



July 21, 2022

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm 1061
Rockville, MD 20852

Submitted via <http://www.regulations.gov>

Re: Docket No. FDA-2022-D-0362, “Blood Pressure and Pulse Donor Eligibility Requirements: Compliance Policy; Draft Guidance for Industry”

Dear Dockets Manager:

AABB (Association for the Advancement of Blood and Biotherapies) and America’s Blood Centers (ABC) are pleased to submit joint comments to the U.S. Food and Drug Administration (FDA) in response to the recently released guidance entitled, “[Blood Pressure and Pulse Donor Eligibility Requirements: Compliance Policy](#)” (the Draft Guidance).

We begin by acknowledging the agency’s response to our requests for regulatory relief with review and consideration of regulations and recommendations that are outdated, duplicative, overly burdensome, and unnecessary to protect the public health. We appreciate the agency’s commitment to help the industry promote a safe and adequate supply of blood and blood products.

Comment 1 is a general comment:

Background, page 2 of the draft guidance:

In November 2009, FDA held a Blood Products Advisory Committee (BPAC or Committee) meeting to seek the Committee’s advice on, among other things, whether available data support the utility of obtaining predonation blood pressure and pulse measurements as predictors of the risk of adverse response to donation . The majority of the Committee responded that data did not establish predonation blood pressure as a predictor of risk of an adverse response; the Committee was divided on whether pulse

measurement was a predictor of adverse reactions. However, many members of the committee stated that pulse and blood pressure measurement should be retained as part of the donor assessment. ... Several members raised concerns of an association between high pulse rates and increased rates of vasovagal reactions. However, it was noted that data have shown that donors with low pulse rates are not at increased risk of reactions.”

Comment 1: Our organizations strongly believe that we must mitigate against donor adverse reactions. Such reactions are harmful to donors and to the blood supply by reducing donor return. That said, we believe that such mitigation should focus on known evidence-based risks including age, blood volume, first-time donor status and gender. We believe that based on an absence of science supporting the process, pre-donation blood pressure and pulse do not play a role in risk mitigation.

Recommendation: Based on the absence of data to support any correlation with risk to the donor, we recommend that FDA not take regulatory action regarding the requirements for performing pre-donation blood pressure and pulse measurement.

Rationale: As described in the draft guidance (above), FDA’s justification for the new blood pressure requirements focused on the discussions of the [2009 BPAC Meeting](#) and described that even though the vote did not support blood pressure measurement as a predictor of risk, many members of the committee stated that “blood pressure should be retained as part of donor assessment.” This “just in case” approach to requirements for blood pressure and pulse is not consistent with today’s standards for evidence-based regulatory decision-making. The BPAC may suggest additional requirements without a scientific basis, as seen in 2019 when the BPAC suggested blood donor centers should continue Zika virus (ZIKV) testing in the documented absence of ZIKV risk for the sole purpose of ZIKV surveillance, but not because it was necessary to protect the safety of the transfusion recipient. We suggest that the agency’s current approach for vital signs is also inconsistent with evidence-based decision-making and does not increase donor safety.

Blood pressure and pulse are poor predictors of adverse reactions in donors; both may be elevated because of anxiety, emotion, exertion, or caffeine. In addition, the value of a single blood pressure measurement has been called into question, especially in the blood donor setting where prospective donors may be anxious; accurate measurement of blood pressure requires specific conditions of a calm and quiet environment and a series of at least three serial blood pressure measurements. Out-of-range blood pressure and pulse measurements are not independent indicators of risk of vasovagal reactions, especially compared to more important factors such as young age, first-time donor status and gender.

Data from a large, independent blood center in Texas (available upon request) accumulated over 10 years (2010-2020), shows that while blood pressure and pulse values examined alone initially appear to predict donor reactions linearly at the extremes of their range, these vital signs actually interact with other factors in determining which donors have reactions. This data encompasses over 1.1 million donations and looks at more than 34,000 reactions in allogeneic donors. For example, reactions due to high pulse occur far more commonly in female donors with low weight. Similarly, low weight and young age are both more predictive of whether a reaction will

occur than any systolic or diastolic blood pressure value. Blood centers have already made accommodations to reduce reactions in younger and smaller donors. Therefore, they should not have to disqualify other donors with a range of vital signs that experience shows will tolerate donation quite well. Additionally, management of such out-of-range measurements places an undue burden on Medical Directors, diverting their attention from more pressing issues.

In the event FDA intends to take regulatory action with respect to the requirements to determine donor eligibility based on blood pressure and pulse measurement, we have the following comments:

Comment 2

IV. DONOR BLOOD PRESSURE AND PULSE ELIGIBILITY REQUIREMENTS – COMPLIANCE POLICY

A. Blood Pressure (21 CFR 630.10(f)(2))

For a donor with blood pressure measurements outside of the specified limits (90-180 mm Hg systolic or 50-100 mm Hg diastolic), we do not intend to take regulatory action with respect to the requirement in 21 CFR 630.10(f)(2) that the donor may be permitted to donate only when the responsible physician examines the donor, when the responsible physician conducts a telephonic or other offsite consultation, and determines and documents that the health of the donor would not be adversely affected by donating. Consistent with 21 CFR 630.5(b)(1)(i)(A) and 21 CFR 630.5(c)(1)(i)(A)(1), the responsible physician must not delegate this determination of the donor's health.

Comment 2: The draft guidance provides minor relief. Although blood pressure may be assessed telephonically/remotely there remains the requirement for the physician to perform this assessment. Therefore, as a practical matter, out-of-range pulse calls to the physician are replaced with out-of-range blood pressure evaluations. Although the guidance allows for donors who would otherwise be deferred for out-of-range blood pressure to be accepted, this remains logistically burdensome, especially when a single physician covers operations in multiple states.

Recommendation: Allow the delegation of out-of-range blood pressure assessment to be performed by qualified designees, when the blood establishment maintains and follows established protocols and/or algorithms as defined in approved standard operating procedures without consultation with the responsible physician.

Rationale: No new data is provided in the draft guidance to support the requirement for medical director assessment of out-of-range blood pressure measurements.

Comment 3

B. Pulse (21 CFR 630.10(f)(4)) and Medical Supervision (21 CFR 630.5(b)(1)(i)(B) and 21 CFR 630.5(c)(1)(i)(A)(2))

For a donor with a pulse measurement below 50 bpm who self-reports being a healthy athlete, we do not intend to take regulatory action with respect to the requirement in 21 CFR 630.10(f)(4) that the donor may be permitted to donate only when the responsible physician determines and documents that the health of the donor would not be adversely affected by donating, and the requirements in 21 CFR 630.5(b)(1)(i)(B) and 21 CFR 630.5(c)(1)(i)(A)(2) that the responsible physician must not delegate this determination of the donor's health. We intend to apply this compliance policy when the blood establishment establishes, maintains and follows SOPs that:

- are approved by the responsible physician of the blood establishment; and,
- allow for donation by a donor with a pulse measurement below 50 bpm who self-reports being a healthy athlete without consultation with the responsible physician.

For a donor with an irregular pulse, we do not intend to take regulatory action with respect to the requirement in 21 CFR 630.10(f)(4) that the donor may be permitted to donate only when the responsible physician determines and documents that the health of the donor would not be adversely affected by donating, and the requirements in 21 CFR 630.5(b)(1)(i)(B) and 21 CFR 630.5(c)(1)(i)(A)(2) that the responsible physician must not delegate this determination of the donor's health. We intend to apply this compliance policy when the blood establishment establishes, maintains, and follows SOPs that:

- are approved by the responsible physician of the blood establishment; and,
- define medical criteria for donation by a donor with an irregular pulse without consultation with the responsible physician.

Comment 3: There is no discretion to allow donation by a donor with a pulse measurement below 50 bpm who reports the use of a beta-blocker.

Recommendation: Allow the delegation for the assessment of a donor with a pulse measurement below 50 bpm who reports the use of a beta-blocker to be performed by qualified designees when the blood establishment maintains and follows established protocols and/or algorithms as defined in approved standard operating procedures without consultation with the responsible physician.

Rationale: Blood centers report a significant number of donors with levels of exercise that would not qualify them as "athletes" and those who report the use of a beta-blocker that is well recognized to be sufficient to lower pulse in these otherwise healthy individuals.

Comment 4: The draft guidance does not allow the assessment of a donor with a pulse measurement above 100 to be delegated/performed by a qualified designee.

Recommendation: Allow the delegation for the assessment of a donor with a pulse measurement between 100 and 110 to be performed by qualified designees when the blood establishment maintains and follows established protocols and/or algorithms (e.g. estimated blood volume, age, gender, first time vs repeat donor status, estimation of anxiety, prior history of reactions) as defined in approved standard operating procedures without consultation with the responsible physician.

Rationale: As described above, in the Texas blood center data, high pulse alone did not predict reactions, only in combination with factors like young age or low body weight.

The Association for the Advancement of Blood & Biotherapies (AABB) is an international, not-for-profit organization representing individuals and institutions involved in the fields of transfusion medicine and biotherapies. Since 1947, AABB has worked collaboratively to advance the field through the development and delivery of standards, accreditation and education programs. AABB is dedicated to its mission of improving lives by making transfusion medicine and biotherapies safe, available and effective worldwide.

Founded in 1962, America's Blood Centers is North America's largest network of community-based, independent blood programs. The network operates more than 600 blood donor centers providing over half of the U.S., and a quarter of the Canadian blood supply. These blood centers serve more than 150 million people and provide blood products and services to more than 3,500 hospitals and healthcare facilities across North America. America's Blood Centers' U.S. members are licensed and regulated by the U.S. Food and Drug Administration. Canadian members are regulated by Health Canada.

Thank you for the opportunity to offer these comments. Questions concerning these comments may be directed to scarayiannis@aabb.org.

Sincerely,

[signatures on file]

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