VoxSanguinis
The International Journal of Transfusion Medicine
ISBT International Society of Blood Transfusion
*Vox Sanguinis* (2021) **116**, 1117–1135

DOI: 10.1111/vox.13113

INTERNATIONAL FORUM

# International Forum on the Collection and Use of COVID-19 Convalescent Plasma: Protocols, Challenges and Lessons Learned: Summary

**Arwa Z. Al-Riyami, Thierry Burnouf, Mark Yazer, Darrell Triulzi, Levent Tufan Kumaş, Levent Sağdur, Nil Banu Pelit, Renée Bazin, Salwa I. Hindawi, Maha A. Badawi, Gopal K. Patidar, Hem Chandra Pandey, Rahul Chaurasia, Roberta Maria Fachini, Patrícia Scuracchio, Silvano Wendel, Ai Leen Ang, Kiat Hoe Ong, Pampee Young, Jarkko Ihalainen, Antti Vierikko, Yan Qiu, Ru Yang, Hua Xu, Naomi Rahimi-Levene, Eilat Shinar, Marina Izak, Carlos Alberto Gonzalez, David Martin Ferrari, Paula Verónica Cini, Robby Nur Aditya, Ratti Ram Sharma, Suchet Sachdev, Rekha Hans, Divjot Singh Lamba, Lise Sofie H. Nissen-Meyer, Dana V. Devine, Cheuk Kwong Lee, Jennifer Nga-Sze Leung, Ivan Fan Ngai Hung, Pierre Tiberghien, Pierre Gallian, Pascal Morel, Khuloud Al Maamari, Zaid Al-Hinai, Hans Vrielink, Cynthia So-Osman, Vincenzo De Angelis, Pierluigi Berti, Angelo Ostuni, Giuseppe Marano, Michel Toungouz Nevessignsky, Magdy El Ekiaby, James Daly, Veronica Hoad, Sinyoung Kim, Karin van den Berg, Marion Vermeulen, Tanya Nadia Glatt, Richard Schäfer, Rita Reik, Richard Gammon, Melissa Lopez, Lise Estcourt, Sheila MacLennan, David Roberts, Vernon Louw & Nancy Dunbar**

## Introduction

Coronavirus disease-2019 (COVID-19), caused by severe acute respiratory coronavirus 2(SARS-CoV-2), has rapidly spread since its first declaration by the World Health Organization (WHO) as a global pandemic in March 2020 [1]. Until vaccination has started to be rolled out in an increasing number of countries, different modalities of treatment were deployed in an attempt to combat this deadly virus but with limited efficacy so far [2]. Collection and use of convalescent plasma for coronavirus disease-2019 (COVID-19) (CCP) treatment for passive immunotherapy had gained interest worldwide and still is considered as a potentially effective therapeutic option when containing high-titre antibodies and administered early in the course of the infection [3,4] including against SARS-CoV-2 variants [5]. Transfusion of CCP itself has been conducted either within a framework of clinical trials or on a compassionate basis in patients with active SARS-CoV-2 infection. CCP may also be fractionated into hyperimmune immunoglobulins for treatment of patients or alternatively for prophylaxis in high-risk individuals such as healthcare providers or individuals who have the underlying risk factors, such as an exposure to persons with confirmed COVID-19 infection.

The medical rationale for transfusing CCP is based on historical perspectives that demonstrated the clinical benefit of transfusing convalescent plasma from recovered individuals in respiratory infections caused by other coronaviruses [6] as well as diseases such as Argentine haemorrhagic fever [7]. The advantages of CCP include its almost immediate availability (once safe recovered donors can be identified) as a local resource in all affected countries worldwide, while specific treatments and vaccines are under development and evaluation. The relative ease of access to CCP from recovered donors, and potential for deployment in different settings, including low- and middle-income countries, made it attractive especially in early stages of the pandemic. Soon after the start of the pandemic, recommendations and 'points to consider' have therefore been published by the International Society of Blood Transfusion (ISBT) to establish and share at a global level to ensure quality and safety, as well as respect of ethical principles, in the collection and use of CCP [8–11]. An emphasis was given to the fact that CCP transfusion was to be considered as an experimental therapy that, whenever possible, should be evaluated within the scope of controlled clinical studies to maximize the knowledge gained, with optimal monitoring of (1) convalescent donors, (2) CCP characteristics and (3) patients outcomes [9].

In addition, there was recognition of variations and gaps existing at a global level in the practices applied to the collection, testing and preparation of CCP [8,12]. ISBT initiated a multidisciplinary working group with representation from all six continents with the aim of reviewing existing practices on CCP preparation and use. It was felt that such information would be invaluable not only to document strategies implemented in CCP collection, but also as a tool for better preparedness against future pandemics.

This Vox Sanguinis International Forum aimed to gather information on the practice and challenges of

collection of CCP on an international level and to draw lessons learned from establishing a CCP collection programme for blood establishments and hospital-based blood services. This international forum was only intended for institutions that collect CCP. Participants were invited to participate in this international forum on 9 December 2020 and were asked to describe the CCP collection programme in their institutions or countries. Responses were collected up to 17 February 2021. The current document is a summary of the findings that have been collected and analysed for practices in place during the specified timeframe.

## Participants

Thirty-eight participants from 34 countries were invited to participate in the international forum. We aimed to cover all WHO regions and include both large national blood suppliers and smaller blood centres. We received 32 responses reflecting practice in 35 centres in 25 countries from around the world (Table 1).

## Responses

### *Describe your institution COVID-19 convalescent plasma (CCP) collection programme*

***Q1: Demographics***

The majority of the institutions had apheresis services, including the hospital-based centres. All hospital-based institutions were in hospitals that treated adults and children and had medical and surgical services. These hospitals ranged in size from 100 beds up to ~2000 beds.

***Q2: What type of CCP donation does your institution perform? How many times is a donor allowed to donate CCP by apheresis, and over what time period? Is the frequency different from routine plasma donation by apheresis? If whole blood (WB) is collected, are red blood cells and/or platelets derived from the WB donation used for standard transfusion?***

All respondents indicated that CCP is collected in their institution using plasmapheresis (Table 2). The frequency of plasmapheresis was variable between institutions. While 20 respondents indicated that the frequency did not differ from that of routine plasmapheresis, five institutions had CCP collection made at a higher frequency than what is permitted routinely. Two respondents indicated that plasmapheresis was an infrequent procedure in their institutions, only used for specific indications (e.g. collection of plasma for IgA-deficient patients) or was only established for CCP collection.

The majority of the institutions ($n$ = 16) allowed plasmapheresis every 2 weeks, while six allowed every week with variable maximum allowable donations per donor. The highest donation frequency was every 48 h reported by three centres. In Héma-Québec (Canada), CCP collection was initially performed at a frequency identical to that of standard plasmapheresis procedures (every 6 days, up to 12 weeks after first donation) for early CCP donations, but decreased to a maximum of 6 weeks after resolution of symptoms, considering the reported decline in the SARS-CoV-2 antibody titre with time [13–15]. In Singapore, the CCP plasmapheresis was initially conducted at the standard plasmapheresis procedure frequency and was subsequently increased to every 2 weeks to allow more frequent donation.

Eight institutions collected WB and plasmapheresis if the donor/units were found to have anti-SARS-CoV-2 antibodies, and donors meet all other donor eligibility criteria. Considering that these donors fulfilled blood donation qualifications and testing for transfusion-transmitted infections, red blood cells and/or platelet components derived from such donated WB were labelled for clinical use. This decision necessitated approval by the institutional ethics committee in Argentina. Two blood centres in the USA (American Red Cross and OneBlood) applied a minimum deferral period of 14 days from the time of resolution of COVID-19 infection for CCP and WB donation. Plasma components from qualified blood donors were labelled as CCP if they met the necessary levels of anti-SARS-CoV-2 antibodies. In Italy, WB collection from recovered COVID-19 individuals was introduced at later stages of the pandemic, and donors were allowed to donate blood after 10 days of recovery. In Norway, the decision to use derived red blood cells (RBCs) and platelets for standard transfusion was based on the European Center for Disease Prevention and Control and European Blood Alliance guidelines recommending accepting WB donors after 28 days following recovery. The same rule was applied in Australia and Israel. In Singapore, only male blood donors who had made standard WB donation with a history of COVID-19 within 6 months before the donation had their samples tested for SARS-CoV-2 neutralizing antibodies. Based on the antibody level present, a decision was made to label the WB-derived plasma as CCP. Derived RBCs and platelet components were labelled for clinical use. Some respondents indicated that the decision of labelling units as for standard components was made based on a lack of evidence of SARS-CoV-2 transfusion transmission (Norway, Australia).

***Q3: Is collected CCP intended for transfusion, prophylaxis, or fractionation purposes? If collected for transfusion, kindly indicate if collected for compassionate-use, trial-use or both?***

All respondents indicated that CCP is collected for transfusion purposes, and one also used it for preparation

**Table 1** Demographics of participating institutions

| Country, Institution | Type of institution | Hospital Beds | RBCs transfused/ year | Approximate number of collections/year |
|---|---|---|---|---|
| Americas | | | | |
| Argentina | Hospital-based BTS/BB | 421 | 587 | WB: 600 |
| Brazil | Hospital-based BS | 510 | 6000 | WB: 5500; Apheresis: 1750 |
| Canada, *Héma-Québec* | National BE | - | - | WB: 220 000; Plateletpheresis: 40 000 |
| Canada, *CBS* | National BS | - | - | WB: 763 319; Plateletpheresis: 11 339 |
| United States, *Vitalant* | Regional blood collector/TS | - | - | RBCs: 87 000; PLT: 25 000 |
| United States, *ARC* | National BE | - | - | WB: 4·4 million; Apheresis: 1·4 million |
| United States, *OneBlood* | Regional BS/BC | - | - | WB: 790 700; Plateletpheresis:48 507 |
| Africa | | | | |
| South Africa, *SANBS* | Regional BS/BC | - | - | WB: 900 000; Plateletpheresis: 18 138 |
| South Africa, *UCT* | Regional BS/BC | - | - | WB: 147 684; PLT: 9265 |
| Eastern Mediterranean Region | | | | |
| Egypt | Hospital-based BS | 100 | 25 000 | Data not provided |
| Israel | National BE | - | - | WB: 265 000, Plateletpheresis:550 |
| Oman | Hospital-based BS | 450 | 18 500 | WB: 12 500, Plateletpheresis: on demand |
| Saudi Arabia | Hospital-based BS | 780 | 12 000 | WB: 12 500; Plateletpheresis: 100 |
| Europe | | | | |
| Belgium | National BE | - | - | RBCs: 160 000; PLT: 11 000 |
| Finland | National BE | - | - | WB: 200 000; Plateletpheresis: 2500 |
| France | National BE | - | - | WB: 2·5 million; Apheresis: 440 000 |
| Germany | Regional BS/BC | - | - | WB: 5849; Plateletpheresis: 379 |
| Italy | National BC | - | - | WB and apheresis: 2 996 264 |
| Norway | Hospital-based BS/BC | - | - | WB: ~175 000; Plateletpheresis: 5000 |
| The Netherlands | National BE | - | - | WB: 413 653; Apheresis 313 811 |
| Turkey, *BUU* | Hospital-based BS | 900 | 22 000 | WB: 20 000; Plateletpheresis: 1700 |
| Turkey, *TRC* | National BS/BC | - | - | WB: 2 766 581; Apheresis: 42 656 |
| Turkey, *AHGH* | Hospital-based BTS/BB | 2129/16 hospitals | 44 465 | WB: 1080; Apheresis: 5800 |
| United Kingdom | National BE | - | - | RBCs: 1·4 million; PLT: 255 000 |
| South-East Asia | | | | |
| India, *AIIMS* | Hospital-based BTS/BB | 2000 | 75 000 | WB: 80 000; Apheresis: 2000 |
| India, *PGIMER* | Hospital-based BTS/BB | 1740 | 135 685 | WB: 57 842 |
| Indonesia | National BS/BC | - | - | WB: 3 523 982 |
| Western Pacific | | | | |
| Australia | National BS/BC | - | - | WB: 690 115; Plateletpheresis 27 024 |
| China, *BRCBC, WHBC, SXBC* | Regional BS/BC | - | - | *BRCBC:* WB: 450 000*;* Plateletpheresis: 68 000<br>*WHBC:* WB: 350 000*;* Plateletpheresis: 70 000<br>*SXBC:* WB:32 000*;* Plateletpheresis: 40 000 |
| Hong Kong, China | Regional BS/BC | - | - | WB: ~215 000; Apheresis: ~10 000 |
| Singapore, *HAS, TTSH* | National BE (*HAS)* Hospital-based BTS/BB (*TTSH)* | >1700 | 15 000 | WB: 117 000; Apheresis: 8000 |
| South Korea | Hospital-based BTS/BB | 2437 | 50 200 | NA |

AHGH, Acıbadem Health Group Hospitals; AIIMS, All India Institute of Medical Sciences; ARC, American Red Cross; BB, blood bank; BC, blood centre; BE, blood establishment; BRCBC, Beijing Red Cross Blood Center; BS, blood service; BTS, blood transfusion service; BUU, Bursa Uludağ University; CBS, Canadian Blood Services; HAS, Health Sciences Authority; PGIMER, Post Graduate Institute of Medical Education and Research; PLT, platelets; RBC, red blood cell; SANBS, South African National Blood Service; SXBC, Shaanxi Blood Center; TRC, Turkish Red Crescent; TS, transfusion service; TTSH, Tan Tock Seng Hospital; UCT, University of Cape Town; WB, whole blood; WHBC, Wuhan Blood Center.

**Table 2** Convalescent plasma donation programmes

| Country, Institution | Intended use of CCP | Method of CCP collection | Frequency of CCP Plasmapheresis | Frequency different from local standard plasmapheresis? | Components used from whole blood? |
|---|---|---|---|---|---|
| Americas | | | | | |
| Argentina | Clinical trials; Compassionate use | Plasmapheresis Whole blood | Every 2 weeks, maximum 1 l/week, 15 l/year; Maximum 600 ml per session | No | Yes |
| Brazil | Clinical trials; Compassionate use | Plasmapheresis | Maximum 4 over 2 months<br>Shorter inter-donation interval can be allowed in specific circumstances<br>Maximum 600 ml per session | No | NA |
| Canada, *Héma-Québec* | Clinical trials | Plasmapheresis | Every 6 days[a] | No | NA |
| Canada, *CBS* | Clinical trials | Plasmapheresis | Every 7 days | No | NA |
| United States, *Vitalant* | Clinical trials; Compassionate use | Plasmapheresis | Medical director discretion, up to every 48 h | No | NA |
| United States, *ARC* | Clinical trials; Compassionate use | Plasmapheresis Whole blood | Every 7 days, maximum of 8 over 3 months | No | Yes |
| United States, *OneBlood* | Clinical trials; Compassionate use | Plasmapheresis Whole blood | Medical director discretion, up to every 48 h | No | Yes |
| Africa | | | | | |
| South Africa, *SANBS* | Clinical trials; Compassionate use; Fractionation | Plasmapheresis | Every 2 weeks, maximum of 24 donations/year | No | NA |
| South Africa, *UCT* | Clinical trials; Fractionation | Plasmapheresis | Every 2 weeks, maximum of 24 donations/year | Not specified | NA |
| Eastern Mediterranean Region | | | | | |
| Egypt | Clinical trials; Fractionation | Plasmapheresis | Every 2 weeks | No | NA |
| Israel | Clinical trials; Compassionate use | PlasmapheresisWhole blood | Every 2 weeks, maximum of 6 per 10 days | Yes | Yes |
| Oman | Clinical trials | Plasmapheresis | Every 7 days, maximum of 4 | NA | NA |
| Saudi Arabia | Clinical trials | Plasmapheresis | Every 7 days, maximum of 2 | Not specified | NA |
| Europe | | | | | |
| Belgium | Clinical trials; Compassionate use | Plasmapheresis | Maximum 2 l/month, 23/year, and 15 l/year<br>Maximum 650 ml per session | No | NA |
| Finland | Clinical trials | Plasmapheresis | Every 2 weeks, maximum of 5 | NA | NA |
| France | Clinical trials; Compassionate use | Plasmapheresis | Every 2 weeks, maximum of 24/year | No | NA |
| Germany | Clinical trials; Compassionate use | Plasmapheresis | Every 2 days (48 h), maximum of 60/year | No | NA |
| Italy | Clinical trials; Compassionate use; Fractionation | PlasmapheresisWhole blood | Every 2 weeks, maximum of 12 l/year<br>600–700 ml per session | No | Not specified |
| Norway | | | Maximum 4 donations over 4 weeks | Yes | Yes |

**Table 2** (Continued)

| Country, Institution | Intended use of CCP | Method of CCP collection | Frequency of CCP Plasmapheresis | Frequency different from local standard plasmapheresis? | Components used from whole blood? |
|---|---|---|---|---|---|
| | Clinical trials; Compassionate use | PlasmapheresisWhole blood | | | |
| The Netherlands | Clinical trials; Compassionate use; Fractionation | Plasmapheresis | Maximum of 26 donations and 25 l/year<br>Maximum 750 ml per session | No | NA |
| Turkey, *BUU* | Compassionate use | Plasmapheresis | Every 10 days, maximum of 8 in 3 months | Yes | NA |
| Turkey, *TRC* | Per direction of Ministry of Health | Plasmapheresis | Every 10 days, maximum of 3 in a month; 1·8 l/month and 8 per 3 months period[b] | Not specified | NA |
| Turkey, *AHGH* | Clinical trials; Compassionate use | Plasmapheresis | Every 10 days, maximum 3 in a month, maximum 8 per 3 month period[b] | Not specified | NA |
| United Kingdom | Clinical trials | Plasmapheresis | Every 7 days, maximum of 24/year | No | NA |
| South-East Asia | | | | | |
| India, *AIIMS* | Clinical trials; Compassionate use | Plasmapheresis | Every 2 weeks<br>Maximum 500 ml per session, 1 l per month | No | NA |
| India, *PGIMER* | Clinical trials; Compassionate use | Plasmapheresis | Every 2 weeks | No | NA |
| Indonesia | Clinical trials | Plasmapheresis | Every 2 weeks, between 3–6 donations | Not specified | NA |
| Western Pacific | | | | | |
| Australia | Clinical trials; Fractionation | PlasmapheresisWhole blood | Every 7 days, up to 12 donations | Yes | Yes |
| China, *BRCBC, WHBC, SXBC* | Clinical trials; Compassionate use | Plasmapheresis | Every 2 weeks, maximum of 24 times/year | No | NA |
| Hong Kong, China | Clinical trials; Compassionate use | Plasmapheresis | Every 2 weeks, maximum of 6 donations | No | NA |
| Singapore, *HAS, TTSH* | Compassionate use | PlasmapheresisWhole blood | Every 2 weeks[c] | Yes | Yes |
| South Korea | Clinical trials | Plasmapheresis | Every 2 weeks | No | NA |

AHGH, Acıbadem Health Group Hospitals; AIIMS, All India Institute of Medical Sciences; ARC, American Red Cross; BRCBC, Beijing Red Cross Blood Center; BUU, Bursa Uludağ University; CBS, Canadian Blood Services; HAS, Health Sciences Authority, NA; not applicable; PGIMER, Post Graduate Institute of Medical Education and Research; SANBS, South African National Blood Service; SXBC, Shaanxi Blood Center; TRC, Turkish Red Crescent; TTSH, Tan Tock Seng Hospital; UCT, University of Cape Town; WHBC, Wuhan Blood Center.

[a]initially allowed for up to 12 weeks after their first donation. Later reduced to up to 6 weeks after resolution of symptoms.

[b]allowed for up to 3 months after recovery.

[c]initially started at allowable frequency as for standard plasmapheresis. Higher frequency is allowed provided donors' serum albumin and globulin levels before each donation was in the reference range.

of minipool CoV immunoglobulin (CoVIg). A total of 20 institutions collected CCP for clinical trials and compassionate use. Of these, four institutions had CCP initially collected for use in clinical trials but later was provided on a compassionate basis (India; Hong Kong; China, in Wuhan; Italy; Table 2).

Eight institutions had CCP collected for transfusion in clinical trials only. Three respondents indicated that the CCP had been used in rare cases on a compassionate basis outside a clinical trial setting (Saudi Arabia; Australia; and the UK). A regional institution in the USA had CCP initially provided for use in both compassionate and study protocols, but since the Mayo Clinic investigational new drug trial was completed, CCP was provided as an investigational new drug.

In Brazil, CCP was collected mostly for use within the setting of clinical trials for patients with severe pneumonia, and to a lesser extent, for compassionate use depending on the physician's request. Two institutions collected CCP solely for compassionate use (Singapore; one in Turkey). In the Netherlands, the compassionate use of CCP was offered for immune-compromised hospitalized patients with persistent and/or severe COVID-19 disease. CCP was also collected for clinical trials and as a source plasma for CoVIg production.

Six institutions have been collecting CCP for fractionation purposes. The use of CCP for fractionation was under consideration in Canada, Norway and France at the time of response to this international forum.

***Q4: Describe the CCP donor eligibility and recovery criteria used in your institution? Do they need to have a confirmatory test result status of past COVID-19 infection before CCP donation? What type of test?***

### *Laboratory confirmation of COVID-19 infection*

The donor eligibility criteria varied dramatically between countries (Table 3). All institutions, except the French and Australian, required proof of a previous COVID-19 infection, either in the form of a positive SARS-CoV-2 polymerase chain reaction (PCR) test (29 respondents) or anti-SARS-CoV-2 antibodies (17 respondents). In France, during the first peak of COVID-19 pandemic, patients with mild clinical symptoms were not systematically tested by SARS-CoV-2 polymerase chain reaction (PCR). The diagnosis of COVID-19 was made presumptively based on patients' symptoms. In Australia, donors had to report that they had a 'laboratory-confirmed COVID-19 infection' as per the national guidelines for a confirmed case (tested positive by RNA or cell culture with PCR confirmation or showed evidence of seroconversion). However, donors were not required to provide the diagnostic report when presenting to donate CCP.

### *Time to donate and confirmatory negative tests*

The vast majority of respondents indicated that donors were accepted for CCP donation 28 days after the resolution of signs/symptoms without any testing. In Italy, this deferral period however needed to be accompanied by a negative SARS-CoV-2 PCR. Alternatively, donors with no prior history of hospitalization could be accepted if SARS-CoV-2 PCR was performed at least 10 days after the onset of symptoms, with negative test results obtained at least 3 days from resolution of signs/symptoms. In Hong Kong, this deferral period was accompanied by a negative SARS-CoV-2 PCR on both nasopharyngeal swab and blood serum within 1 week prior to CCP donation.

Ten respondents indicated that donors were accepted for CCP donation 14 days after the resolution of signs and symptoms without testing. There were some institutions accepting the CCP donor 14 days after resolution of signs/symptoms if they had one negative SARS-CoV-2 PCR on nasopharyngeal swab. Other institutions required two negative test results. In Brazil, donors who remained reactive by the PCR were invited to perform a third PCR test after an additional deferral period of 14 days. If the PCR test remained positive, the donor was deferred from the CCP collection programme [16]. In China and one institution in India, the two SARS-CoV-2 PCR tests had to be performed 24 h apart. The regional blood services/centres in China required a PCR test performed at a minimum of 3 weeks after the onset of symptoms. In the national blood centre and one hospital-based blood service in Turkey, one of the SARS-CoV-2 PCR tests had to be performed within 48 h prior to CCP donation.

Three respondents indicated an acceptance criterion different from the above. In Egypt, donors were accepted after 10 days or more from the resolution of symptoms or if they had two negative PCR tests minimum 24 h apart. In South Korea, CCP collection is allowed 14 days after quarantine release (if no signs and symptoms for 10 days upon confirming the infection). Donors were also tested twice, at least 24 h apart, 14–28 days from quarantine release before donation. In Belgium, donors were accepted 17 days after recovery. In a regional blood centre in Hong Kong, donors had to have a documented SARS-CoV-2 PCR test on nasopharyngeal swab 4 weeks before donation, and a negative SARS-CoV-2 PCR on nasopharyngeal swab and serum within 1 week prior to CCP donation.

### *Evolution of eligibility criteria*

The eligibility criteria evolved in some countries due to testing limitations at certain phases of the pandemic or changes in the definition of a confirmed case. For

**Table 3** CCP donor eligibility and testing

| Country, Institution | Confirmatory test of past COVID-19? | | CCP donor eligibility criteria* | | | | | |
|---|---|---|---|---|---|---|---|---|
| | SARS-Cov-2 PCR | Anti-SARS-Cov-2 Antibody | 14 days after resolution of symptoms | 14 days after resolution of symptoms + 1 negative PCR | 14 days after resolution of symptoms + 2 negative PCR | 28 days after resolution symptoms/ recovery | Pre-donation SARS-CoV-2 testing | Pre-donation anti-SARS-CoV-2 antibody testing |
| Americas | | | | | | | | |
| Argentina | Yes | No | No | Yes[a] | No | Yes[a] | Yes | Yes |
| Brazil | Yes | No | No | Yes | No | No | Yes | Yes |
| Canada, *Héma-Québec* | Yes[b] | No | Yes | No | No | No | No | No |
| Canada, *CBS* | Yes[b] | No | No | No | No | Yes | No | No |
| United States, *Vitalant* | Yes | Yes | No | No | No | Yes | No | Yes[c] |
| United States, *ARC* | Yes | Yes | Yes | No | No | No | No | Yes[c] |
| United States, *OneBlood* | Yes | Yes | Yes[d] | No | No | No | No | Yes[c] |
| Africa | | | | | | | | |
| South Africa, *SANBS* | Yes | Yes | Yes[d] | No | No | Yes | No | Yes |
| South Africa, *UCT* | Yes | Yes | Yes | No | No | No | No | Yes[c] |
| Eastern Mediterranean Region | | | | | | | | |
| Egypt | Yes | Yes | No | No | No | No | No | Yes |
| Israel | Yes | No | No | No | Yes | No | No | Yes[c] |
| Oman | Yes | Yes | No | Yes | No | Yes | Yes | Yes |
| Saudi Arabia | Yes | No | Yes | No | No | No | No | Yes[c] |
| Europe | | | | | | | | |
| Belgium | Yes | Yes | No | No | No | No | No | Yes[c] |
| Finland | Yes | No | Yes[d] | No | No | No | No | Yes |
| France | No | No | Yes | No | No | No | No | No |
| Germany | Yes | Yes | No | No | No | Yes | Yes | Yes[c] |
| Italy | Yes | No | No | No | No | Yes[e] | No | Yes |
| Norway | Yes | Yes | No | No | No | Yes | No | Yes[c] |
| The Netherlands | Yes | No | Yes | No | No | No | No | No |
| Turkey, *BUU* | Yes | Yes | No | No | Yes[f] | Yes | No | Yes |
| Turkey, *TRC* | Yes | Yes | No | No | Yes[f] | Yes | No | No |
| Turkey, *AHGH* | Yes | Yes | No | No | No | Yes[g] | Yes | Yes |
| United Kingdom | Yes | Yes | No | No | No | Yes | No | Yes[h] |
| South-East Asia | | | | | | | | |
| India, *AIIMS* | Yes | Yes[i] | Yes | No | No | No | No | Yes |
| India, *PGIMER* | Yes | No | No | No | Yes[j] | Yes | No | Yes |
| Indonesia | Yes | No | No | Yes | No | No | No | Yes |

**Table 3** (Continued)

| Country, Institution | Confirmatory test of past COVID-19? | | CCP donor eligibility criteria* | | | | | |
|---|---|---|---|---|---|---|---|---|
| | SARS-Cov-2 PCR | Anti-SARS-Cov-2 Antibody | 14 days after resolution of symptoms | 14 days after resolution of symptoms + 1 negative PCR | 14 days after resolution of symptoms + 2 negative PCR | 28 days after resolution symptoms/ recovery | Pre-donation SARS-CoV-2 testing | Pre-donation anti-SARS-CoV-2 antibody testing |
| Western Pacific | | | | | | | | |
| Australia | No | No | No | No | No | Yes | No | No |
| China, *BRCBC, WHBC, SXBC* | Yes | Yes | No | No | Yes[j,k] | Yes[l] | Yes[m] | Yes[m] |
| Hong Kong, China | Yes | Yes | No | No | No | Yes[n] | No | Yes |
| Singapore, *HAS, TTSH* | Yes | No | No | No | No | Yes[o] | No | Yes |
| South Korea | No | No | No | No | No | No | No | No |

AHGH, Acıbadem Health Group Hospitals; AIIMS, All India Institute of Medical Sciences; ARC, American Red Cross; BRCBC, Beijing Red Cross Blood Center; BUU, Bursa Uludağ University; CBS, Canadian Blood Services; HAS, Health Sciences Authority, NA, not applicable; PGIMER, Post Graduate Institute of Medical Education and Research; PCR, polymerase chain reaction; SANBS, South African National Blood Service; SARS-CoV-2, severe acute respiratory syndrome coronavirus-2; SXBC, Shaanxi Blood Center; TRC, Turkish Red Crescent; TTSH, Tan Tock Seng Hospital; UCT, University of Cape Town; WHBC, Wuhan Blood Center.

[a]Initially required negative SARS-CoV-2 PCR on 2 tests, but then accept one test or 28 days post full recovery.

[b]Or presumptive positive.

[c]Testing is done at time of donation.

[d]Initially required negative SARS-CoV-2 PCR, but then accepts 14 days post full recovery without testing.

[e]Along with a negative SARS-CoV-2 PCR (hospitalized patients), or if performed at least 10 days after the onset of symptoms with a negative SARS-CoV-2 PCR at least 3 days from resolution of symptoms (for other symptomatic patients).

[f]One PCR test should have been done within 48 h of donation.

[g]Along with 2 negative PCR tests.

[h]Except for men over 50 years of age (whites) and over 35 years of age (black, Asians and minority ethnic).

[i]By an immunoassay or rapid antigen test.

[j]Minimum 24 h apart.

[k]At least 3 weeks since onset of the symptoms and 2 weeks from time of discharge from hospital.

[l]One centre.

[m]One centre performs SARS-CoV-2 mini-pool or ID-NAT on plasma samples, and tests for anti-SARS-CoV-2 antibodies in-house. Other 2 centres receive test results from recruiting hospitals or perform testing in an external certified laboratory.

[n]Along with a negative nasopharyngeal swab and serum PCR for SARS-CoV-2 within 1 week of the donation.

[o]initially required negative SARS-CoV-2 PCR, but then accepts 28 days post full recovery without testing.

*Other eligibility criteria are applied in Egypt, Belgium and South Korea.

instance, in Norway and France, testing by SARS-CoV-2 PCR was limited at some stages of the pandemic; therefore, presumably recovered patients were allowed to donate CCP and were tested for the presence of antibodies. This criterion was added to the donor eligibility criteria to include donors if a laboratory-confirmed diagnosis was not available. In the Netherlands, a confirmatory SARS-CoV-2 PCR of past infection was required for all donors at the initial stages. This requirement was temporarily removed for CoVIg source plasma donors before it was re-introduced when a lower proportion of these donors were found to have anti-SARS-CoV-2 antibodies compared with apheresis donors (60% vs. 85%).

In the USA, South Africa and Finland, testing was initially required to confirm non-reactivity of SARS-CoV-2 PCR before CCP donation, but this requirement was later removed. In the USA, donors were initially required to have proof of infection in the form of a positive SARS-CoV-2 PCR test and/or antibody test results and be 28 days from infection and symptom-free. The latter criterion was changed to complete resolution of symptoms at least 14 days before the donation [17]. In Argentina, the eligibility criteria initially required negative SARS-CoV-2 PCR on two tests performed 24 h apart, 14 days after resolution of signs/symptoms. This latter criterion was changed to accept donors at least 14 days after symptoms resolution with 1–2 negative PCR tests. Later on, the eligibility criteria included acceptance of donors 28 days post-resolution of symptoms without additional testing. In Singapore, the definition of clinical recovery has evolved with the evolution of the criteria for release from quarantine. Initially, it was defined by the resolution of fever and any clinical symptoms for at least 24 h, along with a negative SARS-CoV-2 PCR from 2 separate nasopharyngeal swabs taken 24 h apart. Since May 2020, non-immune compromised patients could de-isolate 21 days after onset of symptoms if feeling well without further testing. Hence, donors were later accepted 28 days after recovery without testing.

### *Definition of recovery*

The definition of recovery was variable between countries. The majority of the institutions used a complete resolution of symptoms. Other institutions required confirmation of negative SARS-CoV-2 testing and the absence of symptoms. Some institutions relied on the regulatory authorities' definition (e.g. Ministry of Health in Singapore; China; Argentina; and Italy). In the Australian and Norwegian blood centres, donors with residual symptoms (e.g. residual loss of smell and fatigue) could be accepted for CCP donation after medical assessment.

### *Other eligibility criteria*

A few respondents indicated other eligibility criteria for CCP donation. In six countries (Canada; India; Oman; Italy; Egypt; and South Africa), male and nulliparous female donors with no history of pregnancy were accepted as CCP donors. In Italy, other donors were accepted for CCP donation for fractionation purposes. In Finland and the UK, both male donors and female donors tested for anti-HLA-antibodies were accepted. In the UK, potential female donors also had to be tested for anti-HNA antibodies. In the USA, at time of this international forum, individuals who had received the SARS CoV-2 vaccine were accepted to donate CCP if they have had symptoms of COVID-19 and a positive test result from a diagnostic test approved, cleared or authorized by FDA, received the COVID-19 vaccine after diagnosis of COVID-19 and were within six months after complete resolution of COVID-19 symptoms [17].

***Q5: Does your institution test the CCP donor for SARS-CoV-2 by PCR before donation to confirm clearance of the infection?***

The vast majority of the institutions did not perform SARS-CoV-2 PCR testing on the donation, or on the donor, prior to donation to confirm the clearance of the infection (Table 3). However, some specificities were noted in institutions that perform testing. In Brazil, donors should have had a negative SARS-CoV-2 PCR either on nasopharyngeal swab or serum. In Germany, donors were tested for SARS-CoV-2 by PCR during a pre-donation visit (typically 14 days prior to donation). A donation was possible 14 days after a negative PCR test, at the earliest. In regional blood services/centres in China and Hong Kong, testing was performed in the recruiting hospitals. One centre in China performed SARS-CoV-2 NAT test either on a pool of 6–8 plasma samples or ID-NAT [18]. In Hong Kong, donor eligibility criteria required negativity for SARS-CoV-2 on nasopharyngeal swab and serum within 1 week of donation. In Singapore, donor blood samples needed to be tested and confirmed negative for SARS-CoV-2 PCR before CCP donation. However, this requirement was later removed.

***Q6: Does your institution test the CCP donor for anti-SARS-CoV-2 antibodies before donation?***

The practice of testing CCP donors for anti-SARS-CoV-2 antibodies before the donation was variable (Table 3). Sixteen institutions from 13 countries required antibody testing on the donor before the donation, and only those with a predetermined cut-off level were accepted to donate CCP. The system in the regional blood services/centres in China was dependent on the recruiting hospitals in performing testing before referral of the donor to the blood centres for CCP donation. One centre

however performed the testing in-house. Institutions in other countries either performed testing in-house or in an external laboratory. This infers that donors underwent a screening before being accepted for donation. In the institution from Brazil, both SARS-CoV-2 PCR results and the virus-neutralizing antibodies data were made available before medical screening for assessing the donor's eligibility for donation. A total of nine respondents indicated that testing was instead performed at the time of donation. In Singapore, testing was performed at time of donor screening and repeated on the day of donation.

Testing for anti-SARS-CoV-2 antibodies was performed using different testing platforms such as the enzyme-linked immunosorbent assay (ELISA), chemiluminescent assay (CLIA), chemiluminescent microparticle immunoassay (CMIA) and the virus neutralization test (Table 4). A few institutions relied on a rapid screen test of donors for the presence of anti-SARS-CoV-2 antibodies on the day of donation. Some centres used two different testing methods to screen the donors, either using different testing platforms or different manufacturers. In Brazil, both the ELISA and virus neutralization tests were done, but the decision to accept the donation depended on the neutralization test results. In a blood centre in the USA (OneBlood), two CLIA methods were used: a screening test (to detect anti-spike protein) and a confirmatory assay (to detect anti-nucleocapsid protein). If the signal-to-cut-off (S/C) ratio on the screening test was 10 or greater, this result was confirmed by the confirmatory test. In Israel, a rapid test was first performed to screen all donors. Donors with negative results on the rapid test were further tested using a CMIA method.

***Q7: Does your institution test the CCP unit for anti-SARS-CoV-2 antibodies? Are samples collected from the CCP unit and freezed/archived for future assessment?***

A total of 23 institutions tested the CCP units for anti-SARS-CoV-2 antibodies, eleven tested the donor on the donation day (Table 4). Some centres pre-screened the donors by an antibody testing before donation, as described above, and repeated the testing on the unit on the day of donation using the same or additional testing methods. Different test methods were used in qualifying the units, and the cut-off criteria to accept the units varied among centres and testing methodology used, with some institutions using the manufacturer's cut-offs, others a higher cut-off. The specificity of the ELISA, CMIA and CLIA tests used was variable, including viral spike protein, nucleocapsid protein or receptor-binding domain. Moreover, some of these tests were IgG specific, while others were reactive for other antibodies.

Thirteen institutions indicated a virus neutralization test performed on a sample collected on the day of donation &t/or the collected unit (Brazil; Canada; one centre in South Africa; Saudi Arabia; Belgium; Finland; France; Germany; Italy; Norway; Australia; Hong Kong and Singapore). The acceptable level of virus neutralization titre ranged from >1:20 up to >1:320. In Finland and Norway, no cut-off has been set in accepting the donation. In Singapore, the viral neutralization test that is based on antibody-mediated blockage of angiotensin-converting enzyme (ACE)-2 spike protein interaction was done at the time of donor screening using an in-house SARS-CoV-2 surrogate virus [19]. In France, the virus neutralization test was assessed using live SARS-CoV-2 virus, as described by Gallian *et al.* [20].

The criteria to accept donated CCP units for use varies between centres and few centres utilized more than one test or relied on a step-wise approach in qualifying the units. Four institutions decided on diverting the unit to transfusion or fractionation based on titre levels (Australia; one centre in South Africa; Israel; Egypt). Twenty-seven correspondents indicated that samples from the units are archived for future testing.

***Q8: Is CCP subjected to a pathogen-reduction treatment?***

A majority of the institutions (20), located in both high-income countries (HIC) or low- and middle-income countries (LMIC), did not apply any pathogen reduction treatment on the CCP units (Table 4). Among the institutions which performed pathogen reduction, five used the Intercept® Blood system (Cerus Corporation), three used the Mirasol® Pathogen Reduction Technology (Terumo BCT) and three used a methylene blue treatment, including two institutions in China. One institution in Egypt reported the use of caprylic acid, a purification and virus inactivation agent employed in a process to prepare mini-pool CoVIg [21].

***Q9: Does your institution accept recipients of CCP for convalescent plasma donation?***

Nine institutions accepted recipients of CCP as being themselves a donor of CCP (Table 5). Sixteen institutions indicated that these CCP recipients were not allowed to donate CCP (unless as part of a study in one institution in Egypt). In some of these countries, the reason was related to existing donor deferral period after transfusion which exceeds the maximum period allowable for CCP donation as per local protocols. For instance, in Canada, all plasma recipients (including CCP) are deferred from donating blood products for a period of 6 months. As a result, these individuals will not be accepted for CCP donations because of the long delay, which exceeds the 6 weeks post-recovery timeframe for CCP donation. Other respondents indicated that considering that the deferral period for transfusion recipients before allowing them to donate blood is 12 months, recipients of CCP cannot be accepted for convalescent plasma donation (Brazil; India; Turkey; Australia; China; and Singapore). Institutions that allowed

**Table 4** Antibody testing methods and CCP component modification

| Country, Institution | Component antibody testing? | Anti-SARS-CoV-2 antibodies testing methods | | Pathogen inactivation? |
|---|---|---|---|---|
| | | Method | Cut-off criteria to qualify donor/donation | |
| Americas | | | | |
| Argentina | No[a] | ELISA (COVIDAR) | >800 | No |
| Brazil | Yes | VNT<br>ELISA | ≥1:160NA | INTERCEPT® |
| Canada, *Héma-Québec* | Yes | ELISA[b] | >cut-off at 1:100 plasma dilution | No |
| Canada, *CBS* | Yes | VNT | $PRNT_{50}$ titre of ≥1:160 | No |
| United States, *Vitalant* | No[a] | ELISA (Euroimmun) | >cut-off at 1:100 plasma dilution | No |
| United States, *ARC* | Yes | CLIA (VITROS) | S/C ≥ 1·0 | No |
| United States, *OneBlood* | Yes | CLIA (VITROS) *(screening)*<br>CLIA (Elecsys) *(confirmatory)* | S/C ≥ 10 | No |
| Africa | | | | |
| South Africa, *SANBS* | Yes | ELISA[c] | OD ≥ 1·0 *(transfusion)*No cut-off *(fractionation)* | INTERCEPT® |
| South Africa, *UCT* | Yes | VNT | ≥1:160 *(transfusion)* | Mirasol® |
| Eastern Mediterranean Region | | | | |
| Egypt | Yes | Rapid Test (AMEDA)<br>CLIA (MAGLUMI)<br>CLIA (Elecsys) | Reactive<br>≥ 1·0 AU/ml *(transfusion)*<br>≥10·0 AU/ml *(fractionation)*<br>S/C ≥1 *(transfusion)*<br>S/C ≥10 *(fractionation)* | Lipid enveloped virus inactivation by Caprylic Acid for immunoglobulin production |
| Israel | Yes | Rapid Test (PharmaAct)<br>CMIA (Architect) | Reactive<br>S/C > 4 *(transfusion)*<br>S/C > 1·4 *(fractionation)* | No |
| Oman | Yes | ELISA (EUROIMMUN) | OD ≥ 2 | Mirasol® |
| Saudi Arabia | No[a] | VNT | 1:80 | INTERCEPT® |
| Europe | | | | |
| Belgium | No[a] | VNT | >1:320 | Methylene blue |
| Finland | Yes | VNT | None | No |
| France | Yes | ELISA (EUROIMMUN) VNT[d] | OD ≥ 8≥ 1:80 | INTERCEPT® |
| Germany | No[a] | VNT | >1:20 | No |
| Italy | Yes | VNT | ≥1:160 | Yes (type not specified) |
| Norway | Yes[e] | Anti-SARS-CoV-2 commercial tests, In-house multiplex tests, VNT | Not established | No |

**Table 4** (Continued)

| Country, Institution | Component antibody testing? | Anti-SARS-CoV-2 antibodies testing methods | | Pathogen inactivation? |
|---|---|---|---|---|
| | | Method | Cut-off criteria to qualify donor/donation | |
| The Netherlands | Yes | ELISA | OD ≥ 0·1 | No |
| Turkey, *BUU* | No[a] | CMIA (Architect) | S/C > 1·4 | No |
| Turkey, *TRC* | Yes | ELISA (EUROIMMUN) CLIA (Elecsys) | Undisclosed | Mirasol® |
| Turkey, *AHGH* | No[a] | Rapid test | Reactive | INTERCEPT® |
| United Kingdom | Yes | ELISA (EUROIMMUN) | OD ≥ 6 | No |
| South-East Asia | | | | |
| India, *AIIMS* | No[a] | CMIA (Architect) | S/C ≥ 1·4 | No |
| India, *PGIMER* | No[a] | CLIA (VITROS) | S/C ≥ 13·0 | No |
| Indonesia | No[a] | Rapid test (Assure Fastep) | ≥1:80 | No |
| Western Pacific | | | | |
| Australia | Yes[f] | CMIA (Architect) *(screening)* ELISA (EUROIMMUN) *(screening)* VNT | S/C ≥ 1·4 *OD* ≥ 1 ≥1:80 *(transfusion)* ≥1:40 *(fractionation)* | No |
| China, *BRCBC, WHBC, SXBC* | Yes | ELISA (IgG) ELISA (Total) | IgG ≥ 1:160 Total ≥ 1:320 | Variable Methylene blue |
| Hong Kong, China | Yes | VNT | ≥1:80 | No |
| Singapore, *HAS, TTSH* | No[a] | VNT | >1: 80 (Apheresis); >1:40 (WB) | No |
| South Korea | Yes | Rapid test (AFIAS) | COI > 1·0 | No |

AHGH, Acıbadem Health Group Hospitals; AIIMS, All India Institute of Medical Sciences; ARC, American Red Cross; AU, absorbance unit/ml; BRCBC, Beijing Red Cross Blood Center; BUU, Bursa Uludağ University; CBS, Canadian Blood Services; CLIA, chemiluminescence enzyme immunoassay; CMIA, Chemiluminescent microparticle immunoassay; ELISA, enzyme-linked immunosorbent assay; HAS, Health Sciences Authority, NA, not applicable; OD, optical density ratio; PGIMER, Post Graduate Institute of Medical Education and Research; SANBS, South African National Blood Service; SARS-CoV-2, severe acute respiratory syndrome coronavirus-2; S/C, signal to cut-off index; SXBC, Shaanxi Blood Center; TRC, Turkish Red Crescent; TTSH, Tan Tock Seng Hospital; UCT, University of Cape Town; VNT, virus neutralization test; WB, whole blood; WHBC, Wuhan Blood Center.

[a]Testing is done on the donor sample.

[b]Anti-SARS CoV-2 antibodies against total spike protein, neutralization assay, antibody-dependent cell-mediated cytotoxicity assay are done at external collaborators' laboratories.

[c]Initially, samples with sufficiently high OD on ELISA test were tested for neutralizing antibodies, however the later was discontinued.

[d]Neutralizing antibody test is done for CCP units with OD ratio≥ 1·6 (earlier 1·1) and < 8 (earlier 5·6) on Euroimmun anti-SARS-CoV-2 ELISA assay.

[e]For transfusion, the donation must be positive on one of the two screening tests and have a neutralizing antibody titre ≥1:80.

[f]For release for clinical use, the donation must be positive on one of the two screening tests and have a neutralizing antibody titre ≥1:80.

**Table 5** COVID-related modification of blood donor eligibility criteria

| Country, Institution | Recovered individuals allowed to donate blood? | Minimum deferral criteria for donating blood | CCP recipients allowed to donate CCP? | Minimum deferral criteria for a CCP recipient before CCP donation | CCP recipients allowed to donate blood? | Minimum deferral criteria for a CCP recipient before blood donation |
|---|---|---|---|---|---|---|
| Americas | | | | | | |
| Argentina | Yes | 14 days from resolution of symptoms with negative SARS-CoV-2 PCR -*Or*- 28 days from recovery | No | - | Yes | 12 months |
| Brazil | Yes | 60 days after resolution of symptoms[a] | No | - | Yes | 12 months |
| Canada, *Héma-Québec* | Yes | 14 days after resolution of symptoms | No | - | Yes | 6 months |
| Canada, *CBS* | Yes | 21 days after resolution of symptoms | No | - | Yes | 6 smonths |
| United States, *Vitalant* | Yes | 28 days after resolution of symptoms | No | - | No | - |
| United States, *ARC* | Yes | 14 days after resolution of symptoms | Yes | 3 months | Yes | 3 months |
| United States, *OneBlood* | Yes | 14 days after resolution of symptoms | Yes | Not specified | Yes | 3 months |
| Africa | | | | | | |
| South Africa, *SANBS* | Yes | 14 days after resolution of symptoms | Yes | 3 months | Yes | 3 months |
| South Africa, *UCT* | Yes | 14 days after resolution of symptoms | Yes | 3 months | Yes | 3 months |
| Eastern Mediterranean Region | | | | | | |
| Egypt | Yes | 14 days from recovery | No[b] | - | No policy | - |
| Israel | Yes | 28 days after resolution of symptoms | Yes | 6 months | Yes | 6 months |
| Oman | Yes | 28 days after resolution of symptoms | No | - | Yes | 12 months |
| Saudi Arabia | Yes | 28 days after resolution of symptoms, -*Or*- 28 days after the date of the positive swab, if asymptomatic | Undecided | - | Yes | 3 months |
| Europe | | | | | | |
| Belgium | Yes | 28 days from recovery | Yes | 4 months | Yes | 4 months |
| Finland | Yes | 28 days from recovery[a]<br>3 months for hospitalized patients<br>3 months for hospitalized patients | NA[c] | NA | Yes | 4 months |
| France | Yes | 28 ays after resolution of symptoms;<br>4 months for hospitalized patients | No[d] | NA | No | - |
| Germany | Yes | 4 weeks from recovery | No | - | Yes | 12 months |
| Italy | Yes | 10 days from recovery[e] | See note[f] | 4 months | See note[f] | 4 months |
| Norway | Yes | 28 days from recovery | Yes | 6 months | Yes | 6 months |
| The Netherlands | Yes | 14 days from recovery | No[d] | - | No | - |
| Turkey, *BUU* | Yes | 28 days from recovery | No | - | Yes | 12 months |
| Turkey, *TRC* | Yes | 28 days from recovery | No[d] | - | No | - |
| Turkey, *AHGH* | Yes | 28 days from recovery | No | - | Yes | 12 months |
| United Kingdom | Yes | 28 days from recovery | Yes | 28 days from recovery | No | - |

**Table 5** (Continued)

| Country, Institution | Recovered individuals allowed to donate blood? | Minimum deferral criteria for donating blood | CCP recipients allowed to donate CCP? | Minimum deferral criteria for a CCP recipient before CCP donation | CCP recipients allowed to donate blood? | Minimum deferral criteria for a CCP recipient before blood donation |
|---|---|---|---|---|---|---|
| South-East Asia | | | | | | |
| India, *AIIMS* | Yes | 28 days from recovery | No | - | Yes | 12 months |
| India, *PGIMER* | Yes | 28 days from recovery | No | - | Yes | 12 months |
| Indonesia | Yes | 14 days after resolution of symptoms | Yes | Not specified | Yes | 12 months |
| Western Pacific | | | | | | |
| Australia | Yes | 28 days from recovery | No | - | Yes | 12 months |
| China, *BRCBC, WHBC, SXBC* | Yes | 6 months from recovery | No | - | Yes | Minimum 5 years |
| Hong Kong, China | Yes | 180 days from recovery | Undecided | - | Yes | 12 months |
| Singapore, *HAS, TTSH* | Yes | 28 days from recovery | No | - | Yes | 12 months |
| South Korea | Yes | 3 months from recovery | No | - | Yes | 12 months |

AHGH, Acibadem Health Group Hospitals; AIIMS, All India Institute of Medical Sciences; ARC, American Red Cross; BRCBC, Beijing Red Cross Blood Center; BUU, Bursa Uludağ University; CBS, Canadian Blood Services; HAS, Health Sciences Authority, NA, not applicable; PGIMER, Post Graduate Institute of Medical Education and Research; SANBS, South African National Blood Service; SXBC, Shaanxi Blood Center; TRC, Turkish Red Crescent; TTSH, Tan Tock Seng Hospital; UCT, University of Cape Town; WHBC, Wuhan Blood Center.

[a]If they had a mild form of the disease.

[b]Unless if part of a study.

[c]CCP transfusion has not yet started in the country.

[d]Transfusion recipients are not allowed to donate blood.

[e]Including a negative SARS-CoV-2 RT-PCR on nasopharyngeal swab.

[f]Only plasma for fractionation.

CCP recipients to donate CCP had a shorter deferral period post-transfusion (e.g. 3 months in South Africa, 4 months in Belgium). A few institutions do not accept recipients of CCP to donate CCP although they accept other recipients of transfusions (Germany and South Korea). On the other hand, in the UK recipients of CCP are accepted for convalescent plasma donation, although they are not accepted as donors for any other blood components. Three institutions mentioned that no decision was made yet, and one institution (Italy) used the plasma collected from those donors for fractionation purposes only, in line with practice with other blood donors as a means of mitigating the risk of transfusion-related acute lung injury.

***Q10: Does your institution accept individuals recovered from COVID-19 infection for standard WB or apheresis (platelet or plasma) donation? What is the minimum deferral period after recovery before WB or apheresis donation?***

All institutions indicated that they accepted individuals who recovered from COVID-19 for blood donation (Table 5). There were substantial variations in the deferral period applied that ranged from 10 days to 180 days. A majority of institutions implemented a deferral of 14 to 28 days after recovery or resolution of signs and symptoms. In a few institutions, deferral periods of 10 or 14 days were combined with a confirmation of the resolution of the infection by a PCR test on nasopharyngeal swab (in Italy and Argentina, respectively). In two institutions, a longer deferral period of 3 or 4 months was applied for individuals who experienced severe COVID-19 disease or were hospitalized (in Finland and France, respectively).

***Q11: Does your institution accept recipients of CCP for standard WB or apheresis (platelet or plasma) donation? What is the minimum deferral period after CCP transfusion before WB or apheresis donation can be made?***

Most institutions (27; including 3 institutions in China) responded that they accepted recipients of CCP for WB or plasma donations (Table 5). Among these, substantial differences in the duration of the deferral period were noticed, probably reflecting differential perception of the possible risks, if any, to the recipient. The deferral period ranged from 3 months (five institutions), 4 months (three institutions), 6 months (four institutions) and 12 months (thirteen institutions). Three regional blood services/centres in China indicated a period of at least 5 years.

By contrast, five institutions (one regional institution in the USA and the national blood establishments and centres of France; the Netherlands; Turkey; and the UK) had a different regulation and deferred these donors; as part of a general regulation to exclude recipients on blood products as blood donors for some (France and the Netherlands). In Italy, plasma from such donors was used for fractionation, while one institution in Egypt mentioned the lack of a national policy. Institutions located in some countries (USA and Turkey) had different policies in that regard.

***Q12: Describe any challenges faced and lessons learned from establishing a CCP collection programme in your institution?***

The CCP programmes described herein range from single centre-based collection and transfusion up to national programmes. Several institutions faced many challenges in initiating a CCP programme, ranging from operational challenges to communication with the public and the community. Two respondents did not disclose challenges and lessons learned in their facilities.

### *Operations*

Setting up a CCP collection programme as a new service during the pandemic and integrating CCP production planning into operations was reported as a challenge. CCP programmes had to be deployed rapidly early in the pandemic despite the lack of evidence from high-quality clinical trials on its efficacy and safety. Starting a CCP collection programme required test development and/or acquisition, validation, protocol set-up and continuous training. This occurred while many centres were busy maintaining blood inventory and implementing COVID-19-related safety precautions and social distancing, which slowed the facility's operations. In one blood centre in the USA, the challenge was further augmented with the difficulties in predicting the pandemic's effect on the blood supply and the regional and national needs. For such a programme to be deployed, some institutions had to develop specific set-ups involving collaboration with external institutions, thereby bringing additional specific challenges. For instance, in Singapore, the CCP collection was set up in a hospital that was not a blood supplier. The lack of an administrative relationship and service agreement between this institution and the treating hospitals was a challenge. In the USA, the lack of coordination and preparation at the blood centre/hospital level with the national CCP programmes was challenging. Issuing high-titre CCP in South Africa required many operational procedures and system modifications to ensure lower titre convalescent plasma was not issued to patients.

Early and ongoing collaboration between all parties involved in this multi-disciplinary project was a key to overcome these challenges early. This involves the national blood services, hospital blood banks, treating hospitals and the authorities. Respondents highlighted the

need for ensuring early interest within the organization and acceptance of various internal stakeholders to work together to achieve rapid acquisition. Adhesion to the programme underlined a clear understanding and joined efforts to achieve the project's goals from every service involved. The staff's commitment to adapt to the rapid and continuous change in the operations during the pandemic was vital. Enhancing the operations' flexibility during the pandemic to adapt to the new and rapidly changing public health context (e.g. lockdown and social distancing) was stressed. Substantial coordination between hospitals, testing sites and blood establishments/centres was required to facilitate the referral of recovered COVID-19 patients. It was vital to maintain ongoing communication between the cooperating hospitals and the clinicians and blood centre physicians.

### *Resources*

Different challenges regarding scarce resources, especially during the early stages of the pandemic, were described. These included providing additional personal protective equipment (PPE) at times of national shortages and severe supply chain shortages of disinfectants, paper goods and apheresis kits. In one blood centre in the USA, communication challenges in the prioritization of resources were faced. Dependence on single-source suppliers and 'just-in-time' inventory practices added to the challenge of replenishing supplies. Limited apheresis kits and apheresis equipment was faced in different institutions (Finland; the Netherlands; South Africa; and India). Moreover, scarcity in human resources was challenging with staff losses due to COVID-19 illness or mandatory isolation due to case contacts. Another difficulty described was the implementation of a dedicated information technology (IT) supported process for CCP collection, manufacturing and testing (France). One respondent indicated that manual systems during the early development of the programme caused delays and frustration.

Six institutions described occasional competition on the existing resources between WB and apheresis collections, including the staff and space available for donation to maintain social distancing. In South Africa, this led to specific periods of the pandemic requiring careful assessment for the need of CCP collections vs. WB collections. The blood centres in Norway created a separate workflow for handling CCP donors while institutions in India initiated an appointment system for sample collection and donation. An institution in Oman extended the working hours of the blood bank to accommodate CCP donors. In the UK, the CCP national collection programme was supported by 20 new donor centres that were opened to enable the collection of CCP on a national scale.

One of the most important lessons learned is that the rapid implementation of such a programme requires a coordinated effort from every service (such as operation, quality assurance, IT and medical affairs). One large blood centre in the USA (OneBlood) reported that the pre-existence of a robust implementation support structure before the pandemic's onset greatly enhanced the blood centre's responsiveness to the CCP project challenges, and proved to be critical in disaster management. However, there was a need to enhance existing networks and communications pathways at all levels and keep them open. The involvement of research and development staff members was found to be beneficial at the Canadian national blood services. One respondent highlighted the need to be equipped with standardized and homogeneous risk assessment tools at national and international levels and increase the capacity to build up blood components collection programmes in emergencies.

### *Protocol development, testing and product characterization*

Another challenge described was the need to develop a study protocol for CCP collection and use in a short time and define the product specification and therapeutic indications, dose and frequency of administration for COVID-19-infected patients. This was especially the case with the frequently changing donor selection criteria, patient eligibility criteria to receive CCP and the lack of high-quality clinical trials to demonstrate the efficacy of CCP therapy. Delays in ethical board approvals to set up clinical trials was a challenge in some countries.

Another challenge faced by a couple of institutions was the lack of anti-SARS-CoV-2 antibodies licensed tests for donor screening and CCP product characterization, especially at early stages of the pandemic. The development of an in-house test was challenging and time-consuming. Access to neutralizing antibody assays was limited to few institutions. In addition, there was a lack of clear consensus on the cut-off of anti-SARS-CoV-2 antibodies on the different antibody testing platforms and the correlation with the in vitro virus neutralization tests. In Australia, collecting CCP for fractionation before fractionators determined what would likely be a standard level of neutralizing antibody titre required was a challenge.

One participant indicated that communication with international counterparts was invaluable to learn and assess practices and adapt what works best for locals setting in developing CCP collection protocols. The value of collection and storage of donor/product samples for future testing and research was highlighted. Two respondents recommended having trained staff to check updates

on approved tests and identify commercially available serological tests that correlate with in vitro neutralization as they are developed. Clinical trials should be established early in the pandemic before the number of cases starts to drop.

### *Education and training*

Several institutions faced challenges with the limited number of trained staff and lack of experience in collecting CCP, as its collection programme needed to be established quickly. Several institutions reported dependence on the clinicians and trial coordinators in the hospitals to recruit donors from recovered patients, assess and consent patients for CCP in the trial environment. However, the unproven safety and effectiveness of CCP coupled with a lack of other therapeutic modalities for COVID-19 resulted in a level of uncertainty around the availability and use of the product. In the USA, the unfamiliarity of the clinicians with CCP, and with the paths of use under an emergency investigational new drug or expanded access programme to some non-research-based hospitals and blood centres was a challenge. One respondent indicated that educating the ordering physicians about clinical criteria to consent patients was challenging given the wide range of physicians who treated COVID-19 patients.

There was a need for continuous training, especially with the successive changes in the CCP donor eligibility criteria. Training a small group of hospital-based clinicians to obtain consent from the patients was found to be useful in this setting.

### *Donor recruitment and eligibility*

Donor recruitment was a challenge reported by 11 of the respondents, especially during the extended summer holiday and lockdown as reported in South Africa. The lack of access to qualified CCP donor lists due to regulations in some countries to protect patient privacy resulted in inhibition of the hospitals and the health department from sharing needed information and made it challenging to reach recovered patients to donate CCP. One institution in India described the lack of knowledge on CCP donation among COVID-19 patients, while another provided donors with hospital transportation during lockdown. Managing requests of CCP for both clinical trials and compassionate use, and recruitment of donors of specific blood groups to fulfil hospital requests was a challenge in some institutions. An institution in Turkey described that most of the CCP donors were replacement donors due to difficulties in recruiting voluntary donors.

On the contrary to the above, one respondent from South Africa indicated that recovered COVID-19 patients were eager to donate CCP, even if they were not regular blood donors after realizing the possible clinical benefit of CCP. In Argentina, the commitment of the patients to donate CCP was supportive to maintain supplies. The centres in China indicated that CCP donors were very enthusiastic, and almost half became loyal repeat donors. As the media platforms in the Netherlands (social media, messaging services, press releases and TV/radio) were heavily engaged in donor recruitment, this resulted in long waiting lists of donors waiting for the first medical examination and donation.

Nine respondents indicated that donors' unfulfilment of general and CCP donor eligibility criteria was a challenge. This was especially triggered due to many of the recovered COVID-19 patients being new to blood or plasma donations. In addition, the frequent change in donor eligibility criteria for CCP collection further challenged some blood centres to keep up with their donor recruitment efforts. In the early stages of the pandemic in the USA, the FDA required a 28-day donor deferral period after recovery before CCP donation, limiting the number of recruitable donors. In Singapore, the initial requirement of two negative SARS-CoV-2 PCR results resulted in delays in CCP donation. The antibody titres' variable kinetics upon repeat donations in different donors was another challenge. Recruiting donors with the required high anti-SARS-CoV-2 titre was a challenge in the second wave in Canada and South Africa. As community spread level started to decline in Singapore, most recovered patients who were referred for CCP donation were migrants originating from malaria-endemic areas, which posed an additional challenge in finding eligible donors meeting the donor selection criteria in place.

Several respondents reported involving physicians, treating hospitals and public health departments to recruit recently recovered COVID-19 patients. This included educating patients on discharge from the hospital, providing them with information on the importance of CCP donation and streamlining the referral of potential donors. This collaboration should be initiated early and maintained throughout. Respondents expressed the importance of correct marketing to ensure an adequate CCP supply and have a proactive approach in controlling messages to the public using social media, emails and traditional media. One learning lesson was to have a dedicated donor recruitment unit if this does not exist.

The utility of performing point-of-care rapid tests for anti-SARS-CoV-2 antibodies was highlighted to avoid the collection of CCP from people with no or low levels of antibodies. Some institutions further stratified donors for CCP donation, with more data being made available from clinical studies on the dynamics of anti-SARS-CoV-2 antibodies and its relationship with donor factors. Others

focused on recruiting hospitalized patients as they were likely to have higher antibodies titres. A respondent from India applied relaxation of some donor eligibility criteria after careful analysis of risk vs. benefit to enhance the CCP donor pool. In Australia, the use of the same time-frame of acceptance post-recovery for CCP and WB donors allowed the utilization of donated CCP units for regular transfusion, if not meeting the required criteria for CCP.

### *Donor, staff and society concerns*

Insufficient knowledge of COVID-19 and protection measurement required for the collecting staff was reported as a challenge. Inconsistent national messaging regarding disease risk and mitigation, blood donation safety and the need for PPE leading to confusion of donors and staff were described. Several correspondents reported the apprehensiveness of the collection staff to manage CCP donors, especially in the early stages of the pandemic (South Africa; Belgium; the Netherlands; and Hong Kong).

Several respondents expressed concerns of CCP donors on their health post-COVID-19 illness and their worries that CCP donations could affect their immunity to reinfection (South Africa; India; Hong Kong). An institution in India indicated donors' fears of acquiring infections (COVID-19 and non-COVID-19) due to weakened immunity because of COVID-19 illness, resulting in donor's hesitation to donate CCP in hospital-based blood facilities. One respondent from Indonesia reported difficulties in donor recruitment due to social stigma and the inability to meet patients and their families' expectations from the benefit from CCP transfusion. One respondent from South Africa reported some donors concerns from coming to the collection sites, while others used CCP donation to get a SARS-CoV-2 antibody level test rather than being altruistic. Handling fake news on social media was described as a challenge in Argentina.

Donation by apheresis was not a standard procedure in some facilities and was limited to platelet apheresis in others. An institution in India described the hesitation of recovered patients towards CCP donation by apheresis, since plasmapheresis was not routinely practised. Moreover, there were other challenges faced in recruiting recovered patients who were eligible and willing to donate CCP due to the impact of COVID-19 on donor lives and careers.

One respondent indicated that the importance of consistent messaging to the public that the blood centres followed all recommended guidelines for protective measures for the safety of donation. Educating the patients and society on the importance of CCP donation, on the apheresis procedures, and the collection staff on the safety of handling recovered patients was found to be useful. The motivation and continuous reassurance of the recovered patients to donate the CCP by the treating physicians they trust were highlighted.

## Conclusion

Early and rapid deployment of a CCP collection programme during COVID-19 pandemic, at a time when the blood establishments were struggling in meeting blood supply, has brought up unique challenges at different levels in both HIC and LMICs. These challenges spanned a wide range from the lack of resources, short supplies, personnel loss, to operational challenges and the need for inter-organizational collaboration. The challenges also included recruitment of recovered patients who are eligible to donate blood and CCP, while handling staff, donors and society concerns. The World Health Organization recommended that blood services should take steps to assess, plan and respond to the emerging challenges appropriately and proportionately after undertaking a data-driven risk assessment [22]. The role of professional organizations in sharing experiences and providing guidance and recommendations is paramount. We summarize here information on practice of collection of CCP and lessons learned on establishing a CCP collection programme on an international level that can be utilized in developing a framework in facing similar pandemics in the future.

## Acknowledgements

We acknowledge the following members of the ISBT Convalescent Plasma Working transfusion subgroup for their contribution in the development of the International Forum questions: Evan Bloch (Johns Hopkins University School of Medicine, United States), Ruchikha Goel (Johns Hopkins Hospital, Simmons Cancer Institute at SIU School of Medicine and Mississippi Valley Regional Blood Center, United States), Erica Wood (School of Public Health and Preventive Medicine, Monash University and Department of Clinical Haematology, Monash Health, Australia), Mahrukh Getshen (National Blood Bank, Bhutan) and Torunn Oveland (Haukeland University Hospital, Norway).

### *References*

1 World Health Organization. Coronavirus disease (COVID-19) outbreak; 2020. https://www.who.int/westernpacific/emergencies/covid-19 [Last accessed 1st May 2020].
2 Sanders JM, Monogue ML, Jodlowski TZ, Cutrell JB. Pharmacologic treatments for coronavirus disease 2019 (COVID-19): a review. JAMA 2020;323:1824–36.

3 Casadevall A, Tobian AAR. Convalescent plasma for COVID-19 - encouraging signals of efficacy. Br J Haematol 2021;192:681–2.
4 Ripoll JG, van Helmond N, Senefeld JW, Wiggins CC, Klassen SA, Baker SE, et al. Convalescent plasma for infectious diseases: historical framework and use in COVID-19. Clin Microbiol Newsl 2021;43:23–32.
5 Casadevall A, Henderson J, Joyner M, Pirofski LA. SARS-Cov2 variants and convalescent plasma: reality, fallacies, and opportunities. J Clin Invest 2021;131:e148832.
6 Mair-Jenkins J, Saavedra-Campos M, Baillie JK, Cleary P, Khaw FM, Lim WS, et al. The effectiveness of convalescent plasma and hyperimmune immunoglobulin for the treatment of severe acute respiratory infections of viral etiology: a systematic review and exploratory meta-analysis. J Infect Dis 2015;211:80–90.
7 Maiztegui JI, Fernandez NJ, de Damilano AJ. Efficacy of immune plasma in treatment of Argentine haemorrhagic fever and association between treatment and a late neurological syndrome. Lancet 1979;2:1216–7.
8 Bloch EM, Goel R, Wendel S, Burnouf T, Al-Riyami AZ, Ang AL, et al. Guidance for the procurement of COVID-19 convalescent plasma: differences between high-and low-middle-income countries. Vox Sang 2021;116:18–35.
9 Epstein J, Burnouf T. Points to consider in the preparation and transfusion of COVID-19 convalescent plasma. Vox Sang 2020;115:485–7.
10 Epstein J, Martin Smid W, Wendel S, Somuah D, Burnouf T. Plasma-based COVID-19 treatments in low-and middle-income countries and the risk of transfusion-transmitted infections. NPJ Vaccines 2020;5:103.
11 Epstein J, Smid WM, Wendel S, Somuah D, Burnouf T. Use of COVID-19 convalescent plasma in low- and middle-income countries: a call for ethical principles and the assurance of quality and safety. Vox Sang 2021;116:13–4.
12 Al-Riyami AZ, Schäfer R, van den Berg K, Bloch EM, Estcourt LJ, Goel R, et al. Clinical use of convalescent plasma in the covid-19 pandemic: a transfusion-focussed gap analysis with recommendations for future research priorities. Vox Sang 2021;116:88–98.
13 Perreault J, Tremblay T, Fournier M-J, Drouin M, Beaudoin-Bussières G, Prévost J, et al. Waning of SARS-CoV-2 RBD antibodies in longitudinal convalescent plasma samples within 4 months after symptom onset. Blood 2020;136:2588–91.
14 Beaudoin-Bussières G, Laumaea A, Anand SP, Prévost J, Gasser R, Goyette G, et al. Decline of humoral responses against SARS-CoV-2 spike in convalescent individuals. MBio 2020;11:e02590–20.
15 Prévost J, Gasser R, Beaudoin-Bussières G, Richard J, Duerr R, Laumaea A, et al. Cross-sectional evaluation of humoral responses against SARS-CoV-2 Spike. Cell Rep Med 2020;1:100126.
16 Wendel S, Kutner JM, Machado R, Fontão-Wendel R, Bub C, Fachini R, et al. Screening for SARS-CoV-2 antibodies in convalescent plasma in Brazil: Preliminary lessons from a voluntary convalescent donor program. Transfusion 2020;60:2938–51.
17 FDA. Investigational COVID-19 Convalescent Plasma. FDA Guidance for Industry. Center for Biologics Evaluation and Research; 2021. Available electronically at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/investigational-covid-19-convalescent-plasma. Accessed April 23, 2021.
18 Le Chang LZ, Gong H, Wang L, Wang L. Severe acute respiratory syndrome coronavirus 2 RNA detected in blood donations. Emerg Infect Dis 2020;26:1631.
19 Tan CW, Chia WN, Qin X, Liu P, Chen MI-C, Tiu C, et al. A SARS-CoV-2 surrogate virus neutralization test based on antibody-mediated blockage of ACE2–spike protein–protein interaction. Nat Biotechnol 2020;38:1073–8.
20 Gallian P, Pastorino B, Morel P, Chiaroni J, Ninove L, de Lamballerie X. Lower prevalence of antibodies neutralizing SARS-CoV-2 in group O French blood donors. Antiviral Res 2020;181:104880.
21 El-Ekiaby M, Vargas M, Sayed M, Gorgy G, Goubran H, Radosevic M, et al. Minipool caprylic acid fractionation of plasma using disposable equipment: a practical method to enhance immunoglobulin supply in developing countries. PLoS Negl Trop Dis 2015;9:e0003501.
22 World Health Organization. Maintaining a safe and adequate blood supply and collecting convalescent plasma in the context of the COVID-19 pandemic Interim guidance; 2021. Available electronically at: https://www.who.int/publications/i/item/WHO-2019-nCoV-BloodSupply-2021-1. Accessed April 23, 2021.

Guest Editors

Arwa Al Riyami
Sultan Qaboos University Hospital, Oman
Email: arwa.alriyami@gmail.com

Thierry Burnouf
College of Biomedical Engineering, Taipei Medical University, Taipei, Taiwan
Email: thburnouf@gmail.com
On behalf of the ISBT Convalescent Plasma Group

International Forum Editor
Nancy Dunbar
Dartmouth-Hitchcock Medical Center, Lebanon, NH, USA
Email: Nancy.M.Dunbar@hitchcock.org

[Correction added on 28 May 2021 after first online publication: The Guest Editor names and affiliations were previously omitted and have been added in this version.]