

Guidance for Industry

Variations for Blood Collection from Individuals with Hereditary Hemochromatosis

DRAFT GUIDANCE

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Guidance for Industry

Variations for Blood Collection from Individuals with Hereditary Hemochromatosis

This guidance document represents the agency's current thinking on the distribution of blood and blood components from individuals with hereditary hemochromatosis without disease labeling, and collecting blood from such individuals more frequently than every eight weeks without a physical examination on the day of donation. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

I. PURPOSE

This guidance document provides recommendations to blood establishments that wish to distribute blood and blood components collected from individuals with diagnosed hereditary hemochromatosis without indicating the donor's disease on the container label. This guidance also provides recommendations to blood establishments that wish to collect blood from such individuals more frequently than every eight weeks without a physical examination and certification of the donor's health by a physician on the day of donation. This document identifies the conditions under which FDA will consider approving the above as alternative procedures, or variances, to the current regulations, under the provisions of Title 21, Code of Federal Regulations, Section 640.120 (21 CFR 640.120), and provides guidance on what to submit when requesting these variances (Ref. 4). These recommendations apply to all blood establishments, whether or not they hold a U.S. License for the manufacture of blood and blood components.

II. INTRODUCTION

Hereditary hemochromatosis (HH) is an inherited disorder of iron metabolism, with an estimated prevalence of 0.25-0.50% among Caucasians. An epidemiologic study is currently underway to determine the prevalence, as well as the genetic and environmental determinants, of iron overload related to hereditary hemochromatosis in a multiethnic population. This iron metabolism disorder results in the deposition of excess iron in body tissues that can reach toxic levels leading to organ damage. The toxicity can affect most tissues and organs, but particularly the liver, endocrine organs, and the heart. Early initiation of therapeutic phlebotomy before organ damage occurs may restore a normal life expectancy and improve symptoms. (Ref.1, 2)

Treatment of HH typically has two phases. First, the patient undergoes iron depletion therapy, in which excess iron is removed. In one study of current practices, two to three units of blood were withdrawn per month, for approximately one year. In the second phase, maintenance therapy, an average of one unit was withdrawn every two months. In the same study, 76% of respondents reported full or partial insurance coverage of therapeutic phlebotomy charges. Charges ranged from a mean of \$48 for home phlebotomy, \$52 for blood centers, \$69 for physician's offices, to \$90 for hospitals. (Ref. 3)

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On the basis of the currently understood molecular mechanisms of disease, there is no evidence that the use of blood from HH patients for transfusion carries any added risk for recipients from HH. In addition, there is no evidence to support a transfer of a genetic disease by transfusion. Blood from HH patients has been used for transfusion in other countries without reports of adverse reactions in recipients. (Ref. 2)

Currently, the FDA does not prohibit the use of blood from therapeutic bleedings, but requires that blood intended for transfusion be labeled with the donor's disease [21 CFR 640.3(d)]. In addition, the regulations state that a person may donate a unit of blood more than once in eight weeks only after a physical examination and certification of health by a physician [21 CFR 640.3(f)]. (Ref. 4)

Blood establishments that collect blood during a therapeutic phlebotomy have not routinely distributed this blood for transfusion, because consignees have refused to accept blood that is labeled with a disease. Thus, the labeling requirement is considered to be a barrier to the use of blood from HH donors for transfusion, despite evidence that this blood is safe.

There have been several studies that have shown an increase in the prevalence of bloodborne viral pathogens in blood obtained from paid donors as compared to volunteer donors. Therefore, there is concern about creating an incentive for HH patients to donate blood for free, rather than pay for a therapeutic phlebotomy. If a blood establishment charged a fee for therapeutic phlebotomy, but not for a blood donation for transfusion, the HH donor would have an incentive to deny risk conditions that might preclude phlebotomy via cost-free donation. In this circumstance, blood donation provides indirect compensation for medical phlebotomy. (Ref.5)

III. BACKGROUND

On April 29, 1999, the Public Health Service Advisory Committee on Blood Safety and Availability (ACBSA) recommended that the Department of Health and Human Services (DHHS) “create policies that eliminate incentives to seek [blood] donation for purposes of phlebotomy” from patients with diagnosed hemochromatosis who require phlebotomy as therapy for their disease. Further, as undue incentives to donate blood for transfusion (rather than being therapeutically phlebotomized) are removed, DHHS “should create policies that eliminate barriers to using this resource” to augment the country's blood supply. (Ref. 6)

On August 10, 1999, the Commissioner of Food and Drugs made a commitment to consider case-by-case exemptions to existing blood labeling and donor suitability regulations for blood establishments that can verify that therapeutic phlebotomy for hemochromatosis is performed at no expense to the patient (Ref. 7). The Commissioner wrote that as part of any exemption, FDA would request that safety data be collected and submitted to the Agency and that this data would be compared with data gathered on the general donor pool. FDA additionally committed itself to work with the Health Care Financing Administration in ensuring that the financial incentives for persons with HH to donate blood for transfusion are removed. This issue was further discussed at the FDA Blood Products Advisory Committee meeting on September 16, 1999. The statutory authority and scope of jurisdiction of HCFA limits its ability to reduce or eliminate costs of

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treatment for HH patients, many of whom are covered by private insurers, or do not have health insurance. Thus, for the foreseeable future, if blood centers wish to distribute blood collected from donors with HH without disease labeling, they will have the responsibility of removing financial incentives for these donors. Each blood center will have to evaluate the advantages of entering these donors into their donor pool. (Ref. 8, 9)

IV. CONTENT OF VARIANCE REQUESTS.

FDA will consider requests for variances to the labeling and physician examination regulations. FDA believes that variances incorporating the following provisions would be acceptable:

- A. Blood donors with HH would meet the same suitability requirements as allogeneic donors.
- B. To collect blood products from a donor with HH more frequently than every eight weeks a blood center would:
 - 1. collect blood products from a donor who has presented a physician's prescription for iron depletion therapeutic phlebotomy for HH; or,
 - 2. have a blood center physician examine and certify the good health of the donor on the day of donation in accordance with 21 CFR 640.3(f) if the donor has not presented a prescription for therapeutic phlebotomy for HH.
- C. The blood center would not charge a fee for phlebotomies performed on individuals with HH, including those who do not meet allogeneic donor suitability requirements. At the initial donation, the blood center would obtain the donor's written acknowledgement that the donor understands that therapeutic phlebotomy will be provided free of charge.

V. SUBMISSION OF VARIANCE REQUESTS

- A. In accordance with 21 CFR 640.120, the blood collection center must not implement changes at variance to the regulations prior to receiving approval from FDA.
- B. To obtain approval for a variance to 21 CFR 640.3(d) (labeling with the donor's disease) under the provisions of 21 CFR 640.120, the blood collection center should submit a written request to CBER to omit HH labeling. The submission should include a copy of the donor acknowledgement form (informed consent or other written statement), to be signed by the donor, that s/he will not be charged a fee for the phlebotomy even if found to be ineligible as an allogeneic blood donor.
- C. To obtain approval for a variance to 21 CFR 640.3(f) (physician examination) under the provisions of 21 CFR 640.120, the blood collection center should submit a written request to collect blood products from donors with HH more frequently than every 8 weeks without examination by a physician at the time of donation. The submission should include statements that the blood collection center requires a physician's prescription for iron depletion therapeutic phlebotomy for HH, and that the blood collection center physician would examine previously diagnosed HH donors without a prescription (for maintenance phase therapeutic phlebotomy) on the day of donation if less than 8 weeks have elapsed since the last donation.

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- D. These variances may be requested concurrently.
- E. Licensed blood establishments should submit variance requests as major changes (prior approval supplements) pursuant to 21 CFR 601.12(b). Unlicensed blood establishments are not subject to 21 CFR 601.12, but must obtain approval of variance requests under 640.120 before implementing changes at variance with applicable regulations, such as those described in this guidance document.
- F. If the blood collection center discontinues operating under the terms of the approved variance (e.g., starts charging a fee for therapeutic phlebotomies for HH donors who do or do not meet allogeneic donor suitability criteria), the variance would no longer be in effect. The blood center should notify the FDA of this change in writing. Licensed blood establishments may include this notification in their Annual Report.

VI. REFERENCES

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