cGMPs
Current Good Manufacturing Practices

UCSF Blood Bank / Blood Centers

GMP History

- 1906 "The Jungle"
- 1931 Food and Drug Administration
- 1937 Sulfanilamide
- 1938 Federal Food, Drug and Cosmetic Act
- 1958 Thalidomide
- 1963 First draft of the GMPs

GMPs are...

- Legal requirements representing the minimum practices.

CFRs

- CODE OF FEDERAL REGULATIONS
- TITLE 21 FOOD & DRUG
- CHAPTER 1 - GMPS
- SUBCHAPTERS
  - "F"- Biologics (600 Series)
  - "C" - Drugs (200 Series)
  - "H" - Medical Devices (800 Series)

Blood Products

- DRUG (211)
  - Purity
  - Safety
  - Effectiveness
- BIOLOGICS (600)
  - Safety
  - Purity
  - Potency

Consequences of Non-Compliance

- Purity, Potency, Safety compromised
- FDA Citation (483)
- FDA Warning Letter
- FDA Intent to Revoke Licensure
- FDA Consent Decree

Benefits of GMPs

- Improved products and customer satisfaction.
- Consistent, reliable systems for production.
- Decreased product discards, rework, shortages.
- Decreased regulatory problems.
- Improved work environment.

7

GMP Elements

- Record Keeping
- Personnel
- Calibration
- Validation
- Error Management
- SOPs
- Production Controls
- Labeling/Lot Release
- Facilities/Equip/Sup.
- QA and Auditing

8

Record Keeping

- Record Keeping/documentation should provide a complete history of any batch or component, including any process deviations or problems occurring during its life cycle. Effective documentation should provide trackability and traceability of each step. Manufacturing records must be reviewed prior to release of product for distribution.

9

Examples of Record Keeping Errors

- Use of whiteout
- Use of nonindelible ink
- Use of pencil
- Incomplete documentation
- Documentation after the fact
- Use of inappropriate forms
- No review of records

10

Personnel Training and Competency

- Each person engaged in the manufacturing of a product shall have the education, training and experience to perform the assigned functions. Training shall include GMP Training. Supervisors must have necessary education, training and experience, and consultants must be documented.

11

Calibration

- Calibration is the comparison of measurement standard or instrument of known accuracy with another standard or instrument of unknown accuracy in order to confirm, delete, correlate, report or eliminate by adjustment any variation in the accuracy of the item being compared.

12

Calibration

- Documentation of calibration is required.
- Identification of the equipment and standard used.
- Performed at suitable intervals following written procedures.

13

Validation

- Validation establishes documented evidence which provides a high degree of assurance that a specific process will consistently produce a product that meets its pre-established quality and performance specifications.

14

Validation

- Retrospective (relies on historical data)
- Prospective (before implementation)
  - Installation qualification
  - operational qualification
  - product performance qualification
- Revalidation (must take place following any significant change in the equipment, process or procedure.)

15

Validation Protocol

- Specifies
  - Process description
  - Responsibilities
  - Tests to be completed
  - Number of trials
  - Data collected
  - Acceptable criteria

16

Error Management

- Systems must be in place to prevent errors, to detect errors that have occurred, and to take appropriate corrective actions after an error to avoid adverse consequences.

17

Error Management

- Error Management includes deviations, accidents and incidents. The FDA requires a thorough investigation and documentation of any deviation or variation from established SOPs, specifications or records.
- Licensed establishments must report to the FDA all errors and accidents that may effect the safety, purity, or potency of the biologic product.

18

Error Management

- There shall be written records describing handling of all written and oral complaints.
- Recalls must be completely documented.
- Blood collection or transfusion related fatalities must be reported to the FDA ASAP and in writing within 7 days.

19

Examples of Reportable Errors

- Release of :
- Units repeatedly reactive to viral marker testing.
- Units from donors for whom tests results were improperly interpreted.
- Units from donors who are or should have been deferred due to medical history or repeatedly reactive viral marker tests.

20

Examples of Reportable Errors

- Units erroneously released prior to completion of all tests.
- Incorrectly labeled blood components (ABO, expiration date, etc.)
- Microbiologically contaminated.
- Release of wrong unit for transfusion.

21

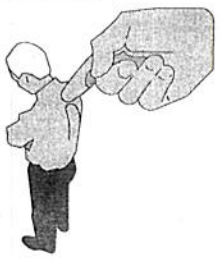
Error Management

- The Responsible Head must be informed of all complaints, errors, product investigations, recalls or regulatory actions.

22

Error Management

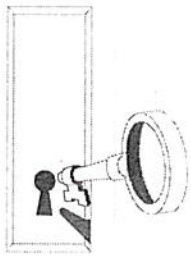
- Non-Punitive!



23

Error Management

- Key to success!



24

Standard Operating Procedures

- Written SOPs shall be maintained for all steps to be followed in the manufacturing of blood.
- Procedures shall be available for use in the areas where the procedures are performed.
- Procedures must be reviewed, approved, and followed.
- Deviations investigated and documented.

25

Responsibilities of the QA Unit

- Assess impact of SOP changes
- Review and approval of SOPs
- Indexing of SOPs
- Archiving obsolete SOPs
- Ensuring SOPs are accessible to staff
- Ensuring validation protocols are written
- Ensuring changes to SOPs are documented

26

Production and Process Controls

- SOPs
- Batch records
- In-process tests
- Quality control

27

Labeling

- Labeling/Lot Release is the system that ensures that each final container is correctly labeled. The labeling system consists of multiple processes, including record review, determination of component suitability for labeling, the labeling process, verification of labeling. A Lot is defined as a unit of blood or blood component.

28

Labeling

- Proper name of the product
- Name, address of manufacturer
- Expiration date, including day, month and year and if dating period is 72 hours or less, the hour of expiration.
- Donor classification, e.g.. "volunteer donor"
- Volume of the product accurate within 10%
- Recommended storage temperature

29

Labeling Controls

- Labeling must be separate from other operations.
- Labels for different products stored separately.
- Obsolete labels destroyed.
- Labels must be clear and legible.
- New labels compared to an approved copy.

30

Labeling Controls

- Labels for blood products must not be altered or removed.
- Instruction circular must be available for distribution.
- Labeled products examined during finishing operations.
- Products unsuitable for transfusion labeled "NOT FOR TRANSFUSION"

31

Facilities/Equipment/Supplies

- Adequate space and design to ensure cleaning, maintenance, and proper flow of operations.
- Equipment be maintained in a clean and orderly manner.
- All supplies and reagents stored in a safe, sanitary and orderly manner, used according to manufacturer's directions.

32

Quality Assurance Program

- A system of all activities necessary to assure and verify confidence in the quality of the process used to manufacture a finished product.
- Blood manufacturers must have a QC/QA unit that reports independently from production to the Responsible Head.

33

QA Auditing

- A mechanism for evaluating the effectiveness of the total QA program.
- Must be documented and must include assessment of effectiveness of corrective action and process improvement.

34

Responsibilities of the QA Unit

- Review and approve all SOPs
- Approval of validation protocols
- Approval of training program content
- Approval of test procedures used in QC
- Error management
- Record review
- Internal audits
- Job description approval

35

Compliance with GMPs...

- ...is everyone's responsibility!

36