Bacterial Contamination of Platelets: A Review of the Policy Making Process

by

Shauna N. Hay

July 5, 2006

A Master’s paper submitted to the faculty of the University of North Carolina at Chapel Hill in partial fulfillment of the requirements for the degree of Master of Public Health in the School of Public Health, Public Health Leadership Program.

Approved by:

Content Reader: Mark E. Brecher, MD

Second Reader: William Williamson, MPH
Shauna Hay

Abstract

On March 1, 2004, the American Association of Blood Banks (AABB) initiated a new standard that required all blood banks to have methods in place that limit and detect bacterial contamination in platelet components. However, the road to achieve this standard was neither quick nor easy. Over the last 15 years, there have been numerous governmental meetings and workshops devoted to the topic of platelet bacterial contamination, however, none of these ever produce a resolution or mandate to reduce the risk. In contrast to the mandates for most viral or newly emerging agents, the push for policy on the issue of bacterial contamination of platelet products has come from within the blood banking community.
Shauna Hay

Introduction:

Assuring the safety of the blood supply is a technologically advanced process requiring multiple federally mandated infectious agent tests, aseptic processing, and stringent quality control measures. However, while the blood supply is exceptionally safe, transfusions are not 100% risk-free. While the threat of viral agent infection has declined in several years, bacterial contamination in blood products, particularly platelet components, has emerged as the greatest infectious threat to patients. Unlike other blood safety issues, the blood banking community has highlighted the issue of platelet bacterial contamination and the impetus for policy has come from within the community as opposed to governmental agencies. On March 1, 2004, the American Association of Blood Banks (AABB) initiated a new standard that required all blood banks to have methods in place that limit and detect bacterial contamination in platelet components. Similarly, the College of American Pathologists (CAP) also recommended (and subsequently required) that laboratories have a method to identify platelet bacterial contamination. Interestingly, to date, there has not been a federally mandated standard regarding bacterial detection.

As much of the recent literature has focused on the methods to detect bacterial contamination, few reports regarding the policy development issues exist. This paper will provide a historical overview of the policy making process for bacterial contamination of platelet components.
Platelet bacterial contamination - a paradigm shift:

The majority of blood products are stored at cold temperatures (i.e., red blood cells 1-6°C, and plasma products <-20°C), however, platelet products must be stored at room temperature (20-24°C) in order to maintain viability. This unique storage temperature makes platelet components more vulnerable to bacterial overgrowth. In addition, the preservative solutions used to prevent coagulation and platelet activation in-vitro provides a source of nutrients for bacteria as well as the platelets themselves.

There are 2 types of platelet product available in the U.S. Random donor whole blood derived platelet concentrates are created from a whole-blood donation and are generally pooled to make a full dose of platelets for patients (5 or 6 concentrates). Platelets are also derived from cytapheresis procedures and are called single-donor or apheresis platelets. Platelets are biologic products intended for replacement therapy (patient deficient in number or function) when there is concern for bleeding or problems with coagulation.

It is currently estimated that 1 in 1000 to 1 in 3000 platelet units are bacterially contaminated, however, in the majority of cases, septic reactions are unrecognized or overlooked in patients. Most platelets are transfused to patients with severe underlying disease (e.g., malignancies) who are frequently receiving a multitude of medications including antibiotics, which may mitigate the effects of a bacterially contaminated unit. In addition, clinical recognition of a septic platelet event is not always detected. Patients exposed to virally contaminated units develop a chronic illness and can then rally for better standards and changes to reduce the risk for others. However, unlike the prolonged patient’s disease course from a virally infected unit, the transfusion of a bacterially
contaminated unit can result in more acute symptoms and possibly lead to death in a matter of hours or alternatively they recover. Thus, there are few victims suffering from the chronic sequelae of the contaminated unit who would demand a solution.

In contrast, to viral marker testing for agents like human immunodeficiency virus (HIV), hepatitis viruses, and West Nile Virus (WNV), bacterial testing cannot be completed prior to “release” of the component to the hospital transfusion service. Routinely, blood products are tested for viral agents soon after collection through donor samples. Units that test positive for a viral agent are disposed of and not shipped to hospitals for transfusion to patients. However, if one were to test for bacteria at collection, one would invariably miss a large number of contaminated units. This is largely due to the small inoculum of bacteria at the time of collection, sampling “error”, and the need to allow the bacteria time to enter growth phase in order to have a detectable quantity of bacteria. In addition, the platelet components themselves have to be sampled, as many cases of bacterial contamination are due to skin contamination, thus testing donors would not, in most cases, reveal contamination.

Currently, the blood banking community has blood components in inventory that are “release” tested negative for viral markers. A release test is an assay that once completed, clears a unit for transfusion or not, whereas a quality control (QC) test does not always affect the decision to transfuse. The criteria used for approval of a release test are more stringent because the device must assure that the products are not contaminated with greater than a certain level of bacteria.

Currently, there is no Food and Drug Administration (FDA) cleared “release” test for bacterial contamination. However, on day 2 of storage, platelet components need to
be sampled and tested by one of the FDA cleared “QC” methods. If a positive result is determined and that unit is still in inventory, it would be quarantined. If the unit has already been transfused, close monitoring of the patient would need to commence. As the storage life of platelets is generally 5 days, waiting for a culture sample to be documented as negative (as in a release test), the life span of the platelet would be over. In all, the testing of platelets for bacterial contamination involves a paradigm shift in the blood banking community as the product is on the shelves of the transfusion service while being tested and is transfused with a test that is often “negative to date”.

*The Precautionary Principle:*

Prioritizing risks has always been a challenge for the medical system, as it is challenging to reduce all risk while attempting to provide the best service possible. Unlike, viral contamination of blood products, there is no media attention for the issue of bacterial contamination or a celebrity spokesperson. Bacterial contamination has not reached high levels of interest even though it remains a far greater threat than Creutzfeld-Jakob disease (CJD), mad cow disease (variant CJD), or WNV. In many cases, the blood banking industry has attempted to provide the public with products that continue to preserve the public’s trust. However, this often means that there are standards established to lessen the fears created out of media attention.\(^7\)

In 1995, Dr. Donna Shalala, as Secretary of the Department of Health and Human Services (DHHS), commissioned the Institute of Medicine (IOM) to review the government’s role in the HIV crisis following a request from Representative Porter Goss and Senators Edward Kennedy and Robert Graham.\(^8\) Overall, the IOM report was
judgmental of public health leadership as they seemed to fail in superseding the conservative nature of the blood bank community. Dr Michael Stoto, Division of Health Promotion and Disease Prevention from the IOM, gave a summary statement before the Committee on Labor and Human Resources of the United States Senate on October 30, 1997. Dr Stoto stated that,\(^8\) "...a failure of leadership in the government and the blood industry led to several missed opportunities to help protect the public from the threat of AIDS. Preventing a similar outcome from a future threat, the committee concluded, will require mechanisms to ensure strong leadership and coordinated, systematic decisionmaking." And, "Policymakers quickly developed a list of clinical and public health options to reduce the risk of AIDS, but because of substantial scientific uncertainty about their harms and benefits, they adopted the least aggressive options consistent with the available scientific information."(Emphasis added) As a part of the IOM report, there were several recommendations including Recommendation 6 that states,\(^9\)

"Where uncertainties or countervailing public health concerns preclude completely eliminating potential risks, the FDA should encourage, and where necessary require, the blood industry to implement partial solutions that have little risk of causing harm."

However, the risk of bacteria remains real and has plagued the blood banking industry while the government has focused on other lesser threats. This is where the precautionary principle is necessary in the development of policies and standards. The European Environment Agency in 1992 stated that:\(^{10}\) "In order to protect the environment, a precautionary approach should be widely applied, meaning that where there are threats of serious or irreversible damage to the environment, lack of full
scientific certainty should not be used as a reason for postponing cost-effective measures to prevent environmental degradation.”

Further,

“The precautionary principle permits a lower level of proof of harm to be used in policy-making whenever the consequences of waiting for higher levels of proof may be very costly and/or irreversible.”

Death from a bacterial contaminated unit is irreversible. Therefore, one may argue that it is unethical to allow patients to die when there are devices available that could help to lessen, if not eliminate the problem. This is not what is to be called “excessive risk aversion” but using sound scientific judgment for preventive action. Moving towards zero-risk is not an easy task, as the closer we get, the more likely we have impacted availability. This is the balancing act that the blood bank industry must tackle. Currently, the FDA allowed shelf life of platelets is limited to 5 days due to fear of bacterial overgrowth over time. However, in the context of platelet bacterial detection, if 7-day expiration of platelets were to come to fruition, the impact of the safety regulations would balance out the impact on availability.

The policy making process:

Over the last 15 years, there have been multiple meetings and workshops devoted to the topic of platelet bacterial contamination, however, none of these resulted in a resolution to reduce the risk. On May 29, 1992, the FDA and CBER held the 36th Blood Products Advisory Committee meeting prompted by an increase in the number of reported septic events from contaminated blood products. At this meeting the Committee discussed the possibility of even shortening the expiration date, however due to the
Shauna Hay

anticipated impact on inventory, which might result in a shortage of platelets; this was felt not to be feasible.\textsuperscript{11}

The Division of Blood Diseases and Resources, the National Heart, Lung and Blood Institute (NHLBI), Center for Biologics Evaluation and Research (CBER), and the FDA held a workshop at the Warren G. Magnuson Clinical Center of the National Institutes of Health (NIH) titled Conference on the Microbial Contamination of Blood Components on September 27, 1995. The main goals of this conference were to review the info available about the causes, detection and prevention of microbial contamination of blood components and to provide guidance for research in these areas.\textsuperscript{12} However, again there was no recommendation or resolution passed to begin limiting the problem of bacterial contamination. At a later conference, Dr. Jay Epstein of the FDA was quoted as saying in regards to this prior workshop that,\textsuperscript{13} "It was of excellent scientific quality, but there was perhaps at that time an aura of disappointment because people were hopeful that we could get more out of it in terms of perhaps solutions to the longstanding problem of bacterial contamination."

Over the next four years, many research projects delved into the problem of bacterial contamination, particularly of platelets. In addition, there were many reports of incidence data in order to gain an accurate risk assessment. The Transfusion Transmitted Disease (TTD) Committee of the AABB issued a set of recommendations that were published June 19\textsuperscript{th}, 1995.\textsuperscript{13} The TTD Committee emphasized the development of screening assays and the development of inactivation protocols, highlighted the preferential use of single donor apheresis platelets instead of a pool of whole blood
Shauna Hay

derived platelets to reduce the risk of bacteria (a function of both the number of needle
sticks and donors), and stressed arm disinfection and aseptic techniques.13

On September 24, 1999, the US DHHS, the FDA, and CBER sponsored another
workshop entitled Bacterial Contamination of Platelets, with the objective to obtain
current information on bacterial contamination of platelets, and then to also encourage
research and development efforts to minimize the transfusion risk.13 Even though
bacterial contamination is a serious risk in the blood banking community, several
speakers were disappointed with the turnout for the workshop. Dr. Mo Blajchman of
McMaster University stated,13 “It seems to me that if this conference had to do with
variance CJD disease where there hasn’t been a single case of transfusion transmission,
this auditorium would be overflowing.” Furthermore to set the tone of the workshop, Dr.
Blajchman is also quoted as saying “We are contributing to the death of many people
unnecessarily, and we’re not doing very much about it.”

Many of the world experts gave presentations at this workshop in order to attempt
to obtain a resolution or mandate on the subject. Dr Mark Brecher of the University of
North Carolina at Chapel Hill stated,13 “When human health or the environment is
threatened, precautionary measures are indicated, even if additional scientific evidence is
needed to establish certain cause and effect relationships.” Brecher is further quoted as
saying, “… the perfect should not be the enemy of the good, and implementation of
partial solutions – and we may not have a perfect one – but partial solutions, and we have
a variety of partial solutions that are currently available and many others that will be
shortly available, that have little risk of causing harm should be encouraged.”
However, even with partial solutions available, there was disagreement as to the implementation of such solutions. Ed Tabor from the FDA stated, "...what we're trying to do is identify the best new technology that can be applied to prevent a serious health problem, and the concept of taking the good without seeking the perfect sounds very nice, but I think we have to keep our eye on the scientific rationale and try to achieve something that meets 1990 standards of accuracy and reproducibility, and that will, in fact, prevent these infections." In addition, Tabor was adamant that this issue be addressed through established scientific data and not "anecdotal experience" as "neither the public nor the medical community will accept that as a basis."

Many of the speakers and experts stressed the significance of having a mandate in order to secure the adoption of bacterial testing. Dr. Blajchman stated, "...what is required at this point is a mandate that requires something to be done for the bacterial sepsis problem..." Dr Ed Snyder from Yale University stressed the importance of governmental buy-in by saying, "FDA regulation versus hoping, which is the appropriate way? And I think it's regulation. Nothing says "I care" like a page of 483s (483s are the citation forms left from an FDA inspection)." Snyder further urged the FDA to consider the role of leadership by stating "...I believe the way this field will move forward is not by the good efforts of the voluntary organizations, but I think the FDA needs to assume a role of leadership and to gently push us into some type of bacterial testing, keeping all of these things going while we're developing inactivation technologies."

In concluding remarks for this workshop, Dr. Jaro Vostal of the FDA continued to stress the importance of surveillance in order to develop accurate risk assessments."
Nevertheless, Vostal did remark that, "...some strong opinions from the audience that the FDA should do something now and not wait for the ultimate test or ultimate solution to the problem. I think having this workshop here is a first step towards doing something because we certainly need to find out what the contaminating rate is and know where we’re starting from. I think it’s fortunate that we’re dealing with a familiar foe, and that’s bacteria. This is in contrast to the issue with CJD where we’re not familiar with the pathogen.” However, even with the explicit discussion of several detection schemes available, there was no mandate or resolution passed at this workshop.

As a follow up to this workshop, the summary was presented at the FDA committee, Blood Products Advisory Committee (BPAC) meeting on March 16, 2000. Dr Chiang Syin stated that the FDA has taken several actions including the establishment of the Bacterial, Rickettsial, and Parasitic Agents staff within the Division of Emerging and Transfusion Transmitted Diseases by the Office of Blood Research and Review to develop a program for bacterial contamination research.14 In addition, the PHS Bacterial Contamination Working Group (BWG) was created by Dr. Jay Epstein to address regulatory and scientific issues as they relate to bacterial contamination.

On February 15, 2002, the BacT/ALERT system and culture bottles (bioMerieux, Durham, NC) was approved by the FDA for the QC testing of leukocyte reduced apheresis platelet units.15 The 510K summary clearly states that this system should not be used in determining suitability for release, thus the system was only cleared as a QC test. Shortly thereafter, Medsep Corporation (a subsidiary of Pall Corp, Covina, CA) also received approval on August 21, 2002 for the Pall BDS system as a QC test for detection of bacteria in platelet components.16
Shauna Hay

The FDA and CBER sponsored a third workshop on August 7-8, 2002. This workshop was called the “Safety and Efficacy of Methods for Reducing Pathogens in Cellular Blood Products used in Transfusion.” Again this meeting was a place of much discussion regarding the issue, but no governmental mandate was thought to be forthcoming even though there was one approved system for QC (the BacT/ALERT) and one system nearing the approval process (Pall BDS).

Following this workshop, several prominent members of the blood banking community including Drs Mark E. Brecher, Jim AuBuchon of Dartmouth-Hitchcock Medical Center, Roslyn Yomtovian of University Hospitals of Cleveland, Paul Ness of Johns Hopkins Medical Institutions, and Mo Blajchman issued an “Open letter to the Blood Collection Community” on August 16, 2002 that called for a program to detect bacteria in platelet to be started immediately (written letter, August 2002, Appendix A). The authors noted that the focus of the prior workshop was on inactivation technologies and “…it is unclear when such inactivation technologies will be available. Bacterial detection technology, however, is currently available and screening via bacterial culture has been shown to be practical and effective.”

Even though this “call to action” came from within the blood banking community, not all members of this community were ready to rally for this issue. For example, Dr Breandnan Moore of the Mayo Clinic submitted a letter to the California Blood Bank Society e-Network Forum that states concern for the lack of a governmental mandate. “The fundamental problem seems to be that there is as yet no agreement on what can or should be instituted as a routine protective measure. It is usually the case that data are presented to the FDA which demonstrate that a particular course of action is wise and
Shauna Hay

that the FDA can logically mandate that all blood collectors institute such a course forthwith. In this particular situation there is no FDA mandate and no real consensus on what steps we should initiate.” Furthermore, Moore expressed his dissatisfaction with the open letter by claiming that, “The presence of this letter of exhortation, however well intended, carries no regulatory “weight” and provides no clear path of action for those being exhorted. Such a situation, though, I am sure, not intended as such, is tantamount to moral blackmail since it implies a less than caring and concerned attitude on the part of any blood bankers who do not “do something”.” Somewhat more lightly, Dr Ronald Domen from the Milton S. Hershey Medical Center of Penn State University College of Medicine expressed his concerns on the e-forum by stating, “I also share concerns that a plea for mandatory bacterial detection has been made without sufficient information and discussion.” The original letter writers offered several rebuttals that included references on bacterial sepsis risk, the need for a consensus, and a solution to the problem.

On January 23 and 24, 2003, the Advisory Committee on Blood Safety and Availability (Committee reports to the Secretary for the US DHHS) held its 18th meeting on “Prioritizing decisions in Transfusion Medicine: Transfusion Transmissible Diseases.” Many speakers discussed risks and how the blood bank industry responds to those risks. Dr. Jay Epstein, from the FDA, gave a summary of a recent BPAC meeting where they recently voted on if they agreed with the “FDA’s proposed statistical approach to providing quality control for platelet contamination. In this case there were zero votes in the affirmative...” In addition, Dr. Epstein further added, “The significant comments from the committee discussion focused on the concern that the medical benefit of a statistical quality assurance approach to monitoring platelet contamination has not been
Shauna Hay

validated in any suitable large-scale study, and that therefore we (the FDA) were advised that we should be shy of promulgating such a recommendation...”

Even without the buy-in from the FDA nor the BPAC, the DHHS Advisory Committee on Blood Safety and Availability did recommend that the “Secretary take steps to encourage and facilitate implementation of available measure that could: a. reduce the risk of bacterial contamination, and b. prevent errors that can result in hemolytic transfusion reactions.”

Over the next 6 months, the AABB Blood Bank/Transfusion Service Standards Program Unit developed a standard that mandated testing of bacteria in all platelet components. The standard, approved March 3, 2003, was to be implemented by March 1, 2004 and reads as follows:

5.1.5.1 The blood bank or transfusion service shall have methods to limit and detect bacterial contamination in all platelet components. Standard 5.6.2 applies.

5.1.5.1.1 Standard 5.1.5.1 shall be implemented by March 1, 2004.

Standard 5.6.2, which is referenced in 5.1.5.1, reads as follows:

5.6.2 The venipuncture site shall be prepared so as to minimize the risk of bacterial contamination. Green soap shall not be used.

Interestingly, Standard 5.1.5.1 was allotted a 1-year time frame for implementation, whereas many Standards are generally published with a 2 to 4 month implementation period (written letter from Dr. Kathleen Sazama to Dr. Christina Beato, February 2004, Appendix B).
Similarly, CAP and their laboratory accreditation program added a Phase I item (recommendation) to the Laboratory Accreditation Checklist in December 2002. This item asks the question, “Does the laboratory have a system to detect the presence of bacteria in platelet components?” Even though this Phase I item was seen as a recommendation, there was controversy that the agency was acting too quickly on the issue, however CAP remained determined to retain the item.

From March 2003 to March 2004, blood centers and suppliers as well as hospital transfusion services developed policies and protocols to implement Standard 5.1.5.1. Many facilities also purchased equipment from FDA approved suppliers to perform the testing on all platelet components.

Even with Standard 5.1.5.1 in place and facilities quickly ramping up to launch platelet bacterial testing, the controversy surrounding this issue had not faded. On February 24, 2004, Dr. Christina Beato, Acting Assistant Secretary for Health from the DHHS, wrote a letter to Dr Kathleen Sazama, President of the AABB, commending the AABB for its progressive action, but requesting that “the AABB carefully consider delay in the implementation until a clear plan is developed.” Dr Beato expressed concern that “the implementation of this standard by the March 1, 2004 may cause potentially serious and possibly unintended effects on the availability of platelet products for patient care.” Dr Beato further recommended that a “round-table discussion” occur with the major stakeholders (written letter from Dr Christina Beato to Dr Kathleen Sazama, February 2004, Appendix C).

Dr Sazama replied to the DHHS concerns on February 27, 2004 in a letter (Appendix B) that stated, “The AABB has provided extensive guidance to its members...
Shauna Hay

on the implementation of this standard, including processes for emergency release of platelets in the event of impending shortages. By this time, most, if not all, of our member facilities have plans to comply with the March 1, 2004 implementation date. For these reasons, after consideration of the issue, the AABB believes that further delaying the implementation of this standard will compromise both patient safety and the public health.” Dr Sazama later stated at an Advisory Committee meeting that, “Given the fact that this standard has been proposed almost a year-and-a-half prior to this date, and that the AABB had provided considerable opportunity for public comment, it came as a surprise to us that HHS would make this request at such an extremely late date.” Even with an attempt to stall the standard at the eleventh hour by governmental officials, the AABB maintained its position and continued with the implementation.

As a direct result of the communication between Drs Beato and Sazama, the 23rd meeting of the Advisory Committee on Blood Safety and Availability on April 7, 2004 had as its major topic the impact of bacterial testing on platelet components. Dr Sazama stated that, “AABB strongly believes that the new bacterial contamination standard will help improve patient care and save lives. We believe that we should stop holding our patients hostage by allowing the perfect to be the enemy of the good. Unfortunately, in the absence of regulation or standard setting, and in the face of limited reimbursement, there has been, and is, little incentive to invest in blood safety advances such as this. AABB believed it was our responsibility to act to serve our patients, even if the FDA had not acted yet in this regard.”

In order to handle the issues raised by bacterial contamination testing and to assist member organizations, the AABB established the Interorganizational Task Force on
Shauna Hay

Bacterial Contamination of Platelets. This Task Force was charged with several objectives including serving as a focal point for bacterial detection issues, providing a forum for discussion between major stakeholders, interacting with test manufacturers, surveying hospitals/blood centers to assess the impact of regulation, and providing guidelines. This group surveyed hospitals and blood center in the Fall of 2004 and determined that the majority of facilities that responded (350 of 900, 38%) that there was little impact on platelet availability due to Standard 5.1.5.1.

Again, on the 24th meeting of the Advisory Committee on Blood Safety and Availability held on August 27, 2004, bacterial detection in platelet components was on the agenda. The FDA voiced several concerns with the newly implemented Standard through spokesperson, Dr. Jaro Vostel. The lack of validated methods for whole blood derived platelets was of particular significance. Dr Vostel stated that, "...we'd like to see standardized methodology for automatic culture systems..." and "We would also like to see application of automatic culture systems to whole blood derived platelets, and this would eliminate the use of non-validated methods for these products." In addition, Dr Vostel commented that, "...we'd like to see a validation of the automatic culture system for a release test claim." (A release test field trial would need to consist of a study of greater than 50,000 units and would cost millions of dollars.) It is interesting that the FDA would have so many recommendations for improving on current standards, when they themselves have not mandated any regulation.

Current status:

Currently, the AABB and CAP have mandated standards for their member agencies that specifically address bacterial contamination of platelets. Furthermore, there
Shauna Hay

is now a licensed system for culturing whole blood derived platelets, thus limiting the 2 tiered safety approaches. Unfortunately, this approach is expensive and wastes platelet product. Until the FDA approves pre-pooling of whole blood derived platelets, there will continue to be a discernable difference in safety between apheresis and whole blood derived platelets.

With the advent of bacterial detection, 7-day platelets have become a reality in certain markets. There are of course specific protocols and waivers that a blood center/transfusion service must follow, however 7-day platelets are on the market and the extended shelf life with culture aids in increasing the safety and availability of platelet products for patients.

Conclusions:

Policies regarding to bacterial contamination of platelet components are currently working to reduce the number of septic transfusion events. However, these policies are still mandated through voluntary accreditation agencies, not by governmental oversight. Interestingly, the FDA has held a number of meeting and workshops on the issue of bacterial contamination, thus deeming it worthy of policy, but never recommending one.

Regulatory control in the US has generally focused on new diseases such as WNV which led to nationally mandated efforts to screen the blood supply with WNV nucleic acid testing. To place this risk into some perspective, in 2002, twenty-three transfusion-transmitted cases of WNV were identified in the US.\(^{23}\) Of these 23 recipients, 7 died, but only 5 of these deaths were associated with WNV meningoencephalitis. During the same period, 17 deaths from bacterial contamination of blood products were reported to the FDA.\(^{24}\) Why has the FDA readily jumped on the theoretical risks of agents such as WNV
or CJD, but disregarded known risks such as bacteria? This question has yet to be answered, but one can speculate that there are multiple answers. Perhaps, the governmental regulatory bodies are dissatisfied that the “ground-swell” for this issue came from within voluntary agencies and was pushed through regulation by non-governmental bodies. Perhaps, the FDA is still waiting on the “perfect” test that will follow “release-testing” and not be just a quality control test. Unfortunately, the HIV crisis and the recommendations from the IOM that the FDA,⁹ “…should encourage, and where necessary require, the blood industry to implement partial solutions that have little risk of causing harm” has been a lesson lost.

While governmental agencies have not followed through with securing the safety of the public blood supply from bacteria, the AABB and CAP should be commended for their work to reduce the risk from bacteria and save patients’ lives.
Shauna Hay

References:


11. Food and Drug Administration, Blood Products Advisory Committee Transcripts, Center for Biologist Evaluation and Research, 36th meeting, May 29, 1992, Rockville MD. [Transcripts available from the FDA, Freedom of Information staff upon request.]


Shauna Hay


August 16, 2002

Open letter to the Blood Collection Community

A recent FDA workshop in Bethesda, Maryland held on August 7 and 8, 2002 addressed the safety and efficacy of methods for reducing pathogens in cellular blood products used in transfusion. At this meeting, the consensus of opinion was that bacterial contamination of platelets represents the largest transfusion transmitted disease risk.

The focus of this meeting was a discussion of inactivation strategies that targeted nucleotides as a means of achieving pathogen reduction. However, it is unclear when such inactivation technologies will be available. Bacterial detection technology, however, is currently available and screening via bacterial culture has been shown to be practical and effective.

In the interim, given the current risk of bacterial contamination of platelets of approximately 1/1000-1/2000 per unit, we call for the blood collection community to immediately initiate a program for detecting the presence of bacteria in units of platelets.

Respectfully,

Mark E. Brecher M.D.  
Director, Transplantation and Transfusion Services  
Professor, Department of Pathology and Laboratory Medicine  
University of North Carolina

Roslyn Yomtovian, M.D.  
Director, Blood Bank-Transfusion Medicine Service  
Associate Professor, Department of Pathology  
University Hospitals of Cleveland

James AuBuchon, M.D.  
E. Elizabeth French Professor and Chair of Pathology and Professor of Medicine  
Dartmouth-Hitchcock Medical Center

Paul M. Ness, M.D.  
Professor, Pathology, Medicine & Oncology  
Director, Transfusion Medicine  
Johns Hopkins Medical Institutions

Morris A. Blajchman, M.D., F.R.C.P.(C.)  
Director, Transfusion Medicine  
Professor, Departments of Pathology and Medicine  
McMaster University
February 27, 2004

Via E-mail and Facsimile

Dr. Cristina V. Beato, M.D.
Acting Assistant Secretary for Health
Department of Health and Human Services
Hubert H. Humphrey Building, Room 716G
200 Independence Avenue, SW
Washington, DC 20201

Dear Dr. Beato:

Thank you for your letter concerning the implementation of AABB standard 5.1.5.1 requiring methods to limit and detect bacterial contamination in all platelet components. The AABB standards are voluntary and are developed through an evidence-based decision-making process. For the last ten years, physicians in the field of transfusion medicine have identified bacterial contamination as one of the most serious risks of transfusion. In the United States, bacterial contamination is considered the second most common cause of death overall from transfusion (after clerical errors) with mortality rates ranging from 1:20,000 to 1:85,000 donor exposures. Indeed, transfusion-associated bacterial sepsis represents the most common cause of death from infectious disease reported to the FDA, with 46 of 277 (16.6%) of all reported fatalities between 1990 to 1998 attributed to sepsis. With approximately 4 million platelet components transfused annually, current estimates are that 50 to 100 platelet recipients die each year as a result of receiving bacterially contaminated platelet units.

Our voluntary standard, initially published for comment on November 1, 2002, addresses this critical safety issue. The final and current wording of the standard was adopted and published on March 1, 2003. Although AABB standards are generally published with an implementation date of two to four months, the AABB allowed a one-year period for implementation of the 22nd edition, in recognition of the challenges inherent in complying with this standard, which, for some, have included a total transition to pheresis platelets.

To address any concerns over potential whole blood derived platelet shortages raised by the standard, the AABB, at the December 12, 2002 Blood Products Advisory Committee, (and again at the March 14, 2003 Blood Products Advisory Committee) specifically requested that the FDA facilitate bacterial detection of whole blood platelets by “reexamining its current thinking under which platelets pooled in either the blood collection facility or the transfusion facility, regardless of the use of sterile methods, cannot be used beyond four hours after pooling.” Extension of the
time frame would allow for pooling at the time of production of whole blood derived platelets which would in turn, provide a mechanism to do culturing. This is a technique used successfully in Europe. At that same meeting, the AABB urged the FDA to “act quickly to consider what data will be required to extend platelet storage to seven days, provided that an acceptable bacterial detection system is used.”

The AABB has provided extensive guidance to its members on the implementation of this standard, including processes for emergency release of platelets in the event of impending shortages. By this time, most, if not all, of our member facilities have plans to comply with the March 1, 2004 implementation date. For these reasons, after consideration of the issue, the AABB believes that further delaying the implementation of this standard will compromise both patient safety and the public health.

The AABB remains committed to seeking the resolution of any regulatory and/or surveillance issues raised by this standard. Our leadership would be pleased to participate in a round table discussion with the Department of Health and Human Services on these issues. Thank you.

Sincerely,

Kathleen Sazama, MD, JD
President

cc: Jerry Holmberg,
Executive Secretary of the Advisory Committee on Blood Safety and Availability
Department of Health and Human Services
Dear Dr. Sazama:

I commend the American Association of Blood Banks for its progressive action to improve the safety of the blood supply by reducing the risk of bacterial contamination of platelet components through the addition of a new standard for accreditation in the 22nd edition of Standard for Blood Banks and Transfusion Services. Although the intent of the standard is laudable, several issues have been brought to my attention that suggest implementation of this standard by the March 1, 2004 may cause potentially serious and possibly unintended effects on the availability of platelet products for patient care. Given the potential public health interests involved in the addition of this new standard, I request the AABB carefully consider delay in the implementation until a clear plan is developed.

In order to address outstanding implementation issues including approved quality control methods applicable to pre-release testing, potential extension of platelet dating, pooling of random donor platelets, and surveillance and reporting protocols for positive test results in patients and donors, I recommend a round table discussion with the Department of Health and Human Services (HHS) agencies, blood centers, transfusion services and manufacturers. Dr. Jerry Holmberg, my Senior Blood Advisor, is available to coordinate HHS' participation at such a round table discussion. Dr. Holmberg can be reached at 301-443-3234.

I strongly support every effort to improve the safety and availability of blood products, including this most recent initiative on reducing bacterial contamination in platelets, and I thank you for your leadership at the AABB.

Sincerely yours,

Cristina V. Beato, M.D.
Acting Assistant Secretary for Health