

# The Quest for Quality Blood Banking Program in the New Millennium the American Way

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## Abstract

For an industry to succeed and satisfy its customers, "QUALITY" must be a primary goal. Quality has been central to blood banking from its inception, with the evolution of a Quality Program since the opening of the first blood bank in U.S. at the Cook County Hospital in 1937. Over the ensuing decades, continuous scientific progress in blood preservation, filters, viral and blood group testing, crossmatching, automation, and computerization including bar coding, etc. has contributed to the quality and safety of the blood products and transfusion service. However, with the advent of the AIDS era, an increasingly sensitized and informed public is continuously demanding that the highest level of quality be achieved and maintained in all processes involved in providing all blood products. The Food and Drug Administration (FDA) introduced the concept of a "zero risk blood supply" as the industry goal. Furthermore, the cost containment and resource-constrained environment have changed the complexity of the quality practice. Both regulatory agencies such as the FDA, the Health Care Financing Administration [HCFA, which was recently renamed as the Centers for Medicare and Medicaid Services (CMS) in July, 2001], and the State Department of Health, and accrediting agencies, such as the American Association of Blood Banks (AABB), the College of American Pathologists (CAP), and the Joint Commission on Accreditation of Healthcare Organizations (JCAHO), require blood banks and transfusion services to establish and follow a Quality Control and Quality Assurance Program for their licensing, certification and accreditation. Every laboratory has to comply with the Clinical Laboratory Improvement Amendments of 1988 (CLIA '88) quality requirements being implemented by the CMS. The FDA guidelines assist facilities in compliance with Current Good Manufacturing Practices (cGMP). The AABB's Quality System Essentials (QSE) are based on these specifications and provide additional guidance in implementing practices that assure quality and compliance with cGMP. AABB and CAP are granted "deemed status" as accrediting organizations under the CLIA '88 program by CMS, as well as JCAHO and some states. The International Standards Organization (ISO) has established international standards in most fields. The U.S. is represented in ISO by the American National Standards Institute (ANSI), and the National Committee for Clinical Laboratory Standards (NCCLS), as a global organization headquartered in the U.S., is a member of ANSI. The FDA and the AABB had begun incorporating many ISO principles into their own regulations and standards. The AABB's 10 QSEs are rooted in the 20 clauses of ISO 9000 series and compatible with their standards. In a Maslow-type model quality hierarchy by Tsiakals, so far the bottom three of the five progressive levels, Quality Control for method control, Quality Assurance for process control, and Quality System for system control have been implemented just to meet the regulatory and accrediting requirements. The next higher level, Quality Management for financial control, and the ultimate highest level, Total Quality Management for strategic control, should be our quest in this new millennium, and with the help of the AABB, ISO, FDA and all other organizations, we will achieve it. We should change our approach to quality issues from detection to prevention. We should improve the quality in transfusion practice itself by effective utilization of blood as a therapeutic resource with clear indication, maximum surgical blood order schedule, alternative transfusion such as autologous transfusion, hemodilution, and intra/post-operative blood salvage, surgical hemostasis, pharmacological hemostasis, and synthetic erythropoietin. Most importantly, implementation of the Quality Program should be something that we want to do rather than simply a burden that we have to do. A well-managed Quality Program is an effective and cost-efficient operation for the blood banks and transfusion services, and will enable us to better serve the patients for whom we exist.

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In 1916, in the midst of World War I, modern blood banking began with the creation of the first blood depot by Oswald Robertson, an American Army officer. In 1937, Bernard Fantus, director of therapeutics at the Cook County Hospital in Chicago, originated the term "blood bank" with the establishment of the first hospital blood bank in the U.S. Within a few years, hospital and community blood banks began to be established across the United States (U.S.), and currently more than 23 million units of blood components are transfused every year.

The U.S. Food and Drug Administration (FDA) [1]'s Center for Biologics Evaluation and Research (CBER) [2] is commemorating the Biologics Control Act of 1902 and 100 years of regulating biological products. Congress enacted this law to ensure the protection of Americans by providing consistently safe biological products. In 1906 the Federal Food and Drugs Act was passed. This Act was later replaced by the 1938 Food, Drug and Cosmetics Act. After 1938, the appropriate provisions of the 1902 and 1938 Acts were used to regulate biological products. FDA/CBER is responsible for regulatory oversight of the U.S. blood supply. FDA issues and enforces standards for blood collection and for the manufacturing of blood products, covering transfusable components of whole blood, pharmaceuticals derived from blood cells or plasma, and related medical devices. FDA also inspects blood establishments and monitors reports of errors, accidents and adverse clinical events. CBER works closely with other parts of the U.S. Department of Health and Human Service (HHS) [3] to establish blood standards, and to identify and respond to potential threats to blood safety or supply.

The 1950s, 60s and 70s were dynamic years for regulation of biologics. Evidence at the time indicated that blood obtained from commercial blood banks, comparing to volunteer ones, carried a greater risk of hepatitis transmission. More careful testing and increased regulation of blood ensued to further protect the blood supply. The blood banks moved toward an all-volunteer blood donor system in 1970. Quality has been central to blood banking from its inception, with the evolution of a Quality Program. Over the ensuing decades, continuous scientific progress in blood preservation, filtration, viral and blood group testing, crossmatching, automation, and computerization including bar coding, etc. has contributed to the quality and safety of the blood products and transfusion service. However, the emergence of the Acquired Immunodeficiency Syndrome (AIDS) in the 1980s threatened the safety of the U.S. blood supply. Transfusions became suspect. An increasingly sensitized and informed public has been continuously demanding that the highest level of quality be achieved and maintained in all processes involved in providing all blood products. Improved screening tests for donated blood were necessary to protect the American people. The Food and Drug Administration (FDA) introduced the concept of a zero risk blood supply as the industry goal. Inspections of blood banks were increased to ensure compliance with strict screen-

ing and processing procedures.

The U.S. Congress passed the Clinical Laboratory Improvement Amendments (CLIA) [4] in 1967 and again in 1988 establishing quality standards for all laboratory testing to ensure the accuracy, reliability and timeliness of patient test results regardless of where the test was performed. The Centers for Medicare and Medicaid Services (CMS) [5] [formerly known as Health Care Financing Administration (HCFA) until July 2001] administers the CLIA laboratory certification program in conjunction with the Centers for Disease Control and Prevention (CDC) [6] and FDA. The final CLIA regulations were published on February 28, 1992 and are based on the complexity of the test method; thus, the more complicated the test, such as in blood banking, the more stringent the requirements. CLIA specifies quality standards for proficiency testing (PT), patient test management, quality control, personnel qualifications and quality assurance for laboratories performing moderate and/or high complexity tests. The CMS survey process is outcome oriented and uses a quality assurance focus and an educational, rather than punitive, approach to assess compliance. Data indicate that CLIA has helped to improve the quality of testing in the U.S. Ongoing efforts by the CDC and CMS are aimed to develop a final CLIA rule, which will reflect all comments received, quality systems and new technologies.

Quality, in all its aspects, is the primary goal and priority for the blood banks and transfusion services. Many discrete activities, such as quality control of reagents, staff competence, laboratory proficiency testing programs, procedures for equipment maintenance, and documentation of error and accident investigations, are standard practice. Thus, for many organizations the foundations for a quality system have been in place for some time.

In 1995, the FDA issued Guideline (first draft in 1991) for Quality Assurance in Blood Establishment. The FDA guidelines assist facilities in complying with Current Good Manufacturing Practices (cGMP) described in Code of Federal Regulations (CFR) [7], 21 CFR and 42 CFR. These guidelines address all aspects of operations and facilities and provide a guide for the development, implementation, and management of a quality program.

In 1962, the College of American Pathologists (CAP) [8] established an Inspection and Accreditation Program, which eventually became the Laboratory Accreditation Program, with Laboratory Improvement Programs. The CAP initiated the Survey Program in 1967. The goal of the CAP Laboratory Accreditation Program is to improve the quality of clinical laboratory services through voluntary participation, professional peer review, education and compliance with established performance standards.

The American Association of Blood Banks (AABB) [9] was established in 1947. The AABB began its Inspection and Accreditation (I&A) Program in 1958 in conjunction with the publication of the first edition of Standards for Blood Banks and Transfusion Services. In

1998 the program redirected its focus to extend beyond the educational and peer review components to include conformance with requirements (AABB Standards and FDA) appropriate for each activity being assessed. The renamed Accreditation Program also changed its approach for performance of the on-site evaluation from a checklist inspection to a quality and operational systems assessment. The AABB Standards [10] defines a Quality System as "the organizational structure, responsibilities, policies, processes, procedures, and resources established by executive management to achieve quality". The AABB Accreditation Information Manual [11] defines Quality System Essentials (QSEs) as "the necessary items of quality system that enables an organization to work efficiently and identifies the parties responsible for the provisions for key quality functions." Business and industry have used the International Organization of Standardization (ISO) [12] standards to describe the elements of a quality system. The AABB QSEs were developed to be consistent with ISO standards and the FDA Guidelines for Quality Assurance in blood establishments. The QSEs listed in the AABB 21<sup>st</sup> edition Standards For Blood Banks and Transfusion Services [10] include the following:

1. Organization
2. Resources
3. Equipment
4. Supplier and Customer Issues
5. Process Control
6. Documents and Records
7. Deviations, Nonconformances, and Complications
8. Assessments: Internal and External
9. Process Improvement through Corrective and Preventive Action
10. Facilities and Safety

The AABB's 10 QSEs are rooted in the 20 clauses of the ISO 9000 series. The AABB's QSEs provide additional guidance in implementing practices that assure quality and compliance with cGMP. According to the AABB Accreditation Program status report [13], as of July 2001, the most frequent nonconformances among the 10 QSEs were seen in Process Control. For a quality Process Control, the AABB Standards requires that the blood bank or transfusion service shall have policies and validated processes and procedures that ensure the quality of the blood, components, tissue, and services. Furthermore, the blood bank or transfusion service shall ensure that these policies, processes, and procedures are carried out under controlled conditions.

Both regulatory agencies, such as the FDA, the CMS and the State Department of Health, and accrediting agencies, such as the AABB, the CAP, and the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) [14], require blood banks and transfusion services to establish and follow a Quality Control and Quality Assurance Program for their licensing, certification and accreditation. AABB and CAP are granted deemed status as accrediting organizations under the CLIA '88 program by CMS (because their requirements are deemed equivalent to or more stringent than

CMS's regulatory requirements) as well as JCAHO and some states. Therefore, AABB and CAP, as approved accrediting organizations, can inspect a blood bank or transfusion service in lieu of CMS and JCAHO.

The FDA and the AABB, key in the development of industry specific standards, had begun incorporating many ISO principles into their own regulations and standards. The ISO, established in 1947, is a worldwide federation of national standards bodies from 140 countries, one from each country. It has established international standards in most fields. This non-governmental organization published first ISO 9000 norms in 1987 with the aim of promoting harmonization of norms of different sectors. The ISO has established a common set of manufacturing, trade, and communications standards that are applicable worldwide and that provide the basis of a quality plan for institutions such as blood banks and transfusion services as well as NASA. The U.S. is represented in ISO by the American National Standards Institute (ANSI) [15], and the National Committee for Clinical Laboratory Standards (NCCLS) [16], as a global organization headquartered in the U.S., is a member of ANSI. The NCCLS, accredited by the ANSI in 1977, is a globally recognized, voluntary consensus standards-developing organization that enhances the value of medical testing within the healthcare community through the development and dissemination of standards, guidelines, and best practices. Although there are many ways to develop and maintain documents, the NCCLS and the AABB embrace the approach based on the ISO 9001 model. Document control based on the ISO 9001 model is the documentation hierarchy [17] - representing the levels of documents in an organization as follows:

Level I: Policies "What to do"

Level II: Processes "How it happens"

Level III: Procedures (SOPs) "How to do it"

Level IV: Forms / Records / Supporting Documents / Data / Quality Control / Records / Templates.

CBER initiated a Blood Action Plan in July 1997, to increase the effectiveness of its scientific and regulatory actions, and to ensure greater coordination with its HHS partners and ISO. The Action Plan addresses highly focused areas of concern such as emergency operations, response to emerging diseases, and updating of regulations. The HHS accepted this plan in March 1998. The plan is being jointly implemented by CBER, other FDA components (i.e., Office of Regulatory Affairs, Office of Chief Counsel, and Office of Policy), CDC, the National Institutes of Health (NIH) [18], and CMS.

On November 7, 2000, the FDA published a final rule of more stringent Biological Product Deviation Reporting (BPDR) by licensed manufactures, unlicensed registered blood establishments, and transfusion services to amend the requirements of reporting errors and accidents in manufacturing of products. The implementation date was May 7, 2001. The amended regulation (at 21 CFR 600.14) and the new regulation (at 21 CFR 606.171) require any event in which the safety, purity,

or potency of a distributed licensed biological product or blood or a blood component may be affected be reported, whether such event occurs during manufacturing, testing, processing, packing, labeling, storing, holding or distributing.

CBER stated that, with continued advancements in medical research and medical technology, it will face new challenges - not just scientific and regulatory, but legal and ethical, and will continue melding strong scientific research with innovative regulations that ensure timely access to safe and effective biological products. In addition to AIDS/Human Immunodeficiency Virus (HIV), the recent public awareness of hepatitis C virus (HCV) and the potential threat for variant Creutzfeldt-Jakob disease (vCJD) to be transmitted through transfusions have heightened public consciousness. On February 27, 2002, the FDA licensed the first pooled and individual sample Nucleic acid amplification (NAT) testing for the detection of HIV-1 and HCV RNA in whole blood donations. The NAT testing has been performed under Investigational New Drug Applications (IND) since 1999, and the risk of transmission through transfusion is currently estimated to be less than 1 in 1,900,000 screened units of blood for HIV, and less than 1 per 1,000,000 for HCV. Scientists are continually researching new technologies to further reduce the transmission of HIV, HCV and others. Examples of emerging technologies include methods to kill viruses in donated blood (viral inactivation) and blood component substitutes.

A few decades ago, disparate regulatory and accrediting agencies had some conflicting regulations and requirements. For example, the required expiration time after thawing of fresh frozen plasma differed depending on the agency. That was a few decades ago; now agencies collaborate to develop quality programs, and the programs are conforming to one another. Abundant templates are available, so it is easier to customize a quality program without reinventing the wheel, and thereby focus on implementing and improving quality care.

So far, the bottom three of the five progressive levels in a Maslow-type model quality hierarchy by Tsiakals [19], Quality Control (1940s-1960s) for method control with PT (1970s), Quality Assurance (1980s) for process control, and Quality System (1990s) for system control have been implemented by the majority of blood banks and transfusion services just to meet the regulatory and accrediting requirements. The next higher level, Quality Management for financial control, and the ultimate highest level, Total Quality Management for strategic control, should be our quest in this new millennium, and with the help of the AABB, ISO, FDA and all other organizations, we can achieve it. Several blood banks and transfusion services have already achieved ISO 9000 certification.

Although there is no way to guarantee error-free processing (zero-defect manufacturing), the goals of the quality program are to significantly decrease error, lend credibility to results, improve product safety and quality

and ultimately improve productivity and reduce costs. Redefining traditional quality assurance along with quality control is a critical response if blood banks are to achieve the standards of excellence needed to cope with the changes facing the blood industry today. Furthermore, cost containment and the resource-constrained environment have changed the complexity of the quality practice. Quality programs include measures to investigate, detect, report, assess, correct, track, trend, and prevent errors. Root cause analysis allows an organization to develop and implement action that will effectively prevent recurrence. The emphasis is on preventing rather than detecting errors. Prevention of errors, deviations, and variation is the key to increase productivity and decrease cost.

The National Blood Data Resource Center (NBDRC) [20] founded by the AABB collects, analyzes and distributes data on all aspects of blood banking and transfusion medicine, hematopoietic, cellular and gene therapies, and tissue transplantation and related procedures. America's Blood Centers (ABC) [21] on March 25 launched the first public online tracking system to monitor blood supply levels of the organization's 75 members around the U.S. and in Quebec, Canada, created at the request of HHS. We need to incorporate these data to a quality management for financial control. Quality and strategic planning should be integrated.

In addition to changing our approach to quality issues from detection to prevention, we should also improve the quality in transfusion practice itself by appropriate and effective therapeutic use of blood and blood products with clear indication, maximum surgical blood order schedule, alternative transfusion such as autologous transfusion, hemodilution, and intra/post-operative blood salvage, surgical hemostasis, pharmacological hemostasis, synthetic erythropoietin, oxygen therapeutics including blood substitutes, and gene therapy.

As time has passed, earlier resistance, skepticism and feelings of over-regulation have turned into more understanding and acceptance. Now let us realize that implementation of the Quality Program should be something that we want to do rather than simply a burden that we have to do. A peer review inspection/assessment is an invaluable learning experience for both the inspectors/assessors and the inspected/assessed. As we put more efforts into implementation of a sound quality program, we appreciate greater value and achievement of better patient care. A well-managed Quality Program is an effective and cost-efficient operation for the blood banks and transfusion services, and will enable us to better serve the patients for whom we exist.

The Quest for Blood Banking Quality Program should encompass quality control, quality assurance, quality system, and continuous quality improvement into a broad-based program, total quality management that ensures application of quality principles and strategic quality planning throughout the operational system of the blood banks and transfusion services in the New Millennium.

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Note: Please refer to the web sites for the most statements associated with regulatory and accrediting agencies.