JUNE 16, 2021

2020-2021 Updates to Blood Donor Eligibility and Testing

1

Recent changes

Updated FDA guidance for donor deferrals

- HIV
- Creutzfeldt-Jakob Disease (CJD)
- Malaria

Updated FDA guidance for donor testing

- Babesia
- Zika
- COVID-19

2

Impact of COVID-19 on Blood Supply

Although most COVID-19 patients do not require transfusion support, the pandemic has had a tremendous impact on the US blood supply

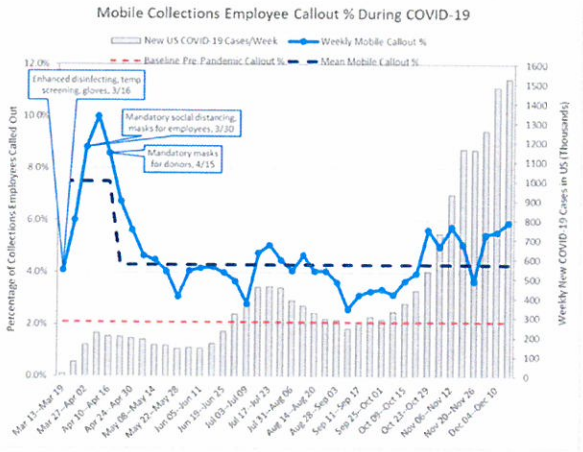
- Cancellation of blood drives
  - March 2020--April 2020
    - 14,000 blood drives cancelled
    - 400,000 planned units uncollected
    - Red Cross was able to collect just 53% of goal
  - Hospitals responded by cancelling elective surgeries, but by mid-May blood usage had surged above pre-COVID levels

https://americanredcrossretirees.wildapricot.org/page-18103/9133611

3

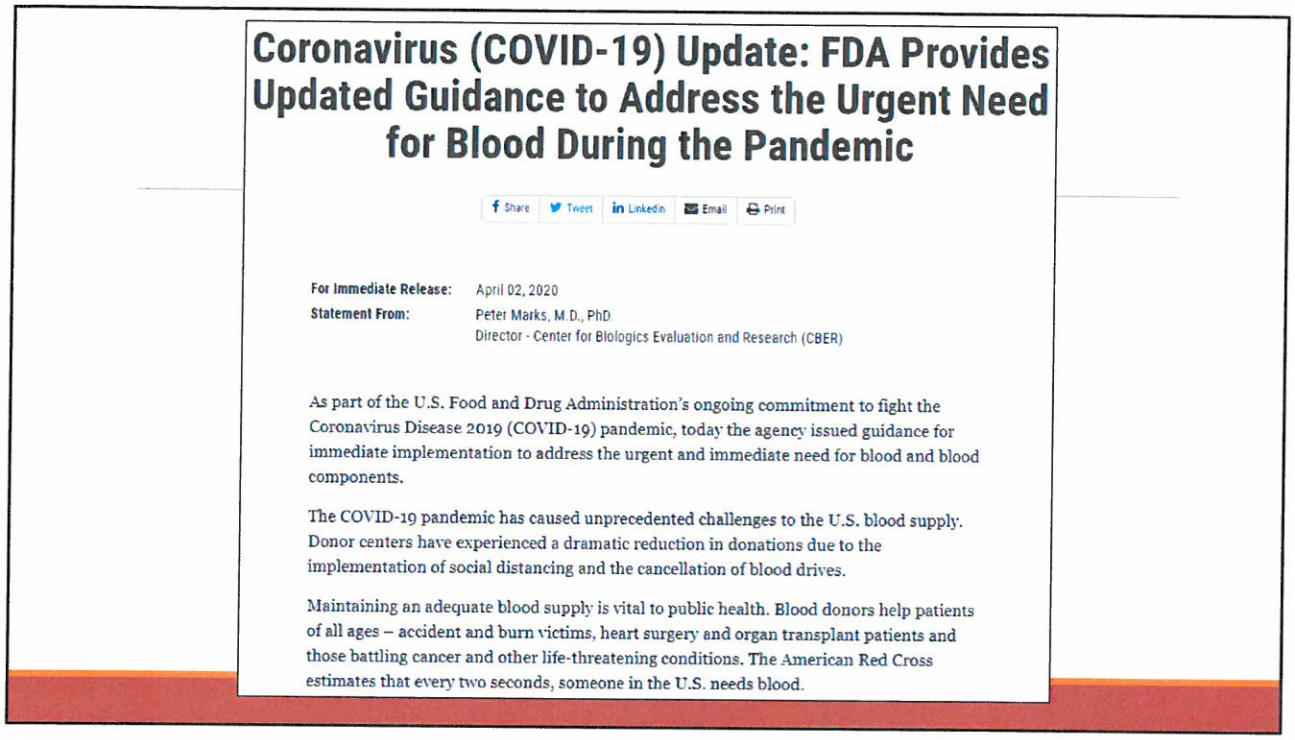
Impact of COVID-19 on Blood Supply

- Social distancing requirements at blood drives (appointment only, removing donor beds and chairs to meet distancing requirements, etc.)
- Donor recruitment challenges
  - Deferral of donors with recent travel, exposure, quarantine, or illness (14-28 days)
  - Some donors uncomfortable scheduling a donation during stay-at-home orders or prior to vaccination
- Blood center staffing challenges due to employee exposures, quarantines, illnesses



https://pubmed.ncbi.nlm.nih.gov/33904604/

4



Coronavirus (COVID-19) Update: FDA Provides Updated Guidance to Address the Urgent Need for Blood During the Pandemic

Share Tweet LinkedIn Email Print

For Immediate Release: April 02, 2020
Statement From: Peter Marks, M.D., PhD
Director - Center for Biologics Evaluation and Research (CBER)

As part of the U.S. Food and Drug Administration's ongoing commitment to fight the Coronavirus Disease 2019 (COVID-19) pandemic, today the agency issued guidance for immediate implementation to address the urgent and immediate need for blood and blood components.

The COVID-19 pandemic has caused unprecedented challenges to the U.S. blood supply. Donor centers have experienced a dramatic reduction in donations due to the implementation of social distancing and the cancellation of blood drives.

Maintaining an adequate blood supply is vital to public health. Blood donors help patients of all ages – accident and burn victims, heart surgery and organ transplant patients and those battling cancer and other life-threatening conditions. The American Red Cross estimates that every two seconds, someone in the U.S. needs blood.

5

FDA Revised Guidance April 2020

Based on recently completed studies and epidemiologic data, the FDA has concluded that current policies regarding certain donor eligibility criteria can be modified without compromising the safety of the blood supply

- High risk behavior associated with **HIV risk**
- Travel and risk associated with **vCJD and CJD**
- Travel related risk associated with **Malaria**

These changes are expected to remain in place after the COVID-19 pandemic ends, with any appropriate changes based on comments received and experience implementing the guidance

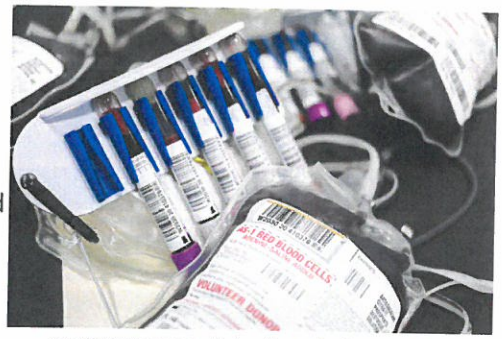
6

HIV Risk Deferral Background

The understanding of risk factors for AIDS in 1983 informed the first blood donor deferral policy

- Indefinite deferral for men who have sex with men (MSM) even once, commercial sex work (CSW), and injection drug use (IDU)
- 12-month deferral for paying for sex, diagnosis of other sexually transmitted infection (gonorrhea/chlamydia), accidental needle stick, blood transfusion, recent tattoo or piercing

Donor education, deferrals, and advances in donor testing reduced the risk of HIV transmission from blood transfusion from 1:2500 to 1:1.47 million



https://www.nbcnews.com/feature/nbc-out/health-experts-urge-fda-ax-outdated-gay-blood-donor-restrictions-n1186276

https://www.fda.gov/media/92490/download

7

2015 Update

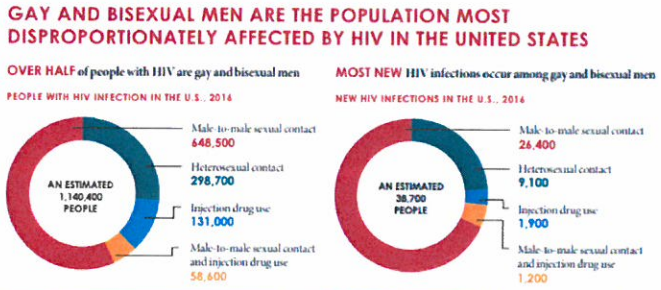
As updated testing methods and further evidence on risk factors for transfusion transmission of HIV became available, the indefinite deferral for MSM was reconsidered:

- The REDS-II Study evaluated four viral markers (HBV, HCV, HTLV, and HIV) in the nation's blood supply to determine the behavioral risk factors associated with donations that tested positive
  - Sex with an HIV-positive partner (132-fold increased risk) and a history of male-to-male sexual contact (62-fold increased risk) remained the two leading independent risk factors for HIV infection in blood donors
  - History of multiple sexual partners of the opposite sex in the last year was 2.3-fold

8

2015 Update

- The Blood Donation Rules Opinion Study (BloodDROPS).
  - MSM comprise ~7% of the population and 2.6% of blood donors
- HIV positivity rate in MSM blood donors was 0.25% compared to estimated 11-12% prevalence in MSM, indicating self-selection of blood donors



https://www.fda.gov/media/92490/download
https://www.cdc.gov/nchhstp/newsroom/docs/factsheets/cdc-msm-508.pdf

9

2015 Update

- Epidemiologic data from countries that changed their MSM policy found no safety concerns
  - Australia reduced MSM deferral from indefinite to 1 year; for 5 year pre- and post-implementation there was no change in risk to blood supply and compliance with the deferral increased
- Based on this evidence, the deferral period for MSM was decreased from indefinite to 12 months in December 2015

10

HIV 2020 Update

- Current change from 12 to 3 months is based on:
  - The Transfusion Transmissible Infections Monitoring System has found no increased risk to the blood supply following the change to a 1-year deferral
  - UK and Canada have now moved to a 3-month deferral for MSM and have had no increase in risk to the blood supply following this change, and there is some evidence that compliance with the deferral has increased
  - Current HIV, HBV, and HCV screening tests including NAT can easily detect each of these viruses within well less than a 3-month period from time of infection

11

Risk Period is now 3 months
Have you ever received money, drugs, or other payment for sex?
Have you ever used needles to take drugs, steroids, or anything not prescribed by your doctor?
In the past 12 months, have you had sexual contact with anyone who has HIV/AIDS or has had a positive test for the HIV/AIDS virus?
In the past 12 months, have you had sexual contact with a prostitute or anyone else who takes money or drugs or other payment for sex?
In the past 12 months, have you had sexual contact with anyone who has ever used needles to take drugs or steroids, or anything not prescribed by their doctor?
In the past 12 months, have you had a blood transfusion?
In the past 12 months, have you come into contact with someone else's blood?
In the past 12 months, have you had an accidental needle stick?
In the past 12 months, have you had a tattoo?
In the past 12 months, have you had ear or body piercing?
Male Donors: In the past 12 months, have you had sexual contact with another male?
Female donors: In the past 12 months, have you had sexual contact with a male who had sexual contact with another male in the past 12 months?
In the past 12 months, have you had or been treated for syphilis or gonorrhea?

12

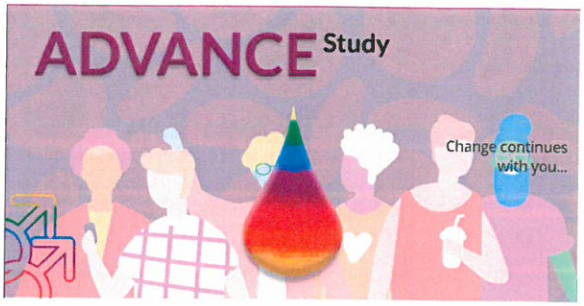
ADVANCE Study

Assessing Donor Variability And New Concepts in Eligibility

American Red Cross, OneBlood, and Vitalant are currently conducting a pilot study funded by FDA that could potentially lead to changes for blood donor eligibility for MSM

The study is focused on evaluating alternatives to determining donor eligibility rather than using time-based deferrals

https://advancestudy.org/



13

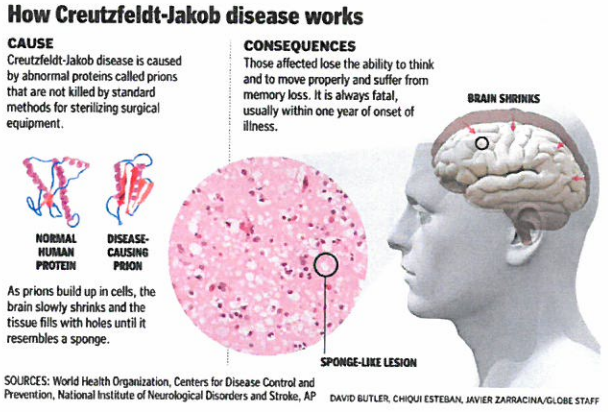
CJD and vCJD Risk Deferral Background

Creutzfeldt-Jakob Disease (CJD)

- Rare and rapidly progressing dementia, generally fatal within 1 year
  - Sporadic (sCJD) 89-95%
  - Familial (fCJD) 5-15%
  - Iatrogenic (iCJD) <1%
    - Dura mater transplant or cadaveric pituitary growth hormone

Variant CJD (vCJD)

- Abnormal protein can be detected in blood and lymphoid tissue
- Reported in the UK in 1996
- Transmitted via consumption of contaminated beef



https://www.fda.gov/media/124156/download

14

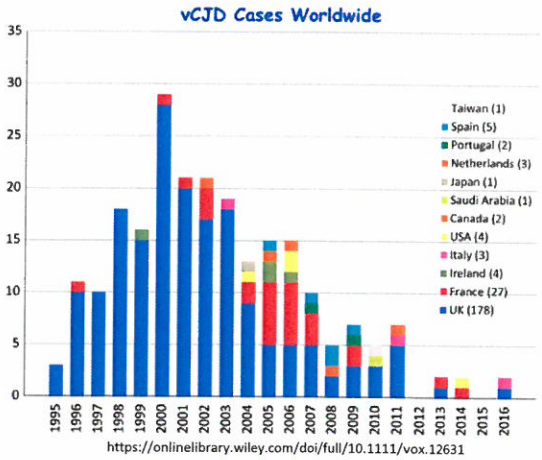
vCJD Background

Bovine spongiform encephalopathy ("mad cow disease") was first recognized in the UK in 1985, peaked in 1992, and fell to low levels by 1996 due to control measures

Four cases of vCJD occurred in the US

- All 4 were former residents of UK or other European countries, none donated blood

The FDA developed a risk model which determined that UK, Ireland, and France account for 95% of the total risk exposure in the US



https://onlinelibrary.wiley.com/doi/full/10.1111/vox.12631

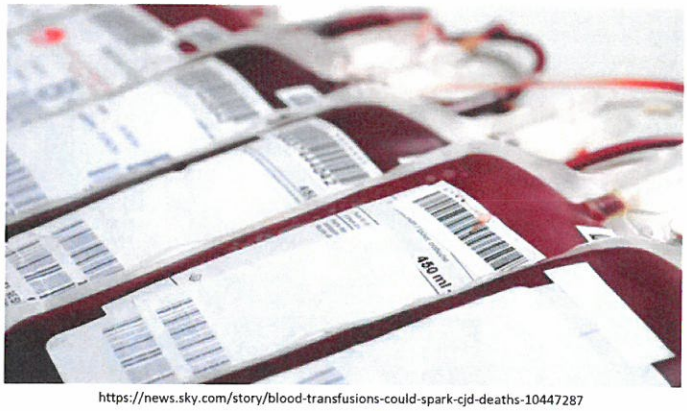
15

vCJD and Transfusion

Of the 178 vCJD cases in the UK

- 18 donated blood
  - 67 transfusion recipients
  - 4 developed transfusion-trasmitted vCJD

No transfusion-transmitted cases of CJD have been described to date and the risk remains theoretical



https://news.sky.com/story/blood-transfusions-could-spark-cjd-deaths-10447287

16

CJD and Transfusion

Lookback studies have identified NO transfusion-transmitted cases of CJD to date, abnormal protein is generally not detectable in blood or lymphoid tissue, and the risk of transfusion-transmission remains theoretical

Almost all cases of CJD are the sporadic form and not familial, and relatives are not at increased risk of developing the disease

Cadaveric pituitary-derived Human growth hormone was available in the US from 1958-1985. All iatrogenic CJD cases in the US were from exposure to hGH. Average incubation period is 15 years with case reports of longer than 30 years

17

CJD/vCJD 2020 Update

Deferral removed

- Question about blood relatives with CJD
- Human growth hormone is now removed from the medication deferral list
  - Donors previously deferred due to hGH use remain deferred as a precaution
- Deferral for Bovine insulin use has been removed
- Deferral for time spent on US military bases in Europe has been removed due to no cases of vCJD

Deferral remains

- Cadaveric dura mater transplant recipients remain deferred due to a remote risk
- Deferral for time spent in UK remains
- Deferral for blood transfusion in UK or France remains, and Ireland was added
- Deferral for time spent in Europe remains, but reduced to France and Ireland

18

CJD/vCJD Old Criteria	CJD/vCJD New Criteria
From 1980 through 1996, donor spent time that adds up to 3 months or more in the United Kingdom (England, Northern Ireland, Scotland, Wales, the Isle of Man, the Channel Islands, Gibraltar, or the Falkland Islands)	No change. Donors remain deferred.
Donor diagnosed with vCJD, CJD or any other transmissible spongiform encephalopathy (TSE)	This question is deleted. Donors remain deferred.
Donor received a human dura mater transplant	No change. Donors remain deferred.
Donor who received an injection of human cadaveric pituitary-derived growth hormone (hGH)	FDA recommends removal of hGH from the medication deferral list, but donors remain deferred.
From 1980 to the present donor received a blood transfusion in the United Kingdom or France	FDA added Ireland to the list of countries.
From 1980-1996, donor spent time on a military base in Europe	FDA deleted this criteria
From 1980 to the present, donor spent time that adds up to five (5) years or more in Europe	FDA reduced list of countries to just France and added Ireland and the timeframe from 1980-2001.
Bovine Insulin	FDA deleted this criteria
Donor who has a blood relative diagnosed with CJD	FDA deleted the question.

19

Malaria Risk Deferral Background

Mosquito-borne parasitic infection caused by Plasmodia species

Eradicated in the US in the 1950s, although locally-acquired mosquito-borne transmission has caused 63 small outbreaks (ranging from 1-32 cases) since 1957, predominantly P. vivax

In contrast, malaria affects millions of people worldwide with infections ranging from asymptomatic to fatal

Transfusion-Transmitted Malaria (TTM) rarely occurs in the US

- The risk of TTM is currently estimated at less than 0.1 per million red blood cell (RBC) transfusion, or about 1 case every 2 years
- Whole blood or RBC components are implicated in most (94%) TTM cases, with the remainder caused by platelet components. Plasma components have not been a source of TTM

https://www.medicalnewstoday.com/articles/150670#what_is_malaria

https://www.fda.gov/media/72243/download

20

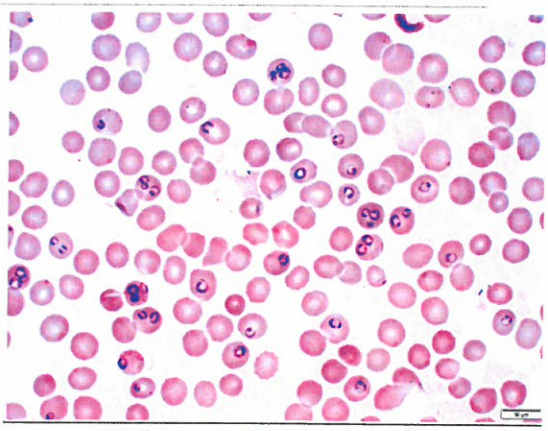
Malaria

No licensed test to screen blood donors for malaria in the US

28 million US residents travel to malaria-endemic countries each year

2,000 imported malaria infections each year

11 cases of TTM between 2000-2017, all implicated asymptomatic donors who were former residents of endemic countries or had a prior history of malaria infection



https://www.pathologyoutlines.com/topic/parasitology malariapfalciparum.html

21

Malaria 2020 Update

Residence=5 years or more, Travel=24 hours to 5 years

Travel to a malaria endemic area by a resident of a non-endemic country

- Deferral reduced from 12 months to 3 months, unrelated to whether the donor took malaria prophylaxis medication

Prior residence in a malaria-endemic country

- 3-year deferral remains after end of residency
- After 3 years, further travel to a malaria-endemic area will result in 3-month deferral

History of malaria infection

- 3-year deferral remains

No deferral required if the donor has been a resident of a non-endemic country for at least 3 years AND is donating platelets or plasma that are treated with Pathogen Reduction

22

Babesia Testing Background

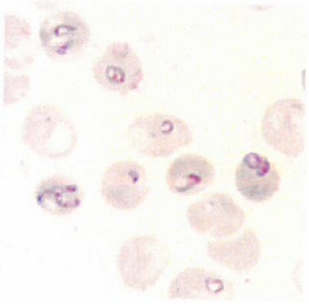
Microscopic parasite that infects red blood cells

Infection most commonly occurs via tick bite

Once inside the rbc, the parasite replicates and causes destruction of red blood cells

Most infected people are asymptomatic, but if symptoms occur they are generally mild
- Fever, muscle aches, fatigue, jaundice, enlarged spleen

In elderly, neonates, immunocompromised, and asplenic individuals, infection may be severe or even fatal



Babesia parasites in red blood cells on a stained blood smear. (CDC Photo: DPDx)

23

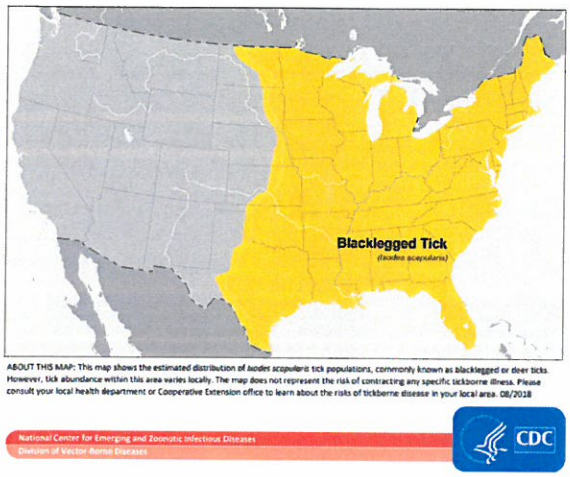
Transmission

Tick bite transmission:
- First US case 1966
- About 2000 cases per year reported to CDC
- Most cases are asymptomatic and not reported, so actual number is likely much higher
- Fatality rate 6%-9% in hospitalized patients, 21% immunosuppressed patients

Transfusion transmission:
- First US case 1980
- More than 200 cases reported
- Fatality rate 20%

https://www.cdc.gov/parasites/babesiosis/index.html

24



BABESIOSIS

Babesia cases reported to CDC in 2016

https://tickencounter.org/tick_identification/guide

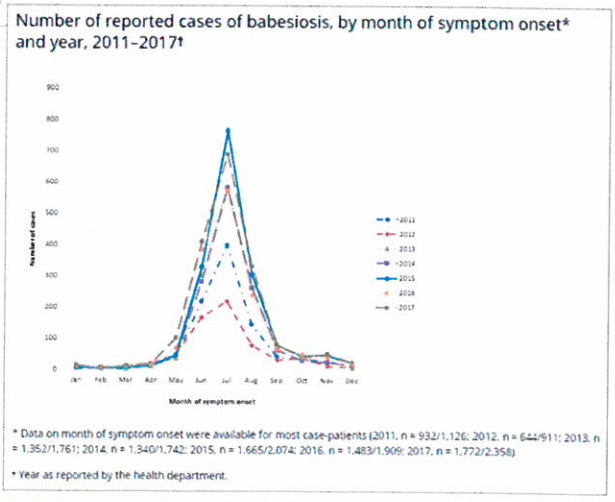
25

Course of infection

Most symptoms appear 1 to 4 weeks after tick bite

Parasitemia lasts from 2 to 7 months, but has been known to persist up to 2 years after infection

86% of donors have DNA clearance within one year, 95% after 2 years



Transfusion. 2019 Feb;59(2):593-600

26

GUIDANCE DOCUMENT

Recommendations for Reducing the Risk of Transfusion-Transmitted Babesiosis

Guidance for Industry

MAY 2019

Blood donors in endemic states must be tested year-round or pathogen reduction must be used

An expert committee had recommended nationwide, year-round antibody testing plus NAT testing for all donations in endemic states

FDA performed an independent risk assessment and determined year-round antibody plus NAT testing only in endemic states only limits risk and balances scope of testing

There is currently no licensed antibody test available for donor screening

Donors who test positive must be deferred at least 2 years

Guidelines go into effect one year from publication of final guidance

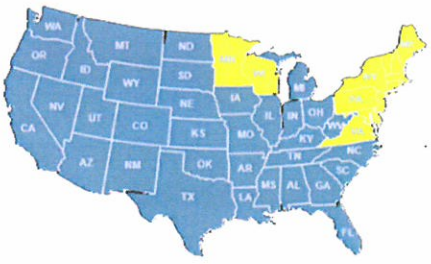
https://www.fda.gov/media/114847/download

27

Babesia 2020 Update

States that now have year-round Babesia NAT:

Connecticut	New York
Delaware	Pennsylvania
Maine	Rhode Island
Maryland	Vermont
Massachusetts	Virginia
Minnesota	Wisconsin
New Hampshire	Washington, D.C.
New Jersey	



28

Zika Background

Viral infection transmitted via mosquito

Most infected individuals are asymptomatic or have mild symptoms including fever, rash, headache, joint pain, muscle pain, red eyes

Can be passed from mother to child during pregnancy, potentially causing severe brain defects (microcephaly) or miscarriage

Prior to 2014, very few travel-associated cases of Zika virus disease were identified in the United States.

In 2015 and 2016, large outbreaks of Zika virus occurred in the Americas, resulting in an increase in travel-associated cases in US states, widespread transmission in Puerto Rico and the US Virgin Islands, and limited local transmission in Florida and Texas. Cases began to decline in 2017

https://www.cdc.gov/zika/index.html

29

Zika

In 2016, Zika was designated a "relevant transfusion-transmitted infection" and FDA recommended nationwide nucleic acid testing for Zika for all blood donations, with pathogen reduction allowed as an acceptable alternative to testing

Since 2018, there have been no reports of Zika virus transmission by mosquitoes in the continental US

Cases have also significantly dropped worldwide

- US travel-associated Zika virus cases have also declined:
  - 437 in 2017, 73 in 2018, 27 in 2019, 4 in 2020
- No countries or territories currently have Zika outbreaks at this time

In 2016, 1.8% of blood donations in Puerto Rico tested positive for Zika. There have been no Zika positive blood donations in the US since March 2018

30

Zika 2021 Update

Zika virus is no longer considered a relevant transfusion-transmitted infection, as it no longer has "sufficient incidence and/or prevalence to affect the potential donor population"

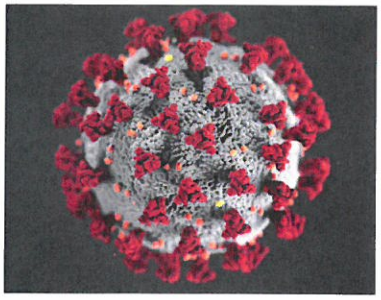
Donor testing for Zika via nucleic acid testing is no longer required

31

COVID-19 Donor Deferral

COVID-19 is not known to be transmitted via transfusion

- FDA does not recommend COVID-19 screening tests for blood donors
- 14-day deferral for confirmed or suspected COVID-19 infection
- No deferral after inactivated COVID-19 vaccines
- 14-day deferral after live attenuated COVID-19 vaccine or if vaccine type is not known



Recent study performed nucleic acid testing for SARS-CoV-2 on 257,809 blood donors

- Positivity rate was 1.13/100,000 donations
- In positive samples, viral load was low and not able to infect cell cultures

https://onlinelibrary.wiley.com/doi/epdf/10.1111/trf.16511
https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/updated-information-blood-establishments-regarding-covid-19-pandemic-and-blood-donation

32

CCP Antibody Testing

Convalescent plasma may be collected from donors

- With a history of symptoms + a positive diagnostic test OR
- Any donor found to have positive antibody test results from 2 different tests

Complete resolution of symptoms for at least 14 days

Male donors, females who have never been pregnant, or females who test negative for HLA

Do not collect from donors who have been vaccinated unless

- They tested positive for COVID-19 BEFORE their vaccine and are within 6 months or less from complete resolution of COVID-19 symptoms

All donors must have a positive antibody test and meet criteria for high-titer based on the individual test

https://www.fda.gov/media/136798/download

33

CCP Antibody Testing

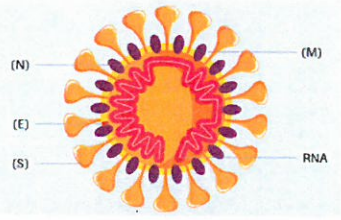
Total Antibody Spike Protein **Positive**

Total Antibody Nucelocapsid **Positive**

High Titer Result **Label as High Titer CCP**

Structure of the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)

- Nucleocapsid protein (N)
- Envelope protein (E)
- Spike protein (S)
- Membrane glycoprotein (M)
- RNA



https://diagnostics.roche.com/us/en/products/params/elecsys-anti-sars-cov-2.html

34

CCP Antibody Testing

CCP demand has decreased dramatically due to decrease in cases, mixed results on studies evaluating the effectiveness of CCP, and alternative therapies now available (Remdesivir, monoclonal antibody therapies, dexamethasone, etc)

Many blood collection centers will be stopping routine antibody screening for all donors in the next few weeks

35

COVID-19 2021 Update

COVID-19 is not transmitted via transfusion and no donor screening test is required

14-day deferral for COVID-19 infection or after live-attenuated vaccine (if one becomes available); no deferral for currently available vaccines

CCP donors must be confirmed to have had COVID-19 via diagnostic test + symptoms or 2 different antibody tests, and must be qualified as high titer

36

Summary

Changes to several donor deferrals were recommended by the FDA in spring 2020 in order to support the US blood supply during the COVID-19 pandemic.

- HIV Risk Factors—Deferral shorted from indefinite or 12 months to 3 months for all risk factors
- CJD/vCJD—Removal of some geographic deferrals and removal of hGH and bovine insulin from the medication deferral list
- Malaria—Travel deferral for residents of non-endemic countries shortened from 12 months to 3 months

NAT for Babesia has been implemented for donors from endemic states, and NAT for Zika was eliminated in spring 2021 due to a significant drop in cases worldwide

COVID-19 is not known to be transmitted via transfusion and routine donor testing is not required; donors are deferred for 14 days after COVID-19 infection. Antibody testing is required to qualify high-titer CCP donors

37

Questions?

38