Guidance for Industry

Recommendations for the Assessment of Donor Suitability and Blood Product Safety in Cases of Suspected Severe Acute Respiratory Syndrome (SARS) or Exposure to SARS

FINAL GUIDANCE

This guidance is being distributed for immediate implementation.

FDA is issuing this guidance for immediate implementation in accordance with 21 CFR 10.115(g)(3). The agency has determined that seeking comments from the public prior to implementation is not appropriate since Severe Acute Respiratory Syndrome may pose immediate safety risks to the blood supply.

FDA invites comments on this document. Please submit comments to Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. You should identify all comments with the docket number listed in the notice of availability that publishes in the Federal Register. FDA will review any comments received and will revise the guidance document as appropriate.

Additional copies of this guidance are available from the Office of Communication, Training, and Manufacturers Assistance (HFM-40), 1401 Rockville, MD 20852-1448, or by calling 1-800-835-4709 or (301) 827-1800, or from the Internet at http://www.fda.gov/cber/guidelines.htm.

For questions on the content of this guidance contact the Division of Blood Applications, Office of Blood Research and Review at (301) 827-3524.

U.S. Department of Health and Human Services
Food and Drug Administration
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Contains Nonbinding Recommendations

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This guidance represents the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

I. INTRODUCTION

This guidance document provides our recommendations for assessing donor suitability and blood product safety with respect to Severe Acute Respiratory Syndrome (SARS). This guidance applies to Whole Blood and blood components intended for transfusion (including red blood cells for immunization) and blood components including recovered plasma, Source Leukocytes and Source Plasma intended for use in further manufacturing into injectable products or non-injectable products. Within this document, "donors" refers to all such donors. The Food and Drug Administration (FDA) developed the recommendations in this guidance in consultation with other Public Health Service Agencies of the Department of Health and Human Services. Within this guidance, "you" refers to blood establishments and "we" refers to the FDA. This guidance does not apply to tissue establishments or to human cells and tissues other than blood. However, tissue establishments may consider implementing similar donor screening practices.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. BACKGROUND

A. Epidemiology and Pathogenesis

The Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO) are investigating a worldwide outbreak of unexplained atypical pneumonia referred to as Severe Acute Respiratory Syndrome (SARS). As of 10 April 2003, over 2,500 suspected cases of SARS have been reported to WHO from nearly 20 countries; in the United

States, over 150 suspected cases (about 5% of cases worldwide) have been reported to CDC from about 30 states. Of the United States cases, about 95% had traveled to outbreak areas listed in the case definition within 10 days prior to the onset of clinical illness, and the remainder had a history of close contact with a person with suspected SARS. Of these cases reported worldwide, approximately 3.5 % (over 100 cases) have been fatal. In the United States, the majority of patients have recovered or stabilized clinically without specific antiviral therapy; no fatalities have been reported as of 10 April 2003 (Refs. 1-4 and unpublished CDC communication).

Laboratories at CDC and elsewhere (SARS Laboratory Network organized by WHO) have detected a new coronavirus in SARS patients (Refs. 5-9). Less often, a paramyxovirus (metapneumovirus) also has been found (Refs. 6, 7, 9). Both are lipid-enveloped, single-stranded RNA viruses. The identification of a novel coronavirus is consistent with a potential etiologic role, but the pathogenesis of SARS remains unclear at the present early stage of research. A co-factor role of paramyxovirus in this syndrome cannot be excluded. A diagnostic test for SARS based on the detection of acute infection with the novel coronavirus is currently under development (Refs. 5-9).

B. Definitions

1. CDC Case Definition of Suspected SARS

Until a diagnostic test is available, CDC's current interim case definition for a United States case of suspected SARS is as follows (Ref. 2):
Respiratory illness of unknown etiology with onset since 1 February 2003, which meets the following criteria:

- Measured temperature > 100.4 °F (>38 °C), AND
- One or more clinical findings of respiratory illness (e.g. cough, shortness of breath, difficulty breathing, hypoxia, or radiographic findings of either pneumonia or acute respiratory distress syndrome), AND
- Travel within 10 days of onset of symptoms to an area with documented or suspected community transmission of SARS (affected areas), OR close contact within 10 days of onset of symptoms with either a person with a respiratory illness who traveled to a SARS-affected area or a person known to be a suspect SARS case.
    - Please consult CDC for the updated list of affected areas (see section II.B.3 below for CDC website and phone number). The list is subject to change. (As of the publication date of this guidance, CDC has defined affected areas as: Peoples' Republic of China (i.e., mainland China and Hong Kong Special Administrative Region); Hanoi, Vietnam; and Singapore. The CDC definition excludes areas with secondary cases limited to healthcare workers or direct household contacts (as is the case at this time in Canada and the United States).)
    - Travel includes transit in an airport in an area with documented or suspected community transmission of SARS.

- Close contact is defined as having cared for, having lived with, or having had direct contact with respiratory secretions and/or body fluids of a patient known to be a suspect SARS case. Please consult CDC for the updated case definitions, including the definition of close contact (see section II.B.3 below for CDC website and phone number).

NOTE: Suspect cases with either radiographic evidence of pneumonia or respiratory distress syndrome or evidence of unexplained respiratory distress syndrome by autopsy are designated as "probable" cases of SARS according to the current WHO case definition (Ref. 4).

2. Use of CDC Case Definition in Guidance

For donor screening purposes, this guidance currently does not distinguish suspected SARS from probable SARS. The phrase "SARS and suspected SARS" as used in this guidance reflects the current lack of an available confirmatory diagnostic test for SARS.

Although WHO and CDC currently use 10 days as the incubation period in their respective case definitions, 14 days may be more appropriate for donor screening as a conservative upper limit of the asymptomatic incubation period (time between exposure to the SARS agent and the onset of clinical symptoms), based on current available information (Ref. 6). This guidance makes recommendations using 14 days as the asymptomatic incubation period.

3. Updated Information on Case Definitions and Areas Affected by SARS

Epidemiologic and laboratory investigations about SARS are ongoing. The case definitions and the list of affected areas worldwide are updated periodically as new information becomes available. The case definitions and the updated list of geographic areas affected by SARS may be obtained at the CDC website or by calling CDC:

Website: http://www.cdc.gov/ncidod/sars/casedefinition.htm
Phone: (888) 246-2675; 8 am - 11 pm weekdays, 10 am - 8 pm weekends

4. Infection Control Guidelines about SARS

Based on clinical and epidemiological experience to date, CDC has developed interim infection control guidelines for use at healthcare and household settings by infection control practitioners and clinicians providing medical care for patients with suspected SARS, including guidelines for triage of potential SARS cases. These guidelines are available at the CDC websites (Refs. 10-12). We recommend that blood center personnel consult these guidelines frequently to keep abreast of evolving CDC recommendations.

C. Impact of SARS on Blood Safety

The potential for transmission of SARS through blood and blood products is not known. The possibility of a viremic period, before the onset of clinical symptoms and/or after symptom resolution, remains an important concern regarding blood safety. The new coronavirus that is the possible cause of SARS has been isolated from infected kidney, lung, and bronchoalveolar-lavage fluid (Ref. 8) but has not been isolated yet from blood or serum of an infected individual (Refs. 5-9), though data are limited. Detection by nucleic acid amplification of this new coronavirus in blood samples from persons acutely infected with SARS has been reported in a single patient (Ref. 9). Because, as in some other early viral infections, persons with SARS could potentially be viremic without symptoms, transfusion transmission of SARS may be possible. Therefore, until more information is known about the epidemiology and pathogenesis of SARS, we recommend, as a preventative measure, the implementation of blood donor deferral for at least 14 days after possible exposure to SARS. Additionally, in cases of suspected SARS, we recommend donor deferral for at least 28 days after symptom resolution and completion of therapy due to the present uncertainty about possible persistence of viremia and/or viral shedding in body fluids (Ref. 9).

At this time, we believe SARS is unlikely to be transmitted through products manufactured from plasma. Lipid-enveloped RNA virus(es), the putative agent(s), should be readily removed and/or inactivated during manufacturing of plasma derivatives (Refs. 13, 14). Licensed plasma derivatives undergo intentional viral clearance procedures that are validated to be effective against lipid-enveloped RNA viruses. These procedures include: filtration, heating, acidification, and detergent treatment. Based on any new scientific information about the safety of plasma derivatives, we intend to revise these recommendations as appropriate.

D. Impact of Guidance on Blood Availability

Currently available epidemiologic data suggest that the implementation of SARS screening as recommended in this guidance will reduce the number of available donors by 0.1 to 0.2% and no more than 0.4%. Our recommendations contained in this guidance reflect recent active consultation with CDC. The recommendations are intended to serve as interim guidance until new scientific information becomes available. We will monitor closely the impact of this guidance on the blood supply. Based on that impact assessment and any new scientific information about the potential risk of transfusion transmission of the infectious agent(s) causing SARS, we intend to revise these recommendations as appropriate.

III. RECOMMENDATIONS

Consistent with existing regulations and applicable guidance, donors must be in good health at the time of donation [21 CFR 640.3(b) and 21 CFR 640.63(b)(3)]. Standard procedures that are already in place should serve as an effective safeguard against the unusual donor who seeks to donate after the onset of clinical illness. The following recommendations apply primarily to the potentially infected person during the asymptomatic incubation period before the onset of clinical symptoms.

A. Donor Interview Questions

At donor interview, we recommend that you ask (orally or in writing) potential donors about:

1. History of SARS, suspected SARS, or treatment for SARS within the previous 28 days. For example, "In the past 28 days, have you been ill with SARS or suspected SARS?"

2. Close contact within the previous 14 days with persons with SARS or suspected SARS. For example, "In the past 14 days, have you cared for, lived with, or had direct contact with body fluids of a person with SARS or suspected SARS?"

3. Travel to or residence in areas affected by SARS within the previous 14 days. Blood collection establishments with existing capture questions (e.g., "Have you traveled outside the United States within the past year?") should review these questions to ensure that they are adequate to identify possible travel to CDC-defined SARS affected areas. Capture questions may be followed up with questions specific to travel to SARS affected areas as necessary.

   If adequate travel capture questions are not currently in use, we recommend that donors be asked a specific question about travel or residence in areas affected by SARS within the past 14 days. For example, "In the past 14 days, have you traveled to, traveled through, or resided in areas affected by SARS?"

   Note that you should read to or show donors a list of affected areas as updated by CDC. See below for CDC contact information

To ensure that the questions used remain consistent with updated case definitions and the list of geographic areas affected by SARS, we recommend that you routinely and periodically refer to the CDC website (www.cdc.gov/ncidod/sars/casedefinition.htm) or call CDC (888-246-2675; 8 am - 11 pm weekdays, 10 am - 8 pm weekends) to obtain the updated information.

B. Donor Deferral Actions

We recommend that donors reporting a history of SARS or suspected SARS be asked about duration of symptoms and any treatment given. We recommend that you defer these donors for a period of at least 28 days after complete symptom resolution AND the cessation of any treatment.

For asymptomatic donors with a history of contact with persons with SARS or suspected SARS, we recommend that you defer these donors for a period of at least 14 days after last exposure. For travel/residence exposure, the donor should be deferred for at least 14 days after arrival in the United States.

C. Post-Donation Information and Lookback Investigation

We recommend that you actively encourage donors to report, post donation, any further information about SARS exposure that may have occurred within 14 days prior to donation, or SARS illness or treatment within 28 days prior to donation. Donors should also be encouraged to report SARS illness or treatment that occurs within 14 days after donation. These recommendations on post-donation information and lookback investigation apply to Whole Blood and blood components intended for transfusion (including red blood cells for donor immunization), and to unpooled units of recovered plasma and Source Plasma, and Source Leukocytes, but not to pooled units of plasma.

1. Product Retrieval and Quarantine

If a donor reports, post donation, a history of SARS disease (as described in section III.A.1, above) that occurred within 28 days prior to blood collection, SARS exposure (as described in sections III.A.2 and III.A.3, above) that occurred within 14 days prior to blood collection, or SARS disease that occurred within 14 days after blood collection, we recommend that blood establishments promptly retrieve and/or quarantine the collected in-date units of Whole Blood and/or blood components and any unpooled units collected for further manufacturing.

NOTE: If the donor is symptom-free more than 14 days post-exposure, product retrieval and quarantine are not necessary.

2. Product Disposition and Special Labeling

Quarantined units should be destroyed in accordance with established procedures, unless distributed for further manufacturing into non-injectable products or for research use under special labeling, as follows:

"Biohazard," AND
"Collected from a donor with SARS exposure or suspected SARS,"

AND

"For laboratory research use only," OR
"Intended only for further manufacturing into non-injectable products."

3. Physician Notification about Potential Transfusion-Transmitted SARS

A blood establishment (including a blood collecting establishment or transfusion service) may receive information that a donor of already-transfused blood or blood components has been exposed to SARS, or became sick with suspected SARS, during the time frames described in section III.A.1-3. We recommend that the establishments consider notifying the treating physician of those recipients about the post donation information, including whether the donor developed suspected SARS.

4. Notification of State or Local Public Health Departments about Suspected Donor Cases of SARS

We recommend that blood establishments report cases of SARS in either donors or blood recipients to their respective state or local public health departments. Also, if a donor reports the existence of clinical symptoms consistent with SARS within 14 days subsequent to donation, and a possible SARS exposure, CDC has asked blood establishments to contact the CDC Division of Viral and Rickettsial Diseases, Assistant Director for Blood Safety (404-639-2775) to determine if retrieved units should be sent to CDC for laboratory studies, under quarantine and specially labeled as indicated above.

IV. BIOLOGIC PRODUCT DEVIATION AND FATALITY REPORTING

Regulations on reporting of product deviations by licensed manufacturers, unlicensed registered blood establishments, and transfusion services are located at 21 CFR 606.171 and 21 CFR 600.14. Pursuant to these regulations, blood and plasma collection establishments (including establishments that collect Source Leukocytes and licensed manufacturers of leukocyte derivatives) must submit biological product deviation reports for events related to SARS, if the establishment distributed the affected product. Additionally, if a suspect donation results in the fatality of a transfusion recipient, blood establishments must report the fatality to the FDA [21 CFR 606.170(b)].

V. IMPLEMENTATION

We recommend that you implement the recommendations in this guidance as soon as feasible, but not later than 30 days after the guidance issue date. Consistent with 21 CFR 601.12, licensed establishments implementing these recommendations should submit by official correspondence a statement in their annual reports indicating the date that the establishment revised and implemented their standard operating procedures, consistent with these recommendations. These changes do not require our prior approval.

VI. REFERENCES

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