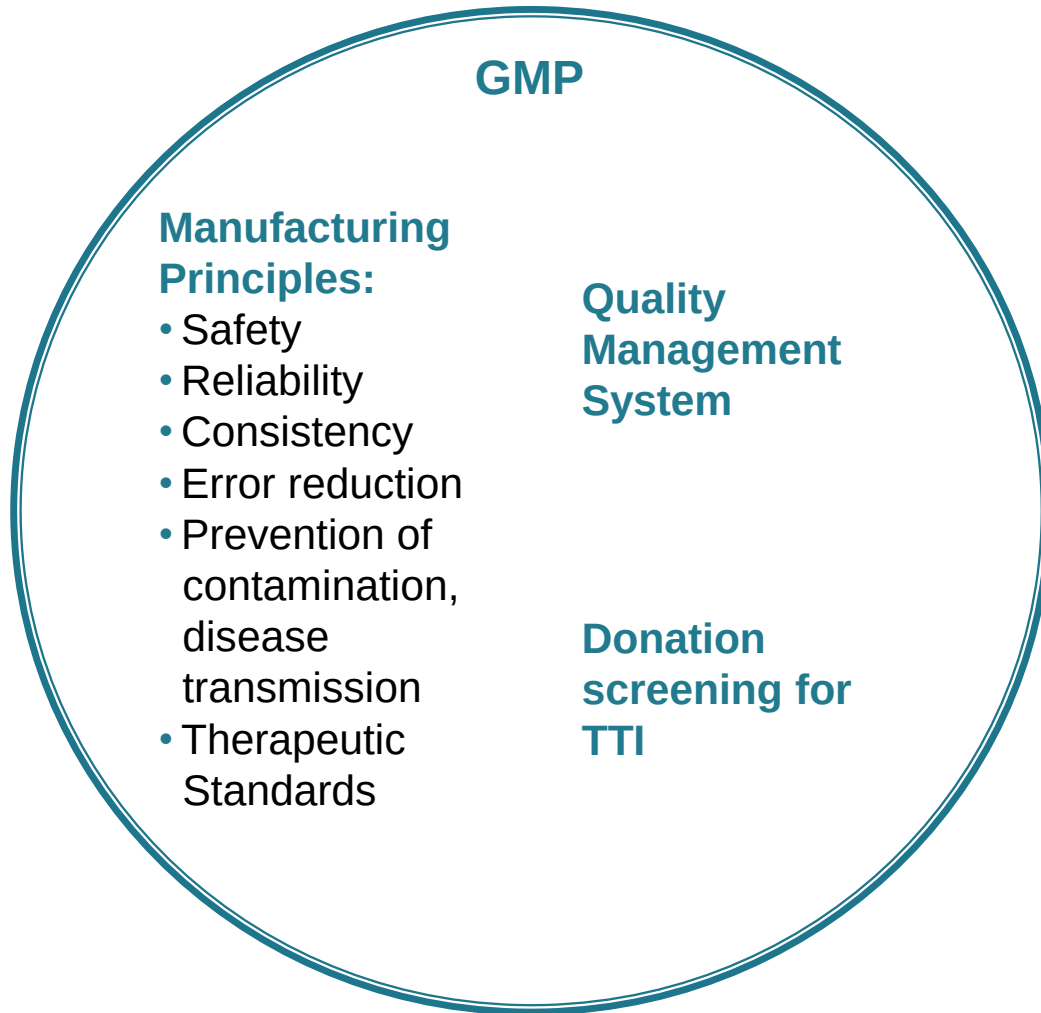
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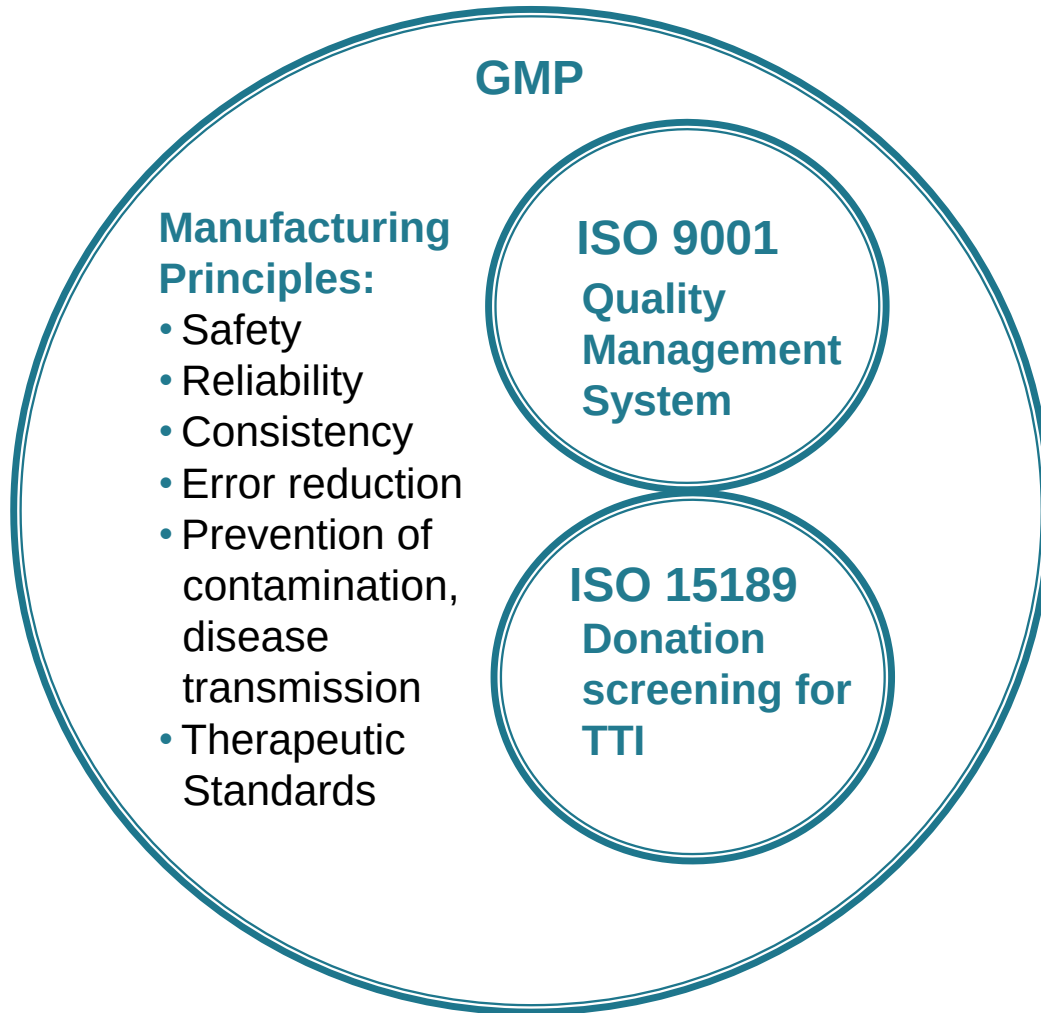
General QS
requirements
(also in ISO
9001)

- Donor Selection / Donation
- TTI Screening
- ABO Rh(D) Testing
- Process Control
- Storage, Packaging and Transport

Blood
manufacture

ISO 15189





GMP > ISO 9001 > ISO 15189

ISO 15189 vs ISO 9001 vs GMP?

► Conclusion:

- ISO 15189 gives you a QS in your screening laboratory but nowhere else
- ISO 9001 gives you a QS for the whole business but not the manufacturing principles that provide safety & control
- GMP gives you a QS for the whole business AND the manufacturing principles that build safety & control into all activities

Essential Principles for Blood

- ▶ So what must we do to reduce risk & ensure safety & quality?
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Blood Standards

- ▶ GMP provides ***principles*** of manufacturing, not the detailed requirements
- ▶ Need a suitable **Blood Standard** to set out minimum accepted specifications for:
 - performance of processes
 - characteristics of components

Blood Standards

EXAMPLE: Donor selection

▶ GMP requirement:

- *The selection of donors and relevant screening tests including those for infectious agents should ensure that the manufactured products are suitable for their intended purpose.*
- *Donors should be selected according to documented procedures defining the selection criteria, infectious disease screening tests and any other relevant tests.*

Ref: Australian cGMP 2013

Blood Standards

EXAMPLE: Donor selection

- ▶ Blood Standard requirement:
 - *Donors must meet the following:*
 - *Acceptable age range – 18 to 65 years old*
 - *Weight ≥ 50 kg*
 - *Hb ≥ 125 g/L (females) ≥ 135 g/L (males)*
 - *No health, travel or lifestyle risk factors*
 - *Not be on certain medications*

Ref: Council of Europe 16 Ed

Blood Standards

- ▶ Blood Standards are complementary to GMP
- ▶ There are several international Standards that can be used:
 - *Council of Europe Guide to the preparation, use and quality assurance of blood components*
 - *AABB Standards*
- ▶ Plasma fractionators can set a specification for plasma that is based on the pharmaceutical/drug Standard they must follow eg:
 - *European Pharmacopoeia*
 - *British Pharmacopoeia*

Closing Summary

- ▶ Blood Service objectives should be based on the essential principle of removing or reducing risks to the safety & well-being of their donors, staff & patients
- ▶ Implementation of a quality system & good manufacturing practice will achieve these objectives by ensuring:
 - Controlled manufacture within a quality framework
 - Reliability & consistency of all components, processes, equipment, materials & staff
 - Improved safety & quality of all components & for all activities
- ▶ The Code of GMP for Blood, & a Blood Standard should be the “go to” documents

The presenter has no conflicting or commercial interests in any of the entities or products referenced in this presentation.

A close-up photograph of two honey bees on Eucalyptus flowers. The bees are positioned on green, unopened flower buds. The background features large, bright yellow Eucalyptus flower heads. A red, textured object is also visible near the bees. The text "Thank you" is overlaid in a white, cursive font.

Thank you

Eucalyptus Tree