

History of Regulation and Quality in the Blood Industry

Holly Rapp, MT(ASCP)SBB, CQA(ASQ)CQM/OE

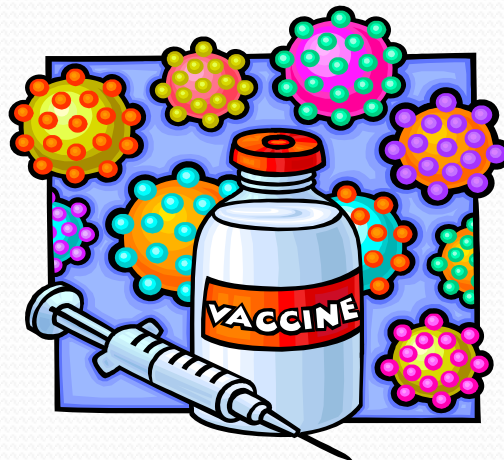
Director, Accreditation and Quality

AABB



The Beginning of Biologics Regulation

- Vaccines used to prevent smallpox and rabies at the end of the 19th century
- Heat killed vaccines used for cholera and plague
- Antitoxins used for diphtheria and tetanus
- Deaths from diphtheria dropped by 50-70%
- Dramatic decline in deaths from other infectious diseases



A Horse named Jim



- In 1901 a serious diphtheria epidemic swept St. Louis; victims were given antitoxin prepared in horses
- A diphtheria immunized horse named Jim had contracted tetanus and had been killed, however his serum was accidentally bottled and used to treat patients
- 13 children died of tetanus because of the tetanus contaminated antitoxin
- As a result, Congress passed the 1902 Biologics Control Act giving the government its first regulation of vaccine and antitoxin production

Biologics Act of 1902

- Intent to ensure the safety, purity and potency of biologics
 - “no person shall sell, barter or exchange..any virus, therapeutic serum, toxin, antitoxin or analogous product applicable to the prevention and cure of diseases of man...unless...prepared at an establishment holding a license.”
 - “any officer...may...enter and inspect any establishment.”





Early Regulations - 1903

- Issuances of licenses
 - Issued and re-issued based on annual inspections
- Inspections
 - Unannounced
 - By commissioned medical officers of the Public Health Service above the grade of assistant surgeon
 - Samples of products examined for purity and potency



Federal Food, Drug and Cosmetic Act

- 1906 Federal Food and Drug Act
- Passed after 107 people died from consuming “Elixir of Sulfanimide” that had been made using diethylene glycol instead of alcohol
 - Drugs must be safe
 - Requires new drug application
 - Manufacturing controls
 - Adulteration and misbranding provisions
- 1938 – FDA regulated food and drugs, NIH regulated biologics using different statutes

World at War

- American Red Cross organized a civilian blood donor service at the request of the Surgeons General of the Army and Navy
 - The first center opened February 4, 1941
 - Over 13 million units of blood were collected during the war





Blood Bank Growth

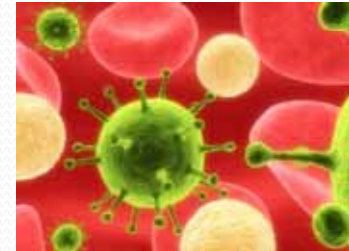
- 1937 Cook County in Chicago established the first “blood bank”
- May 3, 1946 first license issued to the Philadelphia Blood Bank
- 1947 AABB formed
- 1947 start of early blood regulation
 - Safety of the donor
 - Free from disease transmissible by blood
 - Donor history, physical and clinical tests

Court Cases 1960-1970



- Violations included extending the expiration date and shipping unlicensed products
 - Guilty of misbranding and false labeling
- Blood is a drug under the FDC Act
- Blood is a biologic analogous to therapeutic serum
- Court of Appeals ruled that Whole Blood citrated and Red Blood Cells are not analogous to a therapeutic serum – blood is a drug but not a biologic under the current definition
- 1970 Congress modified the definition of biologic to include “blood, blood components or derivatives”

Hepatitis B



- 1967, studies at NIH showed 50% of multiply transfused cardiac patients developed transfusion associated hepatitis primarily due to commercial blood (only 7% with blood from volunteer donors)
- More than 100,000 cases of post-transfusion hepatitis per year
- HBV test developed and licensed
- 1971 NIH issued regulation requiring testing of blood donations for HBV



National Blood Policy

- 1972 President Nixon called for a study and recommendation to develop a safe, fast and efficient system for blood collection and distribution
- 4 goals were recognized
 - Supply – adequate supply to meet needs
 - Quality – attainment of highest standards
 - Accessibility – access to the supply of blood and blood products by everyone in need
 - Efficiency – Efficient collection, processing, storage and utilization



National Blood Policy

- 10 Objectives
 - All voluntary blood donation system
 - Encourage resource sharing and area-wide cooperation
 - Assure ample donation
 - Public-private partnership administered by the American Blood Commission (47 organizations including AABB, ARC, AFL-CIO, AMA)



Bureau of Biologics Regulation

- Brought authority of FDC Act and PHS Act together
- Biologic regulation housed in an agency whose primary mission was consumer protection
 - All establishments manufacturing blood required to register by 1973 – both interstate and intrastate
 - Inspection of establishments
 - Labeling of blood “paid” vs “volunteer”
 - Authority extended from 166 licensed establishments before 1972 to 7000 facilities



cGMP for Blood and Blood Components – part 606

- cGMP for blood and components required through a Final Rule in 1975; preamble stated:
 - Rule intended to minimize hepatitis and assure production of blood and blood components of uniform high quality
 - Applies to all blood banks, transfusion facilities, plasmapheresis centers, etc. that process blood or components...whether for interstate or intrastate commerce use

HIV and the Blood Supply



- 1980-1985 HIV transmission to 30,000 transfusion recipients and 8,000 hemophiliacs
- 1983 PHS issued recommendations for deferral of at risk donors; MSM, IDU
- 1985 HIV test approved
- 1988 Regulation requires HIV testing
- 1995 Institute of Medicine reported “failure of leadership”
- 1997 HHS established a Blood Safety Committee(internal) and HHS advisory Committee for Blood Safety and Availability (external stakeholders)



Quality Systems

- 1995 FDA proposes guidance for quality systems in blood donor centers
 - General information on procedures and practices
 - May be useful to blood establishments in developing and administering a QA program
 - Blood establishment may follow guideline or choose alternative procedures
 - If alternative procedures are chosen, may want to discuss with agency to prevent expenditure of resources on activities unacceptable to FDA





FDA Guideline

- Intended to be used in conjunction with applicable federal standards in 21 CFR
 - Parts 600 through 680
 - Parts 210 and 211
 - Establishments performing laboratory testing must also comply with 42 CFR Part 493 (CLIA requirements)
 - Standards for laboratory personnel, quality control, proficiency testing, patient test management and QA

Quality Assurance

- Term “quality assurance” is not in the CFR
- Regulations clearly require a program of activities to control the manufacturing process to prevent the release of unsuitable products





Quality Control

- Several dimensions of QA include quality control (QC) procedures and current good manufacturing practices (cGMP)
- Adequate QC procedures are an element of conformity with cGMP
 - On-line or in-process monitoring of manufacturing procedures

Quality Control/ Assurance Unit

- Required by 21 CFR 211.22(a)
- Should report to management or designee
- Responsibilities include:
 - Standard Operating Procedures
 - Training and Education
 - Competency Evaluation
 - Proficiency Testing
 - Validation
 - Equipment
 - Error/Accident Reports, Complaints, Adverse Reactions
 - Records Management
 - Lot Release
 - Quality Assurance Audits





Quality System Essentials

- 1997 AABB introduces 10 QSEs
 - Requires implementation of a quality program
 - Intent of a quality program is to ensure quality principles are consistently throughout operations
 - Changes the approach of quality from one of detection to one of prevention



AABB now

- Quality system requirements are imbedded in standards
 - Organization
 - Resources
 - Equipment
 - Supplier and Customer Issues
 - Process Control
 - Documents and Records
 - Deviations, Nonconformances, and Adverse Events
 - Assessments: Internal and External
 - Process Improvement Through Corrective and Preventive Action
 - Facilities and Safety
- Accreditation program is based on ISO/IEC Guide 58:1993 and ANSI/ISO/ASQC Q10013-1995



AABB Accreditation

- 1998 AABB Inspections move to AABB assessments
 - Inspectors become assessors
 - Assessors are resources for facilities
 - Inspections become system audits
 - Deviations become non-conformances
 - Response to non-conformance includes:
 - Immediate corrective action
 - Root Cause Analysis
 - Long term plan

Quality





Questions

