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American Red Cross

June 11, 2021

Dr. Kristen Honey
Chief Data Scientist
Senior Advisor
Office of the Assistant Secretary for Health
Department of Health and Human Services
200 Independence Ave., SW
Washington, DC 20201

Re: Request for Information: Developing the National Public Health Strategy for the Prevention and Control of Vector-Borne Diseases in Humans (HHS-OASH-2021-0001)

Dear Dr. Honey,

AABB, America's Blood Centers, and the American Red Cross appreciate the opportunity to submit comments in response to the request for information intended to inform the development of a national strategy on vector-borne diseases. Collectively, our organizations represent the nation's blood collection establishments, transfusion services, and transfusion medicine professionals. Our organizations strongly support HHS' effort to develop a national public health strategy to address vector-borne diseases, which will include improving surveillance, diagnosis, prevention, treatment, and research.

Blood transfusions are medically necessary, routine treatments for patients with chronic health conditions, life-saving therapies for patients who experience blood loss from trauma or surgery and must be available in emergencies. A variety of human cells, tissues, and cellular and tissue-based products (HCT/Ps) are used as cellular therapies and other biotherapies to treat different diseases or conditions. For instance, hematopoietic stem cells are used to treat leukemia, lymphoma and sickle cell disease.

While methods of transmission vary, some vector-borne pathogens can be transmitted via blood transfusions and may be linked to therapies involving HCT/Ps. Therefore, we urge HHS to integrate the safety and availability of blood and HCT/Ps into the national public health strategy for the prevention and control of vector-borne diseases in humans.

We offer the following responses to the questions presented in the RFI:

1. **What do you recommend as the top priorities to address vector-borne diseases in the United States during the next five years? Why are these the most important priorities?**

The top priorities to address vector-borne diseases in the United States during the next five years include:

(1) Strengthening and investing in surveillance related to vector-borne diseases;
(2) Supporting research to prevent and mitigate the impact of vector-borne diseases; and
(3) Coordinating public and private-sector prevention and response efforts.

In response to the subsequent questions, we explain why these priorities are important and offer goals, objectives and strategies that are aligned with the priorities. As HHS continues to develop the national

public health strategy for the prevention and control of vector-borne diseases in humans, we urge the Department to include considerations related to the safety and availability of blood and HCT/Ps in each priority area.

2. What goals, objectives, and strategies would you propose for each of your top priority areas?

Strengthening and Investing in Surveillance: We propose that HHS set a goal to augment, align, and expand surveillance related to vector-borne diseases. This goal can be achieved through several objectives and strategies, including:

- **Funding and enhancing the national surveillance infrastructure so that it tracks vector and human activities, including the extent and activities of the agents, their vectors and human infections throughout the US, in near real-time.** Such surveillance should also include programs to monitor non-vector borne transmissions including via blood transfusion and therapies involving HCT/Ps. Comprehensive, timely surveillance is key to developing and adopting evidence-based policies and procedures that are proportional to documented risk, mitigating the risks of these vector-borne diseases, and ensuring the availability of safe blood and HCT/Ps. This should include the wide variety of vector-borne agents identified in the US, many of which have been documented to be transmitted by substances of human origin or have the potential to be transmitted. There are numerous examples of these agents in the scientific literature.

  Existing surveillance efforts are flawed. For example, Zika virus (ZIKV) is transmitted by *Aedes* mosquitoes, and can be transmitted through blood transfusion as well as intrauterine, perinatal, and sexual routes. There is also a potential for ZIKV transmission through transplantation of gestational tissues, although the risk posed by ZIKV is unclear. Currently, the Centers for Disease Control and Prevention's (CDC) conducts surveillance to identify areas at "increased risk for" ZIKV. The CDC's website, which is updated as of February 28, 2019, indicates that there are currently no areas in the United States at increased risk of ZIKV transmission through blood or tissue donation. While there are no areas in the world having an outbreak at this time, there are many areas throughout the world classified as "Current or Past Transmission but No Current Outbreak." Notably, CDC indicates that "these counties have a potential risk of Zika, but we do not have accurate information on the current level of risk."[1]

  Even though the CDC's surveillance data are over two-years old and do not reflect current risk levels, the Food and Drug Administration (FDA) continues to rely on this surveillance tool to identify cord blood units that are derived from "ineligible donors" in its guidance entitled, "Donor Screening Recommendations to Reduce the Risk of Transmission of Zika Virus by Human Cells, Tissues, and Cellular and Tissue-Based Products."[2] As a result of this designation, physicians are discouraged from using these cord blood units (only under "Urgent Medical Need"), they cannot be licensed by the FDA, and they cannot be included in and funded by the National Cord Blood Inventory. Thus, investing in and improving real-time surveillance is paramount to protecting the public's health and to advancing evidence-based policies.

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[1] CDC, Blood & Tissue Safety: Geographic areas at increased risk for Zika virus transmission through blood or tissue donation, https://www.cdc.gov/zika/areasatrisk.html (last visited March 16, 2021).

[2] FDA, Donor Screening Recommendations to Reduce the Risk of Transmission of Zika Virus by Human Cells, Tissues, and Cellular and Tissue-Based Products: Guidance for Industry (March 2016, updated May 2018), *available at* https://www.fda.gov/media/96528/download.

- **Dedicating resources to support the screening, testing and surveillance activities conducted by the blood community, which possesses unique, well-established expertise that is critical to the nation's public health infrastructure.** The lack of reliable, community-based national surveillance data is historically quite problematic and limits the nation's ability to understand the epidemiology of vector-borne diseases. Despite the current lack of funding, the blood community has been instrumental in early detection through surveillance, screening, and testing activities related to multiple infectious disease agents, including ZIKV.

  For example, in 2016, FDA classified ZIKV as a relevant transfusion-transmitted infection and issued guidance that required blood collection establishments to test blood donations for the ZIKV. Blood collectors immediately implemented the new testing requirements. Additionally, in the absence of a national surveillance infrastructure, AABB created a Zika Virus Biovigilance Network that enabled blood collection establishments to voluntarily report data on the number of blood donations in the United States from donors with suspected ZIKV infection, and then mapped the information to geographic locations. While AABB established this surveillance tool to support the blood community, many state and local public health departments contacted AABB and used the information in the Zika Virus Biovigilance Network as a proxy for determining the incidence and prevalence of ZIKV in their geographic regions.[3]

  In May 2021, FDA eliminated the requirement that blood establishments test blood donations for the ZIKV. FDA relied on data from CDC as well as the AABB Zika Biovigilance Network to confirm the absence of ZIKV infection in the donor population. Our organizations strongly support this decision and FDA's evidence-based approach to updating the Zika policy for blood establishments.

  However, both the requirements that blood collectors test blood for vector-borne agents and the establishment of associated Biovigilance Networks are unfunded initiatives that cannot be sustained. In December 2017, members of the Blood Product Advisory Committee expressed their reluctance to support discontinuing ZIKV testing although few if any new infections in blood donors were documented (the last in March 2018) due to the loss of important hemovigilance data. We urge HHS to dedicate funding to support the screening, testing, and surveillance activities conducted by the blood community. As described throughout these comments, these efforts are a critical part of the public health infrastructure, can benefit donors, patients, local communities, and the nation, and often support other sectors.

Fund Research: We encourage HHS to set a goal of funding research intended to prevent and mitigate the impact of vector-borne diseases, including research related to the potential risk of transmission through blood and HCT/Ps. Investing in research is essential to strengthening the evidence related to the pathogenicity and transmissibility of vector-borne pathogens transmitted by blood and HCT/Ps, which is needed for improved, evidence-based policymaking that reflects documented risk. Vector-borne pathogens are numerous (hundreds of unique agents), quite diverse, and ongoing research is needed since the methods of non-vector-borne transmission may differ. For instance, while there is evidence that many existing tick-borne disease agents can be transmitted via blood transfusions or therapies involving HCT/Ps, other tick-borne diseases have not been linked to such transmissions.

[3] AABB modeled the ZIKV Biovigilance Network after that used for West Nile Virus (WNV) (established in 2003) and a similar Biovigilance Network that was used for Chagas (established in 2007). The AABB Biovigilance Networks for infectious agents transmitted by blood and HCT/Ps have been used as public health tools in the absence of other real-time networks for reporting.

Coordinate public and private-sector prevention and response efforts: We encourage HHS to continue to improve coordination and communication between Federal agencies and departments, between Federal, state, and local surveillance activities, and between public and private sector efforts. In the absence of a national surveillance infrastructure, it is essential to leverage the expertise that exists within the blood community and the existing structure of blood center screening and testing operations, and to integrate all existing surveillance efforts to support evidence-based policies that protect the public's health.

3. Do you have recommendations on specific research or programmatic efforts to improve surveillance, diagnosis, prevention, and treatment of vector-borne diseases?

We recommend that HHS consider the following research and programmatic efforts to improve surveillance, diagnosis, prevention, and treatment of vector-borne diseases:

- Invest in open data surveillance platforms that can serve multiple public and private stakeholders, such as Federal, state, and local governments; the blood and biotherapies community; researchers and private citizens.

- Ensure that surveillance, research, and other activities are designed to capture and disseminate data on emerging vector-borne disease agents. These emerging diseases potentially present challenges to the safety of blood and biotherapy recipients. Research, surveillance and other activities should specifically address the magnitude of the risk for transmission and outcomes from infections from vector-borne disease agents via blood transfusion or by HCT/Ps.

- Provide CBER with the opportunity to offer input into the design of surveillance, research, programs, and other activities so that these efforts are constructed in a manner that can inform, update and support evidence-based policies impacting the blood and biotherapies community. Additionally, implement a process that ensures that findings from research, surveillance efforts, other programs and activities are immediately made available to CBER. In addition, building on efforts of federally funded, multisite research involving blood centers including the NIH-funded REDS, the FDA-sponsored TTIMS, FDA-sponsored ADVANCE and the CDC-funded MASS-BD, further multicenter research will help ensure that policies regulating blood and biotherapies improve patient care and are (1) implemented and continuously updated to protect the safety and availability of blood and HCT/Ps; (2) not overly burdensome in the absence of data implicating transmission risk by blood or HCT/Ps; and (3) support the availability of blood and HCT/Ps.

  For instance, FDA's "Recommendations for Reducing the Risk of Transfusion-Transmitted Babesiosis; Guidance for Industry" takes a risk-based, regional approach to regulating blood donations. Currently, FDA requires blood collection establishments to test blood donations when collected in 14 states (Connecticut, Delaware, Maine, Maryland, Massachusetts, Minnesota, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, Vermont, Virginia, Wisconsin) and Washington, D.C. Since the epidemiology of vector-borne diseases is continuously evolving, additional funding for studies and expanded surveillance efforts can be used to inform and update FDA's policies.

- Research should include economic studies and operational activities related to the costs associated with preventing transmission and mitigating the risk of vector-borne diseases. For instance, the targeted approach to regional testing of blood donors for evidence of babesiosis has been a crucial public health function carried out by blood operators to effectively mitigate risk in

states with the highest risk, eliminating transfusion-transmitted babesiosis, thus far. The current funding model is flawed and is not aligned to support this public health role. We believe that it is important to understand the positive economic impact of this type of public health activity, and to dedicate funds and develop reimbursement policies to support the function. Additionally, research may focus on cost-effective methods to develop and implement multiplex and microarray technologies that simplify and streamline testing or to further develop and implement FDA-approved pathogen inactivation technologies.

4. Any additional topics you wish to provide input on.

As HHS continues to develop a national strategy on vector-borne diseases, we encourage the Department to consult with individuals with expertise related to the impact of vector-borne diseases on the safety and availability of blood and HCT/Ps. Experts in blood transfusion safety as well as the transmission of diseases via HCT/Ps can contribute epidemiological and clinical research information related to blood and HCT/P donor collections and testing processes. Additionally, individuals from the blood and biotherapies community can explain operational considerations associated with risk mitigation.

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If you have any questions or need additional information, please contact Leah Stone (lmstone@aabb.org, 301-215-6554), Diane Calmus (dcalmus@americasblood.org, 202-654-2988) or Julie Manes (Julie.manes@redcross.org, 202-417-5147).

Sincerely,

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