INTERVIEW

An Overview of Regulatory Guidelines and Scientific Evidence Guiding Our COVID-19 Response

Featuring
Sue Grondin, Associate Director, Clinical Project Management
Brianna Schoen, PhD, Scientific Director
Brad Taylor, PhD, Global Marketing Director

Brad Taylor, Ph.D.: My name is Brad Taylor and I am Director of Global Marketing at HemaCare, A Charles River Company. We at HemaCare have been closely monitoring the COVID-19 pandemic and have consistently reacted with the safety and wellbeing of our donors, employees, and clients in mind. We are an essential business and, thus, have continued to support your research with our cryopreserved materials throughout this crisis. Since California has initiated a phased reopening approach, our advisory committee has determined that we can safely resume operations in our donor facility as well.

Today we have prepared a few slides and I have invited two guests who were influential to this decision to sit with me and discuss some of the guidance and data that weighed into the development of our reopening strategy so that you understand the steps we are taking to ensure the safety and quality of our products.

REGULATORY GUIDELINES

Brad Taylor, Ph.D.: First, I would like to introduce Sue Grondin who is the Associate Director of Clinical Project Management. Welcome Sue.

Sue, what regulatory guidance has been issued to date and how has that affected HemaCare's plan for resuming operations?

Sue Grondin: Thank you for the introduction, Brad. Let's start by looking at the current information that the FDA has issued in relation to COVID-19, and later we'll discuss the measures that HemaCare is taking in response to that information.

The FDA issued out a general information statement initially on February 14, 2020 and then issued an update to that statement on April 1, 2020. The sections from those statements relative to HemaCare's operations are summarized on this slide. FDA noted that, to date, there have been no reported cases of transmission of the virus through transfusion or transplant, but they did acknowledge that there have been trace amounts of viral RNA detected in blood samples from patients who are severely ill with the virus. They also reiterated that at this time, the routine screening measures currently in place to assess a donor's eligibility to donate blood or tissues are sufficient to detect possible infection with the virus. These measures include a physical exam of the donor, measurement of body temperature, and assessment of the donor's overall health prior to donation. In addition to these routine screening measures, they noted that facilities may also wish to further investigate the possibility that a potential donor may be at an increased risk for exposure to the virus. As noted in this slide, these additional measures include asking if a potential donor has had close contact with anyone diagnosed with or suspected of having COVID-19 in the past 28 days and, of course, not allowing anyone to donate who was themselves diagnosed with or suspected of having COVID-19 for at least 28 days.

Brad Taylor, Ph.D.: Is the FDA the primary source for guidance on this issue?

Sue Grondin: In addition to the FDA information, the accrediting bodies and other expert organizations in the field of cell therapy and tissue transplant have also issued out statements related to COVID-19.

AABB, which is HemaCare's accreditation agency, is currently deferring to the FDA guidelines. FACT and NMDP issued out brief statements which, in essence, defer to the FDA guidelines.

Both organizations pointed out that since COVID-19 is a respiratory virus, it is not likely to be transmitted by blood. These organizations are also pointing out the same additional considerations as the FDA with regards to taking some extra measures to ensure that donors who may be at an increased risk of exposure are not allowed to donate for at least 28 days following the possible exposure to the virus.

Brad Taylor, Ph.D.: How about other regions outside of the United States, for instance, what guidance has Europe issued on this matter? They have also seen a large number of cases and death during this pandemic?

Sue Grondin: We have also looked into what actions may be suggested in the EU with regards to COVID-19 and donor eligibility assessment for cell and tissue donation and have found information similar to what the FDA has issued. The ECDC (the equivalent to our CDC) issued out statements noting that COVID-19 is being treated like other respiratory viruses and that it has not been reported to be transmitted by transfusion or transplant. They also indicate that testing of donors is not recommended based on this information.

Brad Taylor, Ph.D.: Thanks for that insightful information Sue. It certainly provides some great context for the structure of our reopening plan.

Next, I would like to introduce Brianna Schoen, Ph.D., Scientific Director at HemaCare. Welcome Brianna and thanks for joining me today.

SCIENTIFIC EVIDENCE

We have heard from Sue about the regulatory bodies and their guidance. Certainly, that guidance is based on firm scientific data. Of course, there is still much to be understood about this virus, but what do some of the most current findings tell us about the virus and transmission?

Brianna Schoen, Ph.D.: A study published in the high impact medical journal "Lancet" examined a cluster of pneumonia cases in Wuhan in late 2019 where 41 admitted hospital patients were confirmed to have infection with SARS-CoV-2. Of these patients, RNA could be detected by RT-PCR in 15% of patients. However, the cycle threshold was high, indicating a low level of viral RNA in plasma.

Another study published in the "Lancet" reported similar results in a family cluster of COVID-19 infection, where RNA could only be detected in one of the 6 patients. Again, a high cycle threshold confirms that only low levels of viral RNA were present in the serum.

In line with this publication, a study published in the Journal of the American Medical Association, examined presence of SARS-CoV-2 RNA in multiple tissues, including blood, across 205 inpatient SARS-CoV-2 patients across three hospitals in China. Viral RNA was only detected in 3 out of 307 blood samples investigated by RT-PCR. For these samples, the cycle threshold was again high, indicating an extremely low level of viral RNA.

Brad Taylor, Ph.D.: Thanks Brianna for walking us through those studies. One can certainly see why FDA guidelines are aimed at detection and preventing spread but don't seem to make recommendations about testing materials such as blood, plasma, or cells that we would encounter in our donor room.

Do you think these studies are a good summary of published data to date? What other considerations should we take into account when working with donor materials?

Brianna Schoen, Ph.D.: These studies represent the most relevant information currently available in high-impact peer-reviewed journals. To summarize, viral RNA could only be detected in blood, serum, or plasma of a small subset of hospitalized COVID-19 patients. Viral RNA detection always required high RT-PCR cycle threshold values, indicating that only low levels of viral RNA were present.

Now we should keep in mind that even though SARS-CoV-2 RNA could be detected in some blood-derived specimens from patients, the detection of viral RNA by RT-PCR is not equivalent to the detection of intact infectious virus.

It is also important to keep in mind that there have not been any documented cases of SARS-CoV-2 infection through blood-derived products. As SARS-CoV-2 is a recently discovered emerging virus, it is prudent to also consider whether other related viruses may have been shown to be transmitted through blood. To date, there have been no documented cases of transmission of other related coronaviruses, such as SARS-CoV or MERS-CoV via blood.

As SARS-CoV-2 research continues and with improvements to SARS-CoV-2 testing, it is possible that new data and guidelines may emerge. That is why at HemaCare, we continually monitor and assess information and regulatory guidelines as they develop.

Although the risk of transmission of SARS-CoV-2 via blood-derived materials remains extremely low, it is important to always treat any human blood-derived material as potentially infectious. Therefore, regulations for the treatment of infectious materials must always be followed and appropriate PPE must always be used when handling human blood-derived materials.

Brad Taylor, Ph.D.: Thanks again Brianna for sharing that information. Sue as we say so often here, the health and safety of our donors is paramount as it is their generosity and donation of materials that is really the foundation of the development of so many life-saving therapies.

HEMACARE'S RESPONSE AND STEPS TO ENSURE SAFETY

Sue, we have detailed information available online, but would you mind walking us through some of the steps we have put in place to achieve this goal?

Sue Grondin: Sure, first, let's talk about

Facility Entry and Lobby

- Prior to entering the facility, donor temperature will be measured.
- Additional screening questions will be asked to assess their risk of exposure to COVID-19.
- Donors will be required to wear personal protective equipment (PPE) supplied by HemaCare.
- Extra protective barriers have been installed in the reception to supplement supplied PPE.
- Seating areas have been clearly demarcated to ensure proper social distance is maintained.

Donor Screening and Collection

- After entry, donor temperature confirmation prior to donation using validated and calibrated thermometers.
- Licensed medical staff ask more questions to assess possible exposure to the virus.
- Donor health exam performed with complete blood count (CBC) panel.
- Donor beds and canteen seating configured for proper social distancing.
- Strict disinfection and sanitization of areas between collections.
- Protocols in place to minimize the need for touching common surfaces such as entertainment equipment and snacks.

Donor Deferrals

- Donors will be deferred for 28 days if they report any of the situations listed:
  - Were in contact with COVID-19 positive or suspected patients.
  - Had a diagnosis of COVID-19 infection.
  - Were under self-quarantine orders.
  - Show symptoms indicative of infection even if not tested.
- Follow-up process with donors to inform of exposure or diagnosis of COVID-19 within 1-month following donation.

Preventing the Spread Internally

- Travel is discouraged for HemaCare employees.
- We are encouraging social distancing in the office place.
- This includes working from home for all employees when possible.
- Dedicated entry and exit.
- Daily temperature checks.

Though we will continue to monitor the current AABB, FDA, EMA, and FACT guidelines diligently, there is currently no evidence to support the spread of COVID-19 via blood, blood products, or via the implantation, transplantation, infusion, or transfer of human cells, tissues, or cellular or tissue-based products (HCT/Ps). If these guidelines change, we will notify our client base and take appropriate steps and precautions where warranted.

Brad Taylor, Ph.D.: Thank you Sue and Brianna for giving us this overview and details about the reopening plan and the safety measures we have implemented. As stated, we will continue to monitor the situation closely over the next weeks and as always, we will adhere strictly to regulatory guidelines. And thank you all for joining. I hope we have been able to answer questions concerning our plan to resume operations. For more information, please visit our website or, as always, reach out to your local BDE for technical support or assistance.

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