

BLOOD PRODUCTS ADVISORY COMMITTEE
100th Meeting, April 28-29, 2011
Hilton Washington DC/North,
620 Perry Pkwy., Gaithersburg, MD

Topic III: Blood Donor Written Statement of Understanding

Issue

FDA seeks advice from the Committee on the appropriate elements of a written statement of understanding for Whole Blood donors, and the best methods to present this information to the donor.

Background

In the United States, about 9 million blood donors provide approximately 15 million donations of Whole Blood each year (1). The blood donor screening process involves measures to ensure the safety of the donor and recipient. The blood donation process in the United States is typically safe and uneventful. However, the process of obtaining consent to phlebotomy and donation of Whole Blood varies from state to state, with individual establishment variations, as well.

Although the FDA has regulations requiring “informed consent” for Source Plasma, plateletpheresis and plasmapheresis donors, the FDA has not required that blood establishments inform Whole Blood donors about the blood donation procedure. In a 2007 proposed rule on Human Blood and Blood Components for Transfusion and Further Manufacturing Use, FDA included a proposed requirement for blood establishments to provide all donors with a Written Statement of Understanding. This proposal would create new requirements for providing information to Whole Blood donors in part to ensure blood safety while protecting the health of the donor. The proposed elements for the statement of understanding are:

- 1) The donor has received and reviewed the educational material regarding relevant transfusion-transmitted infections, including the fact that relevant transfusion-transmitted infections present potential risks to the safety, purity, or potency of the blood supply.
- 2) The donor agrees not to donate if the donation could result in a potential risk to the safety, purity, or potency of the blood supply as described in the educational material.
- 3) A sample of the donor’s blood will be tested for specified relevant transfusion-transmitted infections and for syphilis.
- 4) If any of the tests is reactive, the sample of blood will be tested further.
- 5) If the donation is determined to be not suitable or if the donor is deferred from donation, the donor’s record must identify the donor as ineligible to donate and

the donor must be notified of the basis for the deferral and the period of deferral.

- 6) The hazards and risks of the donation procedure.
- 7) The donor has the opportunity to ask questions and withdraw consent at any time.

FDA would require that the collecting establishments provide a written statement to the donor, to read and sign before performing phlebotomy. This statement would be written in a clear and understandable terminology and not include language that would waive any of the donor's legal rights.

Elements of the Written Statement of Understanding

Educational materials

The proposed rule for the written statement of understanding includes a requirement for providing the donor with educational materials to be read prior to the donation. FDA proposed a requirement for collecting establishments to provide to all donors, before donation, information about behaviors that increase risks of relevant transfusion-transmitted infections, signs and symptoms of such infections, and consequent risks to the safety of the blood and blood components. Collecting establishments can provide this information in oral, written, or multimedia form in a manner designed for the donor to understand, in appropriate language and literacy level, and taking into account any disabilities. When screening for behavioral risk factors associated with a relevant transfusion-transmitted infection (for example, HIV, HBV, or HCV), the material would instruct donors to self-defer if they determine that they have participated in an increased-risk behavior for, or show signs or symptoms of that relevant transfusion-transmitted infection. FDA may issue additional guidance on educational materials in the future. FDA solicited comments on this provision, particularly on how comprehensive the educational material should be, and its presentation format or style.

The intent of prescreening educational material is to educate donors about relevant transfusion transmitted infections so that they can self defer or seek clarification from the blood collection staff if they are unsure of a particular risk. AABB introduced the concept of educational materials in 1984. FDA first recommended the use of educational materials to inform donors about HIV in 1990. Subsequently, AABB adopted FDA recommendations into their education materials (2). FDA describes its current recommendations for educational materials in the memorandum entitled "Revised Recommendation for the Prevention of Human Immunodeficiency Virus (HIV) Transmission by Blood and Blood Products," issued April 23, 1992 (3). In this memo, FDA recommends, but does not require, that establishments provide educational material to inform potential donors of the risks of HIV transmission and the need for self-deferral of donors at increased risk. FDA officially recognizes version 1.3 of the educational materials created by the AABB donor task force (appendix 1). It contains information on the donation process, a definition of sexual contact, and information on HIV, HIV/AIDS risk behaviors and the handling of positive tests. The National Center for Health Statistics

(NCHS) included the AABB educational materials in a study to evaluate if the information provided to donors was clear and simple. The NCHS investigators concluded that the AABB donor task force had achieved its goal of creating simple and clear material (2). Many blood establishments use the AABB educational materials. They are permitted to add additional material at the end but may not delete or rearrange the materials in the FDA recognized version. The current practice is to present educational materials to donors in either written or electronic format.

Risks and hazards of blood donation

Though the blood donation process is generally safe and well tolerated, mild to severe adverse reactions may occur. Studies have demonstrated that approximately 3% to 10% of blood donors will experience an adverse reaction or injury after the donation (4). However, reaction rates vary depending on the study design and the population surveyed.

If a post-donation interview is conducted and mild reactions are solicited, the rate of adverse reactions appears to be quite high. In a study of 1000 randomly selected blood donors, investigators asked about seven adverse reactions using a post-donation interview. Donors with one or more adverse reactions ranged from 30% – 43%. The common complications were bruises (23%), sore arms (10%), fatigue (8%), and donor reactions (7%). Donor weight and age were significant contributors to donor reaction rates (5, 6).

Record reviews yield a lower incidence of adverse reactions. Wiltbank et al (7) reviewed the records of 422,231 allogeneic whole blood donations over a 9-month period and assessed for pre-faint and faint reactions. They found a total of 6,049 adverse events; a rate of 1.43 %. Of this total, the percent of mild, moderate or severe reactions was 63%, 29% and 8% respectively. Predictors of these reactions were age, sex, race, blood volume, blood pressure, pulse, and body mass index. The strongest predictors of a reaction were donor blood volume of less than 3500 mL, age, and first time donor status.

Kamel et al (8) studied and reported on delayed adverse reactions in blood donors. The prevalence of moderate to severe reactions was 41 in 10,000 donations; 24% of these reactions were delayed, and 12% occurred offsite. Delayed reactions were associated with female gender. Off-site reactions, particularly in female donors, were more likely to be associated with a fall, with head trauma, with other injury, and with the use of outside medical care. Low estimated blood volume, youth, and first-time donor status were major risk factors for immediate and delayed reactions. Women were more likely than men to report delayed reactions.

Eder et al (9) analyzed adverse reactions recorded in the American Red Cross donor hemovigilance program in 2006. Excluding large hematomas, adverse reactions occurred at a rate of 7.4, 5.2, and 3.3 per 10,000 collections for whole blood, apheresis platelet, and 2-unit automated red cells. The need for donors to seek outside medical care was recorded at a similar rate for both whole blood and automated procedures (3.2 and 2.9 per 10,000 donations respectively). Major syncopal-type reactions (long loss of consciousness, loss of consciousness or presyncope with injury, and prolonged recovery)

accounted for 46% of all reactions associated with seeking further medical care. The authors noted that regional center variation in addition to donor age, gender, and donation status was an independent risk factor for adverse events, but identified imprecise coding of adverse events and overlapping definitions of donor complications as limitations of hemovigilance efforts.

The proportion of young (<18 years old) blood donors continues to increase. Studies show that these donors are more likely to experience donation related vasovagal reactions, and that age and donation status are strong predictors of the risk of vasovagal reactions after whole blood donation (10).

Finally, multiple studies conclude that frequent blood donations contribute to iron deficiency among blood donors. The REDS II donor iron study examined factors that predicted iron deficiency among blood donors. Factors examined included frequency of donation, menstrual status, age, weight, iron supplementation, diet, race, and hemochromatosis genotype. Results from this study show that donation intensity, sex and/or menstrual status, weight, and age are important independent predictors of absent iron stores and iron deficient erythropoiesis (11).

Current practice of “donor consent” in blood establishments

AABB introduced donor consent in the 8th edition (1976) of the AABB Standards for Blood Banks and Transfusion Services (SBBTS). The current 26th SBBTS edition requires donor consent (Standard 5.2.3). The donor consent standards include the following elements: the donation procedure, risks of the procedure, tests performed to reduce the transmission of infectious diseases to the allogeneic recipient and an opportunity to ask questions and to give or refuse consent for donation (12).

Published literature on elements of blood donor consent

Currently, practices of informing the donor about the donation process and the possible risks and hazards of the procedure vary. While the FDA accepted AABB education material educates the donor on infectious risks and high-risk behavior, and briefly describes the donation process, it does not mention the risks and hazards of donation.

Since publication of the proposed donor eligibility rule, there have been several publications in the literature on consent in blood donation. Shaz et al (13) reviewed blood donor consent or parental consent forms and educational material provided to US blood donors. The authors sought to determine if blood establishments provided whole blood donors with the generally accepted elements of informed consent, as described in the FDA Guidance for institutional review boards and clinical investigators conducting clinical investigations. (Note that FDA’s informed consent regulations and guidance are applicable only to investigational studies.) The authors found that none of the whole blood allogeneic donation consents surveyed contained all the elements of informed consent described for investigational research. They concluded that there is a need for a uniform approach to consent for whole blood donation.

Wherli and Sazama (14) recently wrote a commentary advocating for improved donor safety by adopting a uniform donor education process and documents. The authors note that the current donor consent practice varies among blood collection facilities and that donor comprehension of the consent and educational material may be limited. They encouraged the blood community to engage in creating standardized, expanded education materials and to standardize the donor consent process and documents.

Published literature on blood donor comprehension

It is important to ensure that the blood donor understands the information presented to them at the time of donation. Alashuisi et al (15) performed a study to assess the level of comprehension of their whole blood donors with various aspects of the donation process. They distributed a questionnaire to whole blood donors at various donation sites. The questions consisted of demographic information, donor opinions of information content, length, and comprehension; and a short quiz pertaining to donor risks and eligibility. They found that greater than 90% of donors comprehended that dizziness or fainting are risks of donation, that certain medications affected donor eligibility, that having lived in certain countries can affect eligibility, and that acquired immunodeficiency syndrome could potentially be spread even if they felt well and had a negative human immunodeficiency virus test. Less than 50% of donors, however, seemed to not fully comprehend that they could potentially be placed on a blood donor deferral registry, could obtain a positive result for infectious disease blood tests, or be referred to a physician for additional evaluation. The authors suggested that information presented to the donor in multiple formats could improve comprehension.

Current FDA consent requirements or recommendations for blood donors (other than Whole Blood)

Source Plasma donors

For Source Plasma donors, a requirement for informed consent is codified in 21CFR 640.61. This requires that the written consent of a prospective donor shall be obtained after a qualified licensed physician has explained the hazards of the procedure. In addition, the FDA issued “Guidance on Informed Consent Recommendations for Source Plasma Donors Participating in Plasmapheresis and Immunization Programs” (16) describes relevant regulatory requirements and recommendations concerning informed consent in plasmapheresis donors.

Plateletpheresis and plasmapheresis donations

For plateletpheresis and plasmapheresis donors, the requirement for informed consent is codified in 21 CFR 640.21(c) and 21CFR 640.31(b), respectively. In addition, the FDA “Guidance for Industry and FDA Review Staff: Collection of Platelets by Automated Methods” recommends that the plateletpheresis procedure should be described to the donor; the donor should be given information about potential side effects of the

procedure, and information indicating that there are limitations to the number and types of components that can be donated per year (17).

Apheresis red blood cell donations

For red blood cell apheresis donors, the FDA issued “Guidance for Industry: Recommendations for Collecting Red Blood Cells by Automated Apheresis Methods - Technical Correction February 2001” recommends the use of an informed consent form describing the procedure, donation frequency, and any reasonable risks or discomforts that might occur. (18).

Previous public discussions concerning donor consent

In December 2008, the HHS Advisory Committee on Blood Safety and Availability recommended that consent in blood and plasma donors needed improvement. They noted that donor consents, while performed nationally, lacked consistency in terms of a defined set of elements. They recommended that at a minimum, known risks of donation including the effects of repeat donation in the general population, the gender specific effects of iron deficiency on donors, the effects of collecting blood from anemic men using current donation thresholds and the disproportionate prevalence of adverse events in the youngest donors should be included in consent forms. They also recommended consideration of the method and frequency of effective consent for repeat donations (19).

Discussion

FDA is seeking advice from the committee on the elements of a written statement of understanding for Whole Blood donors, the need to establish minimum standards for explaining the risks and hazards of blood donation, and the best techniques available to present the statement of understanding to the blood donor. This discussion will not include the issues of informed consent for research in the blood donation setting.

Intent of a written statement of understanding

A written statement of understanding that includes required elements helps ensure that blood establishments inform a donor about the entire donation process. France et al (20) in a study of 89,597 allogeneic blood donors revealed that vasovagal reactions had an overall negative impact on donor return with moderate and severe reactions reducing donor return by as much as 50%. In another study, the same authors note that providing a donor recruitment brochure containing potential adverse reaction information resulted in decreased donor anxiety, more positive attitude, higher self worth and greater intention regarding blood donation (21). Sazama and Wehrli (14) in their commentary note that it is not clear if the donors in this study understood the risk of these adverse events and that it is unknown if this would impact donor return rates for those who experienced adverse events. On August 28, 2008, AABB published Association Bulletin #08-04 which addressed strategies to reduce adverse reactions and injuries in younger donors. The bulletin indicates that pre-donation information, consent for donation and understanding

how to manage postdonation issues are critical to providing a satisfying donation experience and ensuring that the donor returns for future donation. Recognizing that younger donors have a higher incidence of reactions, the bulletin recommends the presentation of educational materials in other adolescent-friendly formats, such as videos (22).

The requirement of a written statement of understanding also ensures minimum standards for the content of such documents across blood establishments. As reported by Shaz et al (13), the content of blood donor consent forms and parental consent forms vary especially when communicating the risks and hazards of donation.

Donor comprehension of the written statement of understanding is essential. The proposed rule indicates that the written statement should be written in a clear and understandable terminology. NCHS evaluated the current AABB educational materials for content and comprehension and concluded that the material was simple and clear (2). However, it is unclear if other consent material provided to donors is clear and understandable. Also, there is a suggestion that presenting some of the information in multiple formats is useful. Alashuisi et al in their study examining comprehension among blood donors concluded that “presenting information to the donor in multiple formats leads to greater comprehension of the donation process”. Another study on donor comprehension also suggested donor level of understanding depends on how the information is presented (23).

Questions for the Committee:

1. Please comment on the seven proposed elements of the written statement of understanding as listed in FDA’s 2007 proposed donor eligibility rule.
2. Does the Committee agree that the data support a need for minimum standards for the explanation of the risks and hazards of Whole Blood donation to the donor?
3. Please comment on what methods are acceptable for presenting the written statement of understanding to the donor, and how the donor should acknowledge receipt of this statement.
4. Please comment on when blood establishments should administer the written statement of understanding.
 - a) Before donor questions?
 - b) Before physical examination?
 - c) Before phlebotomy?
5. Please comment on how often blood establishments should administer the written statement of understanding to Whole Blood donors.

References

- 1) Whitaker BI, Green JA et al. 2007 National Blood Collection and Utilization Survey.
- 2) Fridey JL, Townsend MJ, Kessler DA, Gregory KR. A question of clarity: redesigning the American Association of Blood Banks blood donor history questionnaire--a chronology and model for donor screening. *Transfus Med Rev.* 2007 Jul;21(3):181-204.
- 3) <http://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/OtherRecommendationsforManufacturers/MemorandumtoBloodEstablishments/UCM062834.pdf>
- 4) Eder A, Goldman M, Rossmann S, Waxman D, Bianco C. Selection criteria to protect the blood donor in North America and Europe: past (dogma), present (evidence), and future (hemovigilance). *Transfus Med Rev.* 2009 Jul;23(3):205-20.
- 5) Newman, B. and Roth, A. Estimating the probability of a blood donation adverse event based on 1000 interviewed whole-blood donors. *Transfusion.* 2005; 45: 1715–1721
- 6) Newman, B., Pichette, S., Pichette, D. and Dzaka, E. Adverse effects in blood donors after whole-blood donation: a study of 1000 blood donors interviewed 3 weeks after whole-blood donation. *Transfusion.* 2003; 43: 598–603.
- 7) Wiltbank TB, Giordano GF, Kamel H, Tomasulo P, Custer B. Faint and pre-faint reactions in whole-blood donors: an analysis of predonation measurements and their predictive value. *Transfusion.* 2008 Sep;48(9):1799-808.
- 8) Kamel H, Tomasulo P, Bravo M, Wiltbank T, Cusick R, James RC, Custer B. Delayed adverse reactions to blood donation. *Transfusion.* 2010 Mar;50(3):556-65.
- 9) Eder AF, Dy BA, Kennedy JM, Notari EP, Strupp A, Wissel ME, Reddy R, Gible J, Haimowitz MD, Newman BH, Chambers LA, Hillyer CD, Benjamin RJ. The American Red Cross donor hemovigilance program: complications of blood donation reported in 2006. *Transfusion.* 2008 Sep;48(9):1809-19.
- 10) Eder AF, Hillyer CD, Dy BA, Notari EP, Benjamin RJ. Adverse reactions to allogeneic whole blood donation by 16- and 17-year-olds. *JAMA* 2008;299:2279-86.
- 11) Cable RG, Glynn SA, Kiss JE, Mast AE, Steele WR, Murphy EL, Wright DJ, Sacher RA, Gottschall JL, Vij V, Simon TL. Iron deficiency in blood donors:

analysis of enrollment data from the REDS-II Donor Iron Status Evaluation (RISE) study. *Transfusion*. 2011 Mar;51(3):511-522.

- 12) Price TH, editor. Standards for blood banks and transfusion services. 26th ed. Bethesda (MD): AABB; 2009.
- 13) Shaz, B. H., Demmons, D. G. and Hillyer, C. D. Critical evaluation of informed consent forms for adult and minor aged whole blood donation used by United States blood centers. *Transfusion*. 2009 Jun;49(6):1136-45..
- 14) Wehrli G, Sazama K. Universal donor education and consent: what we know and where we should go. *Transfusion*. 2010 Nov;50(11):2499-502.
- 15) Alaishuski LA, Grim RD, Domen RE. The informed consent process in whole blood donation. *Arch Pathol Lab Med*. 2008 Jun;132(6):947-51
- 16) <http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Blood/ucm073433.htm>
- 17) <http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Blood/ucm073382.htm>
- 18) <http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Blood/ucm076756.htm>
- 19) <http://www.hhs.gov/ash/bloodsafety/advisorycommittee/recommendations/resdec08.pdf>
- 20) France CR, Rader A, Carlson B. Donors who react may not come back: analysis of repeat donation as a function of phlebotomist ratings of vasovagal reactions. *Transfus Apher Sci* 2005;33:99-106.
- 21) France CR, Montalva R, France JL, Trost Z. Enhancing attitudes and intentions in prospective blood donors: evaluation of a new donor recruitment brochure. *Transfusion*. 2008 Mar;48(3):526-30.
- 22) AABB association bulletin: strategies to reduce adverse reactions and injuries in younger donors. Association bulletin. Bethesda (MD): AABB; 2008. Report No.: 08-04.
- 23) Lindstrøm TC, Røsvik A. Ambiguity leads to uncertainty: ambiguous demands to blood donors. *Scand J Caring Sci*. 2003 Mar;17(1):74-7.

Appendix 1: AABB Donor Educational Materials

Blood Donor Educational Materials: **MAKING YOUR BLOOD DONATION SAFE**

Thank you for coming in today! This information sheet explains how **YOU** can help us make the donation process safe for yourself and patients who might receive your blood. **PLEASE READ THIS INFORMATION BEFORE YOU DONATE!** If you have any questions now or anytime during the screening process, please ask blood center staff.

ACCURACY AND HONESTY ARE ESSENTIAL!

Your **complete honesty** in answering all questions is very important for the safety of patients who receive your blood. **All information you provide is confidential.**

DONATION PROCESS:

To determine if you are eligible to donate we will:

- Ask questions about health, travel, and medicines
- Ask questions to see if you might be at risk for hepatitis, HIV, or AIDs
- Take your blood pressure, temperature and pulse
- Take a small blood sample to make sure you are not anemic

If you are able to donate we will:

- Cleanse your arm with an antiseptic. **(If you are allergic to iodine, please tell us!)**
- Use a new, sterile, disposable needle to collect your blood

DONOR ELIGIBILITY – SPECIFIC INFORMATION

Why we ask questions about sexual contact:

Sexual contact may cause contagious diseases like HIV to get into the bloodstream and be spread through transfusions to someone else.

Definition of “sexual contact”:

The words “have sexual contact with” and “sex” are used in some of the questions we will ask you, and apply to any of the activities below, whether or not a condom or other protection was used:

1. Vaginal sex (contact between penis and vagina)
2. Oral sex (mouth or tongue on someone’s vagina, penis, or anus)
3. Anal sex (contact between penis and anus)

HIV/AIDS RISK BEHAVIORS AND SYMPTOMS

AIDS is caused by HIV. HIV is spread mainly through sexual contact with an infected person OR by sharing needles or syringes used for injecting drugs.

DO NOT DONATE IF YOU:

-Have AIDS or have ever had a positive HIV test

- Have ever used needles to take drugs, steroids, or anything not prescribed by your doctor
- Are a male who has had sexual contact with another male, even once, since 1977
- Have ever taken money, drugs or other payment for sex since 1977
- Have had sexual contact in the past 12 months with anyone described above
- Have had syphilis or gonorrhea in the past 12 months
- In the last 12 months have been in juvenile detention, lockup, jail or prison for more than 72 hours
- Have any of the following conditions that can be signs or symptoms of HIV/AIDS:
 - Unexplained weight loss or night sweats
 - Blue or purple spots in your mouth or skin
 - Swollen lymph nodes for more than one month
 - White spots or unusual sores in your mouth
 - Cough that won’t go away or shortness of breath
 - Diarrhea that won’t go away
 - Fever of more than 100.5 °F for more than 10 days

Remember that you CAN give HIV to someone else through blood transfusions even if you feel well and have a negative HIV test. This is because tests cannot detect infections for a period of time after a person is exposed to HIV. **If you think you may be at risk for HIV/AIDS or want an HIV/AIDS test, please ask for information about other testing facilities. PLEASE DO NOT DONATE TO GET AN HIV TEST!**

Travel to or birth in other countries

Blood donor tests may not be available for some contagious diseases that are found only in certain countries. If you were born in, have lived in, or visited certain countries, you may not be eligible to donate.

What happens after your donation:

To protect patients, your blood is tested for hepatitis B and C, HIV, certain other infectious diseases, and syphilis. If your blood tests positive it will not be given to a patient. You will be notified about test results that may disqualify you from donating in the future.

Please do not donate to get tested for HIV, hepatitis, or any other infections!

Thank you for donating blood today!

(Donor Center Name)

(Telephone Number)